Interventions to improve screening for latent TB: effectiveness and outcomes

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Which is the odd one out?
BHIVA guidelines 2011
HIV patients at risk of latent TB requiring screening

• High incidence - Sub-Saharan Africa ≥500/100,000
  – ARTs <2 years irrespective of CD4 count

• Medium TB incidence country 40-499/100,000
  – ARTs <2 years and CD4 <500

• Low incidence country <40/100,000
  – Not on ART
  – Or ART <6 mths and CD4 <350

*2011 World Health Organization*
British HIV Association (BHIVA) 2011 guidance on HIV/TB co-infection

- Patients should be offered screening with IGRA if they belong in one of these groups and would benefit from chemoprophylaxis

- IGRA positive: patient should be offered chemoprophylaxis, if active TB infection excluded
Flow Chart 1 Algorithm for screening for latent tuberculosis (TB)

*Medium incidence regions include Eastern Europe, Central Asia, North Africa and the Middle East, South Asia, East Asia, and the Caribbean.

HAART, highly active antiretroviral therapy; IGRA, interferon-γ release assay.
Communicable Diseases
Academic Directorate (GUM & ID)
Audit 2013

844 patients HIV patients 2007-2013
109 met screening criteria
7% screened (8/109 ) – target 100%
25% Quantiferon positive (2/8)
1 treated
Interventions

• Leadership
  – appointing a lead for the initiative
  – Multi-professional team: reception, nurses, data manager, medics

• Educational
  – inform staff of guidelines, risks of latent TB and poor audit results

• Process
  – early identification of new patients, reminders in existing patients’ notes

• PDSA cycle
  – Feedback
  – Intermediate presentation of results
  – e-mail reminders to nursing and medical staff
## Process actions

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Action</th>
<th>Person Responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of patients eligible for Quantiferon test</td>
<td>Stickers in notes to remind the clinician to offer Quantiferon test to the existing patients</td>
<td>HIV Specialist nurses implemented since 01/01/2015</td>
</tr>
<tr>
<td>All new HIV patients fulfilling the criteria should have a Quantiferon test as part of their initial assessment</td>
<td>BHIVA guidelines algorithm to be included in new HIV patients’ notes in order to identify those that should be offered Quantiferon test</td>
<td>HIV clinicians and Specialist nurses implemented since 01/01/2015</td>
</tr>
<tr>
<td>Display the BHIVA guidelines algorithm in clinics to raise awareness for the test</td>
<td>Print leaflets for the clinics</td>
<td>Project supervisor implemented since 01/01/2015</td>
</tr>
</tbody>
</table>
## Eligible patients

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Screening</th>
<th>ID</th>
<th>GUM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Still eligible from previous screening</td>
<td>65</td>
<td>41</td>
</tr>
<tr>
<td>01/01/2014-31/12/2014</td>
<td>New eligible within 2014</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Total eligible</td>
<td>41</td>
<td>78</td>
</tr>
<tr>
<td>01/01/2015</td>
<td>Implementation of interventions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients excluded due to active TB, lost to follow-up, transfer care or no longer eligible i.e. ART &gt; 2 years</td>
<td>20</td>
<td>45</td>
</tr>
<tr>
<td>31/12/2015</td>
<td>Total eligible for analysis</td>
<td>21</td>
<td>33</td>
</tr>
</tbody>
</table>
## Improvement in screening

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Compliance (%)</th>
<th>Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-interventions</td>
<td>Post-interventions</td>
</tr>
<tr>
<td>patients at risk had Quantiferon test</td>
<td>7%</td>
<td>65% (35/54)</td>
</tr>
<tr>
<td>patients with positive Quantiferon test</td>
<td>100%</td>
<td>63% (5/8)</td>
</tr>
<tr>
<td>offered prophylaxis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients with positive Quantiferon test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>received prophylaxis</td>
<td>50%</td>
<td>100% (5/5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Results by group

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Standards</th>
<th>Pre-intervention Compliance (%)</th>
<th>Post-intervention Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HIV patients at risk offered Quantiferon test</td>
<td>Group A</td>
<td>7 % (6/84)</td>
<td>62% (29/47)</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>11% (1/9)</td>
<td>80% (4/5)</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>6% (1/16)</td>
<td>100% (2/2)</td>
</tr>
</tbody>
</table>
## Results by service

<table>
<thead>
<tr>
<th>Criteria</th>
<th>ID Total patients</th>
<th>ID Quantiferon test requested</th>
<th>GUM Total patients</th>
<th>GUM Quantiferon requested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>18</td>
<td>78% (14/18)</td>
<td>29</td>
<td>52% (15/29)</td>
</tr>
<tr>
<td>Group B</td>
<td>1</td>
<td>100% (1/1)</td>
<td>4</td>
<td>75% (3/4)</td>
</tr>
<tr>
<td>Group C</td>
<td>2</td>
<td>100% (2/2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>81% (17/21)</td>
<td>33</td>
<td>55% (18/33)</td>
</tr>
</tbody>
</table>
Treatment

• Quantiferon test positive: 24% (8/34) (1 declined test)

• Treatment
  – 3 not offered treatment
    • 1 frailty, 1 patient has recently started ART with high pill burden, 1 patient defaulted follow-up
Future Interventions

- **Leadership**
  - Develop sustainable system

- **Educational**
  - inform staff of improved results and need for further improvement

- **Process**
  - Add to baseline screening tests on new patient test request
  - enable or block order according to eligibility
  - use of EPR when implemented to create reminders
Significance of study-or so what?

- Is it important to screen patients for latent TB in a time of earlier treatment and cost restraints?
- Is it worth the effort of measuring outcome?
  - Who has audited their own results?
  - What were they like?
  - Have they improved them?
Was the effort worthwhile?

- Nearly a quarter of those tested had latent TB
- QI approach resulted in same proportion positive but greatly increased number tested
TB Europe

countries and cities (2012)

TB rates per 100,000 population

Berlin: 9.1
Germany: 5.2
Stockholm: 8.7
Sweden: 6.7
Milan: 15.4
Italy: 5.2
Amsterdam: 16.5
Netherlands: 5.7
Paris: 20
France: 7.6
Madrid: 12.5
Spain: 13
Brussels: 27.4
Belgium: 8.9
London: 14.2
UK: 14.2
Lisbon: 41.2
Portugal: 48.2

London has the highest TB rate per 100,000 population, with 48.2. Portugal has the second highest rate, with 41.2.
TB numbers 2014
New guidance

• Collaborative TB strategy 2015-2020
  – Offer screening to new entrants who were born or lived in Sub Saharan Africa or countries with an estimated TB incidence of greater than 150 per 100,000 and who arrived in the UK within the last five years

• NICE 2016
  – screen adults who are severely immunocompromised, such as those with HIV and CD4 counts of fewer than 200 cells/mm³
  – people who have recently arrived from a high-incidence country
  – people younger than 65 years from under-served groups
Recommendations

- Use a quality improvement approach to increase identification of cases of latent TB
- BHIVA guidelines need to be updated as a matter of urgency to comply with new TB screening recommendations and NICE guidance

Should we do opt-out testing – test unless there is no risk?
BHIVA guidelines 2011
HIV patients at risk of latent TB and requiring screening - time for change

• High incidence - Sub-Saharan Africa ≥500/100,000
  – ARTs <2 years irrespective of CD4 count
• Medium TB incidence country 40-499/100,000
  – ARTs <2 years and CD4 <500
• Low incidence country <40/100,000
  – Not on ART
  – Or ART <6 mths and CD4 <350

2011 World Health Organization
Which is the odd one out?
14.8% of all new TB cases in adults are attributable to HIV infection worldwide.

79% of all TB/HIV co-infections are found in Africa.

In 2007, 456,000 people globally died of HIV-associated TB.

All patients with TB, regardless of their perceived risk of HIV infection, should be offered an HIV test.

doi:10.1086/651493
• 18.3% of adults with TB were HIV co-infected

• 17–25% of adults with TB were HIV co-infected in London

• Compared with the immune-competent population, TB/HIV-infected patients with active pulmonary TB are more likely to have normal chest radiographs or to have sputum that is smear negative but culture positive
**Discussion**

- Individuals with HIV infection are at an increased risk of developing active TB
- Treatment of latent TB infection helps to prevent progression to active disease in HIV positive populations
  
  *Corbett et al, Arch Intern Med 2003;163:1009-21*

- Recent data from England, Wales and Northern Ireland confirms that TB incidence in HIV-infected individuals is higher than background HIV-uninfected population rates and that this risk declines with time on ART
  
  *Gupta et al, CROI 2014*
References

• **British HIV Association guidelines for the treatment of TB/HIV coinfection 2011**


### Results (1)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Standards</th>
<th>Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HIV patients at risk for latent TB should be offered a Quantiferon test</td>
<td>Group A</td>
<td>6/84 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>1/9 (11.1%)</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>1/16 (6.25%)</td>
</tr>
</tbody>
</table>
## Results (2)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Standards</th>
<th>Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HIV patients at risk for latent TB had a Quantiferon test performed</td>
<td>100%</td>
<td>8/109 (7.3%)</td>
</tr>
<tr>
<td>All HIV patients at risk for latent TB with positive Quantiferon test should be offered anti-tuberculosis prophylaxis</td>
<td>100%</td>
<td>2/2 (100%)</td>
</tr>
<tr>
<td>All HIV patients at risk for latent TB with positive Quantiferon test received anti-tuberculosis prophylaxis</td>
<td>100%</td>
<td>1 /2 (50%)</td>
</tr>
</tbody>
</table>
Pathway for management of HIV patients offered TB screening using IGRA test

Assess for clinical symptoms of TB (See box 2)

Asymptomatic

IGRA test, see box 1

negative

positive

Reassure patient that screening test for TB is negative. Reassess if new symptoms occur.

homes

Box 1:

Indications for use of IGRA for TB screening:

- From Sub-Saharan Africa, on ART <2 yrs, any CD4 count
- From medium risk country, on ART <2 yrs, CD4 <500
- From low risk country, no ART or <6/12, CD4 <350

Box 2:

Clinical symptoms of TB:
- Cough > 4/52
- Fever
- Night sweats
- Weight loss
- Unexplained abdominal pain and distension

Repeat test, ensure tubes mixed well

If remains inconclusive monitor clinically, including repeat CXR at 3/12

Symptomatic

Asymptomatic for TB

CXR Normal

Refer for routine review at ID unit at RHH

Give patient TB alert leaflet about latent TB. Reassure likely dormant infection, no risk of transmission to others

CXR Abnormal

Refer for urgent review at ID unit at RHH

Fax referral to: 0114 226 8875

Symptoms consistent with TB disease

CXR Normal

Admit to ID unit at RHH

Contact ID reg via STH switchboard 0114 2711900

CXR Abnormal

Asymptomatic

repeat test, ensure tubes mixed well

If remains inconclusive monitor clinically, including repeat CXR at 3/12

Request Chest X-ray, reassess for symptoms
# Agreed interventions and action plan

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<tr>
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<tbody>
<tr>
<td>Educational activities for further improvement of adherence with the BHIVA HIV/TB coinfection guidelines at the ID and GUM departments</td>
<td>Presentation of re-audit results at the educational meetings and the HIV viral load MDT meetings in ID and GUM</td>
</tr>
<tr>
<td>Distribution of the HIV/latent TB management pathway to healthcare professionals involved in the management and care of patients with HIV infection outside the Sheffield Teaching Hospitals NHS Foundation Trust in order to raise awareness</td>
<td>E-mail the HIV/latent TB management pathway to participants attending the South Yorkshire HIV Network (SYHN) meeting</td>
</tr>
<tr>
<td>Include Quantiferon test in new HIV positive patient baseline screening tests</td>
<td>Create an ICE proforma for HIV positive patient’s first attendance including the Quantiferon test with criteria to enable or block order according to eligibility criteria following discussion with the Virology department and/or use of Lorenzo facilities once available to create reminders for latent TB screening when appropriate</td>
</tr>
</tbody>
</table>
TB risk definition

- **High incidence** countries with a TB incidence ≥ 500 cases/100,000
- **Medium incidence** countries with a TB incidence 40-499 cases/100,000
- **Low incidence** countries with a TB incidence <40 cases/100,000

**Data source**

*Estimated incidence (all forms) per 100 000 population, 2011 World Health Organization TB data*

## Improvement in screening

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<td>2/2 (100%)</td>
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</tr>
<tr>
<td>patients with positive Quantiferon test received prophylaxis</td>
<td>1 /2 (50%)</td>
<td>100% (5/5)</td>
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</table>
## Results

<table>
<thead>
<tr>
<th>Criteria</th>
<th>ID</th>
<th>Total patients</th>
<th>ID Quantiferon test requested</th>
<th>GUM Total patients</th>
<th>GUM Quantiferon test requested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>47</td>
<td>9% (4/47)</td>
<td>37</td>
<td>5% (2/37)</td>
<td></td>
</tr>
<tr>
<td>Group B</td>
<td>3</td>
<td>33% (1/3)</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>6</td>
<td>0</td>
<td>10</td>
<td>1/10 (10%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>9% (5/56)</td>
<td>53</td>
<td>6% (3/53)</td>
<td></td>
</tr>
</tbody>
</table>