Latent tuberculosis infection screening and treatment in HIV: insights from evaluation of UK practice

Latent TB infection (LTBI) screening and treatment in HIV-positive individuals in the UK is advocated by the British HIV Association (BHIVA) and National Institute for Health and Care Excellence (NICE), although each recommends differing strategies. We undertook an evaluation of UK practice, relating the responses to the local HIV/TB disease burden. 162 of 188 (86%) UK geographical areas responded; only 93/162 (57.4%) offer LTBI testing with considerable heterogeneity in practice, and no difference in HIV/TB burden between areas offering testing and those who do not. Only 33/93 (35.5%) and 6/93 (6.5%) reported full compliance with BHIVA and NICE guidance respectively. A uniform national guideline is required.

INTRODUCTION

HIV-positive individuals are at an increased risk of acquiring TB and progressing to active disease through reactivation of latent TB infection (LTBI).[1] Analysis of the incident TB rate in the UK HIV-positive cohort demonstrates that there are high rates in Black Africans, those with a low blood CD4 count, and that rates are also higher in white individuals than in the background HIV-negative white population. This is despite access to, and widespread use of, antiretroviral therapy (ARV).[2]

An increasing drive by the WHO to identify and treat LTBI in HIV-positive individuals as part of TB control,[3 4] particularly in high HIV prevalence/low-income settings, is supported by a Cochrane meta-analysis that found treating LTBI in this group reduced the risk of active TB by 32%.[5] Since mortality from HIV/TB remains high in the UK,[6] there are calls for expanded LTBI screening and treatment here.[2]

Currently, LTBI screening in HIV-positive individuals is advocated by the British HIV Association (BHIVA)[7] and the National Institute for Health and Care Excellence (NICE). The NICE guidance in place at the time of this evaluation was from 2011.[8] BHIVA recommends screening selected individuals with an interferon gamma release assay (IGRA) dependent upon a combination of criteria including the region of origin, duration of receipt of ARV and the CD4 count. NICE advocates screening all those with a CD4 count of 200–500 cells/mm^3 with an IGRA plus the additional option of a tuberculin skin test (TST), with a definite recommendation of IGRA plus TST in those with CD4 <200 cells/mm^3. Chemoprophylaxis is advocated by both if LTBI is diagnosed. Little is known about whether, and how, HIV healthcare providers implement these guidelines. A national evaluation of UK practice is therefore highly topical and policy relevant with respect to understanding how screening is provided, the level of adherence to current guidance and whether the HIV/TB burden in different centres has any impact on practice.

METHODS

Questionnaire design

An online questionnaire was devised and one HIV professional working for each HIV healthcare provider organisation in the UK was invited to participate in the evaluation.

HIV prevalence and TB incidence data

A total of 188 geographical areas in the UK were identified and had data available on HIV prevalence and TB incidence data.

Full details of the methods are available in the online supplementary information.

RESULTS

Response rate

Responses were obtained from 116 individuals, representing 162 UK geographical areas, since some respondents provided HIV care for more than one geographical area. The overall response rate was therefore considered to be 162/188 (86%).

HIV and TB burden in all geographical areas

There was no difference in HIV/TB burden between those geographical areas who did, and did not, respond to the survey (p=1.000).

Size of HIV cohort in responding areas

The total number of patients reported as being treated within their HIV centres by the 116 respondents was 73 395 (90% of total HIV cohort reported by Public Health England in 2014[9]). The median was 300, range 10–8000 and IQR 170–700.

Coverage of screening HIV-positive patients for LTBI

Only 93/162 (57.4%) of geographical areas reported offering any form of LTBI screening, with no difference in HIV/TB burden between the geographical areas who offered screening and those who did not (p=0.22) (table 1).

Table 1 HIV/TB categories by latent TB infection screening

HIV prevalence and TB incidence rate category	Offer screening n (%)	Do not offer screening n (%)
High HIV/high TB*	17 (18.3)	17 (24.6)
High HIV/low TB†	8 (8.6)	3 (4.3)
Low HIV/high TB‡	2 (2.2)	5 (7.2)
Low HIV/low TB§	66 (71)	44 (63.8)
Total	93 (100)	69 (100)

*High HIV: >2/1000 HIV prevalence; High TB: >20/100 000 TB incidence.
†High HIV: >2/1000 HIV prevalence; Low TB: ≤20/100 000 TB incidence.
‡Low HIV: ≤2/1000 HIV prevalence; High TB: >20/100 000 TB incidence.
§Low HIV: ≤2/1000 HIV prevalence; Low TB: ≤20/100 000 TB incidence.

Selection of patients to screen for LTBI

Of the geographical areas offering any kind of LTBI screening, 57/93 (61.3%) reported using the current CD4 count as a screening criterion, with 53/57 (93%) screening adults with a CD4 count of ≤200 cells/mm^3 but decreasing numbers offering screening at higher CD4 counts (table 2). 75/93 (80.6%) used the patient's country of origin, with all screening those from high TB incidence countries, but fewer than two thirds screening from any other region. The duration of receipt of ARV treatment was the least used criterion.

LTBI screening tests

IGRA tests were implemented most commonly; 44/93 (47.3%) and 42/93 (45.2%) of geographical areas reported using QuantiFERON and T.SPOT tests, respectively. Other screening methods or combinations of tests were used infrequently.

Adherence to national guidance

Only 33/93 (35.5%) and 6/93 (6.5%) reported complete adherence to BHIVA and NICE guidelines, respectively. No geographical area reported using any non-UK guidelines.

Multifactorial reasons for not screening

Of the geographical areas not offering screening, 31/69 (45%) believed their cohort was at low risk of LTBI, 20/69 (29%) cited a lack of confidence in the existing guidelines, 12/69 (17.4%) reported that the tests were too expensive, with 10/69 (14.5%) and 8/69 (11.6%) reporting unavailability of T.SPOT TB and QuantiFERON Gold In-Tube test (or other version), respectively. A few areas cited reasons such as wanting a cost-effectiveness analysis, concern over

Table 2 Criteria used to guide latent TB infection screening

Screening criteria	n (%) Total n=93 geographical areas offering screening
CD4 count criteria	57 (61.3)
CD4 count ≤50	53/57* (93)
CD4 count ≤100	53/57* (93)
CD4 count ≤200	53/57* (93)
CD4 count ≤350	51/57 (89.5)
CD4 count ≤500	45/57 (79)
CD4 count >500	33/57 (57.9)
Other reported CD4 count criteria—individual assessment	4/57 (7)
Country of origin criteria	75 (80.6)
High TB incidence country >40/100 000 pop.	75/75 (100)
Medium TB incidence country 20–40/100 000 pop.	49/75 (65.3)
Low incidence TB country <20/100 000 pop.	35/75 (46.7)
Other reported criteria—Eastern European countries	1/75 (1.3)
Duration receiving ARV criteria	52 (60)
Under 6 months	48/52 (92.3)
Under 1 year	42/52 (80.8)
Under 2 years	42/52 (80.8)
Other reported criteria—individual assessment	4/52 (7.7)

*53 centres offering screening to patients with a CD4 count of ≤200 are the same centres offering screening to those with CD4 counts in the ≤100 and ≤50 categories.
ARV, antiretroviral therapy.

chemoprophylaxis efficacy, toxicity/drug–drug interactions and conflicting local advice.

Management of LTBI

Eighty-eight of the 93 (94.6%) geographical areas undertaking LTBI screening offer chemoprophylaxis. The most common regimens reported were 6 months isoniazid (62/88, 70.5%), 3 months combined isoniazid/rifampicin (49/88, 55.7%), 9 months isoniazid (5/88, 5.7%) and combined rifampicin/isoniazid/ethambutol (1/88, 1.1%).

Future intention to offer LTBI screening and treatment

Of the 69 geographical areas not currently offering LTBI screening, 22 (31.9%) indicated a future intention to do so.

Full details of the results are available in the online supplementary information.

DISCUSSION

This national evaluation, covering over 90% of HIV-positive adults in the UK, is the first to evaluate LTBI screening in this population. It reveals that screening practices are highly heterogeneous in terms of the screening criteria and the tests used and often deviate from published national guidance, although these are themselves non-congruent. Additionally, screening policy was not dependent on the local burden of HIV/TB.

Most cases of active TB in the UK occur through the reactivation of LTBI in foreign-born individuals. Identification and treatment of LTBI in high-risk populations (such as those with HIV infection) in the context of a low-burden TB setting such as the UK, where there is relatively little ongoing exposure to *Mycobacterium tuberculosis*, has the potential to augment TB control and prevent morbidity and mortality. However, our work indicates that despite two national guidelines, a relatively low proportion (57.4%) of areas in the UK currently perform any kind of systematic LTBI screening, although a further 14% have expressed a future intention to do so.

Interestingly, the most commonly reported explanation for not offering LTBI screening was a perception that the cohort was at low risk of TB infection, although a quarter of geographical areas not offering screening, have high HIV prevalence/TB incidence.

A lack of confidence in the published guidance and a view that the current guidelines are too complex were also cited. Although not explicitly stated by the respondents, having two different published guidelines on the same topic may well cause confusion and uncertainty among clinicians. Unavailability or high cost of screening tests was the next most reported explanation, raising questions about equitable resource allocation.

Although observational and epidemiological cohort data support antiretroviral use with wider LTBI screening in HIV-positive individuals to prevent active TB, there is an urgent need to prospectively asses which individuals to offer screening to, the optimal screening strategy and the cost-effectiveness of screening in an era of widespread antiretroviral therapy use, thereby informing future national guidance.

Helena A White,[1,2] Robert F Miller,[3] Anton L Pozniak,[4] Marc C I Lipman,[5] Iain Stephenson,[1] Martin J Wiselka,[1,2] Manish Pareek[1,2]

[1]Department of Infection and Tropical Medicine, Leicester Royal Infirmary, Leicester, UK
[2]Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK
[3]Research Department of Infection and Population Health, University College London, London, UK
[4]HIV Department, Chelsea and Westminster Hospital, London, UK
[5]UCL Respiratory, Division of Medicine, University College London, London, UK

Correspondence to Dr Manish Pareek, Department of Infection, Immunity and Inflammation, University of Leicester, Leicester LE1 5WW, UK; mp426@le.ac.uk

Acknowledgements The following are thanked for providing HIV and TB epidemiological data: Venkata Polavarapu and Debora Pedrazzoli (Public Health England), Eisin McDonald and Lesley Wallace (Health Protection Scotland), Brian Smyth and Cathriona Kearns (Health and Social Care in Northern Ireland).

Contributors The survey was conceptualised by HAW and MP. HAW designed the survey tool, undertook it in entirety, and the results were collated by HAW and MP but interpreted by all authors. HAW wrote the first draft, but all authors critiqued and adjusted the paper and agreed the final draft.

Funding HAW received a Research Award from Gilead/British HIV Association, (awarded in 2013). This report is independent research supported by the National Institute for Health Research (NIHR Post-Doctoral Fellowship, Dr Manish Pareek, PDF-2015-08-102). The views expressed in this publication are those of the author(s) and not necessarily those of the National Health Service, the National Institute for Health Research or the Department of Health.

Competing interests ALP reports being the Chair of BHIVA HIV/TB guidelines committee and a member of BTS joint committee on TB. RFM reports personal fees from Merck, personal fees from ViiV, personal fees from Gilead and personal fees from Janssen, all outside the submitted work. He is coauthor of the BHIVA HIV/TB Guidelines 2011 and additionally is a member of the BHIVA HIV/TB Guidelines 2016 writing group.

Provenance and peer review Not commissioned; externally peer reviewed.

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2016-209063).

To cite White HA, Miller RF, Pozniak A L, *et al*. *Thorax* Published Online First: [*please include* Day Month Year] doi:10.1136/thoraxjnl-2016-209063
Received 20 June 2016
Revised 30 August 2016
Accepted 21 September 2016

Thorax 2016;**0**:1–3.
doi:10.1136/thoraxjnl-2016-209063

REFERENCES

1 Lin PL, Flynn JL. Understanding latent tuberculosis; a moving target. *J Immunol* 2010;185:15–22.
2 Gupta RK, Rice B, Brown AE. Does antiretroviral therapy reduce HIV-associated tuberculosis incidence to background rates? A national observational cohort study from England, Wales and Northern Ireland. *Lancet* 2015;2:e243–51.
3 World Health Organization. *WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders*. Geneva: World Health Organization, 2012.
4 World Health Organization. *Guidelines on the management of latent tuberculosis*. Geneva: World Health Organization, 2015.
5 Akolo C, Adetifa I, Shepperd S, *et al*. Treatment of latent tuberculosis infection in HIV infected persons. *Cochrane Database Syst Rev* 2010;(1): CD000171.
6 Zenner D, Abubakar I, Conti S, *et al*. Impact of TB on the survival of people living with HIV infection in England, Wales and Northern Ireland. *Thorax* 2015;70:566–73.
7 Pozniak AL, Coyne KM, Miller RF, *et al*. British HIV Association guidelines for the treatment of TB/HIV coinfection 2011. *HIV Med* 2011;12:517–24.
8 National Institute for Health and Clinical Excellence. *Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control [CG117]*. London: NICE, Mar 2011.
9 Public Health England. National HIV surveillance tables. HIV: surveillance, data and management. 2014. https://www.gov.uk/government/statistics/hiv-data-tables (accessed 9 Nov 2015).