

Supplementary Information

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

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ADDITIONAL METHODS

Questionnaire design

The online questionnaire (available in full below) was devised by HAW using SurveyGold software (© 2014 Golden Hills Software, Inc, Colorado Springs, USA), incorporating skip logic (“conditional branching”) functions to allow respondents to skip to relevant subsequent questions conditional on answers submitted to specific initial questions. Free text space was also provided at certain points of the questionnaire, to enable respondents to clarify or augment their answers. The predominant themes of the questionnaire were to identify, in the respondent’s centre, whether testing for LTBI was offered to HIV positive adults, and if so, whether either published UK national guidelines or other criteria were used to guide testing, which screening tests were used, whether chemoprophylaxis was given if LTBI was diagnosed, and if so, which drug regimen was offered. Finally, if respondents reported that no current screening for LTBI was undertaken, future intentions to provide screening for, and treatment of, LTBI were explored.

Administration of questionnaire

One HIV professional working for each HIV healthcare provider organisation in the UK was identified through personal contacts, and by contacting healthcare organisations directly. Most organisations nominated the Head of HIV service, or another HIV physician, with a minority nominating a specialist HIV nurse. A request for participation in the survey was also advertised in the BHIVA newsletter. If an organisation such as an NHS Trust did not provide direct HIV care to its local population, then providers supplying HIV care on behalf of these organisations were identified, and contact details obtained. Each identified

professional was approached by email by HAW, explaining that the purpose of the questionnaire was to investigate current national practice as part of a research degree. Participation was invited either by following a web link and completing the questionnaire online, or by arranging a telephone interview with HAW, who recorded the responses. The questionnaire was piloted amongst five HIV providers known to the authors. Minor adjustments to the wording of questions were made following feedback, and the final participation emails were sent in April 2014.

Statistical methods

All data were extracted on to a standardised database. Continuous data were summarised with median and interquartile range (IQR), and compared using the non-parametric Mann-Whitney U-test. Categorical responses were expressed as a simple descriptive percentage and comparisons made using Pearson's chi-square test (or Fisher's exact test if appropriate). All analyses used STATA 9.2 (StataCorp, College Station, TX). All tests were two tailed; p-values ≤ 0.05 were considered significant.

HIV prevalence and TB incidence data

HIV prevalence information categorised by healthcare provider was not available for England and therefore surrogate data on HIV prevalence (3) for Upper Tier Local Authorities (UTLA) (4) was obtained from PHE. The most recently available data at the time of the study design were from 2012. Data for 3-year average tuberculosis reports and rates for 2010-12 by English UTLA were provided by PHE (5).

HIV prevalence information for 2012 was obtained for each Welsh (6) and Scottish (7) Health Board, and Northern Irish Health and Social Care Trust (HSCT) (8), with matched data extracted from 3-year average tuberculosis reports and rates for 2010-12 (9-11).

Each UTLA, Health Board and HSCT (hereafter referred to as ‘geographical areas’) was assigned a category dependent upon their local HIV prevalence per 1,000 and TB incidence rate per 100,000 population respectively. An HIV prevalence of >2 per 1,000 or ≤ 2 per 1,000 was designated High HIV and Low HIV, respectively. A TB 3 year incidence rate of >20 per 100,000 or ≤ 20 per 100,000 was designated High TB and Low TB, respectively.

Each UTLA in England was then matched with the NHS Trust(s) providing health care in that geographical area. Several sources were used to enable the matching; a map from the Office of National Statistics showing every LA in the UK; a comprehensive map detailing all NHS facilities in the UK (12), and individual NHS Trust websites.

The matching led to the identification of 174 geographical areas in the UK. 12 geographical areas had more than one organisation providing HIV care to the local population and in these situations, each organisation was considered separately. Thus the number of geographical areas was inflated to a total of 188.

Definition of compliance with BHIVA/NICE guidance on LTBI testing

Reported screening criteria, together with associated free text comments were assimilated by two authors (HAW and MP) in order to determine the proportion of geographical areas offering screening at different criteria thresholds. For example, a respondent who answered that they followed the BHIVA guidelines on screening for LTBI was categorised as offering screening to individuals with a CD4 count ranging between 0–500 cells/mm³ and those reporting use of NICE guidelines were categorised as offering screening to individuals with any CD4 count (including those >500 cells/mm³)

Ethical approval

HAW discussed the questionnaire with the Nottingham 2 Research Ethics Committee (REC) who confirmed that this was an evaluation of service and no ethical approval was required.

ADDITIONAL RESULTS

Professional status of respondents

Of the 116 respondents 81 (70%) were genitourinary medicine physicians, 30 (26%) were infectious diseases physicians, three (2.4%) were respiratory physicians, one (0.9%) was an HIV nurse specialist and one (0.9%) was an immunologist providing HIV care.

HIV and TB burden in all geographical areas

Table 2. HIV/TB categories of English Upper Tier Local Authorities, Welsh and Scottish Health Boards and Northern Irish Health and Social Care Trusts ('geographical areas')

HIV prevalence and TB incidence rate category	Responded to survey n (%)	Did not respond n (%)	Total n (%)
High HIV/High TB*	34 (21)	5 (19.2)	39 (20.7)
High HIV/Low TB	11 (6.8)	2 (7.7)	13 (6.9)
Low HIV/High TB	7 (4.3)	1 (3.9)	8 (4.3)
Low HIV/Low TB	110 (67.9)	18 (69.2)	128 (68.1)
Total [^]	162 (100)	26 (100)	188 (100)

*High HIV: >2/1,000 HIV prevalence; High TB: >20/100,000 TB incidence; Low HIV: ≤ 2/1,000 HIV prevalence; Low TB: ≤ 20/100,000 TB incidence

[^] Total number and percentage reflects the distribution of HIV/TB burden across all geographical areas

Future intention to offer screening and treatment for latent tuberculosis in HIV patients

Of the 69 geographical areas not currently offering LTBI screening, 22 (31.9%) indicated that they were planning to do so in the future. The intended guidelines to be followed in the future, together with planned screening tests and treatment, are shown in Table 3.

Table 3. Intended future screening strategies

Planned screening guideline*, screening test* and chemoprophylaxis strategy*	n (%) Total n = 22 geographical areas intending to perform future screening	
British HIV Association guidelines	16	(72.7)
NICE guidelines	8	(36.4)
Other – awaiting better/revised guidance	5	(22.7)
Scottish guidance (pending)	1	(4.5)
International guidelines	0	(0)
Testing strategy^		
Unsure of future screening strategy	9	(41)
T.SPOT only	7	(31.8)
QuantiFERON (all types) only	3	(13.6)
QuantiFERON then T.SPOT if QuantiFERON negative or equivocal	3	(13.6)
Mantoux then QuantiFERON if Mantoux negative	1	(4.5)
Mantoux and T.SPOT together	1	(4.5)
Chemoprophylaxis to be offered		
6 months isoniazid	11	(50)
Unknown future treatment regime	5	(22.7)
Other – awaiting further studies	3	(13.6)
4 months rifampicin or rifabutin	3	(13.6)
3 months isoniazid/rifampicin	1	(4.5)
9 months isoniazid	0	(0)

* Respondents could select as many answers as were applicable, therefore total >100%

^ Other combinations of tests listed in the survey have been omitted here as no respondents selected them; e.g. QuantiFERON and T.SPOT together

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* deceased

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Survey Gold participant survey
Screening HIV positive individuals for latent tuberculosis infection

Instructions

Thank you for participating in this survey. It should take no longer than 5 minutes to complete.

Location

1. Which organisation(s) do you work for, when providing HIV care?

(Select all that apply)

- (Organisations listed in alphabetical order – respondents tick relevant boxes)
- Other: (free text box)

Number of patients attending care

2. For approximately how many HIV positive adults (>16 years) does your organisation provide regular HIV care?

(Provide only one response)

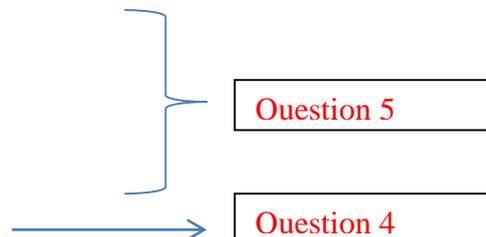
(free text box)

Profession

3. In which of the following capacities do you work whilst caring for individuals with HIV infection?

(Select only one)

- As an infectious diseases physician
- As a genitourinary medicine physician
- As a respiratory physician
- As an HIV nurse specialist
- Prefer not to say
- Other



Other profession

4. In what other capacity do you work when caring for individuals with HIV?

(Provide only one response)

(free text box)

Current screening practices for latent tuberculosis

5. Does your organisation currently offer any form of latent tuberculosis screening to any HIV positive individuals?

(Select only one)

- Yes
- No



Question 8



Question 6

Reasons why LTBI screening is not offered

6. What are the reasons why your organisation does not currently offer screening for latent TB infection to HIV positive individuals?

(Select all that apply)

- Mantoux test is unavailable
- QuantiFERON Gold In-Tube test (or other version) is unavailable
- T-SPOT.TB test is unavailable
- The tests are too expensive
- Lack of physician or nursing time to arrange the tests
- Lack of confidence in the existing guidelines
- The guidelines are too complex
- Our cohort of patients is considered to be at low risk of latent TB infection
- We would not treat a positive result in an asymptomatic patient
- Other: (free text box)

Future intentions to offer screening

7. Does your organisation have any future plans to offer screening for latent TB infection to HIV positive individuals?

(Select only one)

- Yes
- No



Question 37



Question 43

BHIVA guideline

8. When screening for latent TB, does your organisation follow the BHIVA screening guidelines incorporated into the "British HIV Association guidelines for the treatment of HIV/TB coinfection" 2011 document?

(Select only one)

- Yes, in entirety
- Yes, partially
- No



Question 26



Question 9



Question 10

Partial use of BHIVA guidelines

9. Please explain how your organisation partially follows the 2011 BHIVA screening guidelines

(Provide only one response)

(free text box)

NICE guideline

10. When screening for latent TB in HIV positive individuals, does your organisation follow the guidelines included in the NICE (National Institute for Health and Care Excellence) "Clinical diagnosis and management of tuberculosis and measures for its prevention and control" 2011 document?

(Select only one)

- Yes, in entirety
- Yes, partially
- No



Question 26



Question 11



Question 12

Partial use of NICE guidelines

11. Please explain how your organisation partially follows the 2011 NICE screening guidelines

(Provide only one response)

(free text box)

International guideline use

12. Does your organisation follow any international guidelines when screening HIV positive individuals for latent TB?

(Select only one)

- Yes
- No



Question 13



Question 14

Explanation of international guidelines

13. Please explain which international guidelines your organisation follows

(Provide only one response)

(free text box)

Any other guideline use

14. Does your organisation follow any other guidelines when screening HIV positive individuals for latent TB?

(Select only one)

- Yes
- No



Question 15



Question 16

Explanation of other guideline use

15. Please explain which other guidelines your organisation follows

(Provide only one response)

(free text box)

Using CD4 count as a criterion

16. Is the CD4 count a criterion for offering screening for latent TB infection in your organisation?

(Select only one)

- Yes
- No



Question 17



Question 19

Specification of CD4 count used as a criterion

17. Which criterion do HIV positive individuals have to meet, in order to be offered latent TB screening in your organisation?

(Select only one)

- Screening offered only if CD4 count is 50 or below
- Screening offered only if CD4 count is 100 or below
- Screening offered only if CD4 count is 200 or below
- Screening offered only if CD4 count is 350 or below
- Screening offered only if CD4 count is 500 or below
- Other (free text box)



Question 19



Question 18

Further specification of CD4 count criterion

18. Please specify which alternative CD4 count criterion is used to offer screening in your organisation

(Provide only one response)

(free text box)

Using country of origin as criteria

19. Is the individual's country of origin a criterion for offering screening for latent TB infection in your organisation?

(Select only one)

- Yes
- No



Question 20



Question 22

Specification of country of origin as criteria

20. Which criteria are used when offering latent TB screening in your organisation?

(Select all that apply)

- Screening offered to those from sub-Saharan Africa
- Screening offered to those from the Indian sub-continent
- Screening offered to those from a country with a high incidence of TB (> 40 per 100,000 population)
- Screening offered to those from a country with a medium incidence of TB (20-40 per 100,000 population)
- Screening offered to those from a country with a low incidence of TB (< 20 per 100,000 population)

- Other (please specify): (free text box)

21. If you wish to, please add any additional comments about using countries of origin as criteria for offering screening

(Provide only one response)

(free text box)

Using duration of ARVs as a criterion

22. Is the duration of time an individual has received anti-retrovirals for, a criterion for offering latent TB screening in your organisation?

(Select only one)

- Yes
 No



Question 23



Question 25

Specification of duration of ARVs as a criterion

23. Which criterion do individuals have to meet in order to be offered latent TB screening in your organisation?

(Select only one)

- Screening offered to those receiving anti-retrovirals for under 6 months only
 Screening offered to those receiving anti-retrovirals for under a year only
 Screening offered to those receiving anti-retrovirals for under 2 years only
 Other (please specify): (free text box)

24. If you wish to, please add any additional comments about using the duration of anti-retroviral therapy as a criterion for offering screening

(Provide only one response)

(free text box)

Any other criteria for offering screening

25. If you wish to, please comment on any other criteria used by your organisation when deciding which HIV positive individuals to screen for latent TB

(Provide only one response)

(free text box)

Screening strategies

26. Which screening strategies for the diagnosis of latent TB infection are currently utilised in your organisation?

(Select all that apply)

- Mantoux testing alone
 QuantiFERON Gold In-Tube test alone
 T-SPOT.TB test alone
 Mantoux and sequential QuantiFERON Gold In-Tube test only if the Mantoux test is negative

- Both Mantoux and QuantiFERON Gold In-Tube test irrespective of the result of the Mantoux
- Mantoux and sequential T-SPOT.TB test only if the Mantoux test is negative
- Both Mantoux and T-SPOT.TB test irrespective of the result of the Mantoux
- QuantiFERON and sequential T-SPOT.TB if QuantiFERON is negative or equivocal
- T-SPOT.TB and sequential QuantiFERON if T-SPOT.TB is negative or equivocal
- Both QuantiFERON and T-SPOT together
- Mantoux, QuantiFERON and T-SPOT.TB together
- Other: (free text box)

27. If you wish to, please enter any comments you may have about the screening strategy used in your organisation

(Provide only one response)

(free text box)

Screening in low CD4

28. Is a different screening strategy utilised in individuals with a CD4 count under 200, compared to those with a CD4 count greater than 200?

(Select only one)

- Yes
- No



Question 29



Question 30

Explanation of differing strategy in low CD4 count

29. Please explain the difference in screening strategy offered for those with a CD4 count below 200

(Provide only one response)

(free text box)

Offering treatment

30. Are individuals diagnosed with latent TB infection (either through systematic screening or ad-hoc screening) offered treatment?

(Select only one)

- Yes
- No



Question 34



Question 31

Reasons why treatment is not offered

31. What are the reasons why your organisation does not currently offer treatment to HIV positive individuals diagnosed with latent TB infection?

(Select all that apply)

- Lack of confidence in the treatment guidelines
- Uncertainty as to which treatment regime to use
- Uncertainty as to the cost-effectiveness of treatment
- Treatment is too expensive
- Other: (free text box)

32. If you wish to, please elaborate further on the reasons why treatment is not offered in your organisation

(Provide only one response)

(free text box)

Survey end

33. Thank you very much for completing this survey.

(Select only one)

- Please take me to the end of the survey so that I can submit my answers



Question 44

Treatment regimes

34. Which of the following treatment regimes are offered in your organisation to HIV positive individuals diagnosed with latent TB infection?

(Select all that apply)

- 6 months of isoniazid
 9 months of isoniazid
 3 months of rifampicin and isoniazid
 Other (please specify): (free text box)

35. With reference to your previous answer, please comment on which treatment regime is preferred in your organisation, and why

(Provide only one response)

(free text box)

Survey end

36. Thank you very much for completing this survey.

(Select only one)

- Please take me to the end of the survey so that I can submit my answers



Question 44

Future screening plans

37. Upon which existing guidelines are you intending to base your future screening?

(Select all that apply)

- "British HIV Association guidelines for the treatment of HIV/TB coinfection" 2011
 NICE (National Institute for Health and Care Excellence) "Clinical diagnosis and management of tuberculosis and measures for its prevention and control" 2011
 International guideline (please specify which in the free text box)
 Planning systematic screening but not using any specific guideline
 Planning ad hoc screening only
 Other (please specify): (free text box)

Future screening plans 2

38. Which screening strategies for the diagnosis of latent TB infection will be planned for use in your organisation?

(Select all that apply)

- Mantoux testing alone
- QuantiFERON Gold In-Tube test alone
- T-SPOT.TB test alone
- Mantoux and sequential QuantiFERON Gold In-Tube test only if the Mantoux test is negative
- Both Mantoux and QuantiFERON Gold In-Tube test irrespective of the result of the Mantoux
- Mantoux and sequential T-SPOT.TB test only if the Mantoux test is negative
- Both Mantoux and T-SPOT.TB test irrespective of the result of the Mantoux
- QuantiFERON and sequential T-SPOT.TB if QuantiFERON is negative or equivocal
- T-SPOT.TB and sequential QuantiFERON if T-SPOT.TB is negative or equivocal
- Both QuantiFERON and T-SPOT together
- Mantoux, QuantiFERON and T-SPOT.TB together
- Unsure
- Other: (free text box)

39. If you wish, please comment further on the screening strategies which are planned in your organisation

(Provide only one response)

(free text box)

Future screening plans 3

40. Which of the following treatment regimes will your organisation offer to those HIV positive individuals diagnosed with latent TB infection?

(Select all that apply)

- 6 months of isoniazid
- 9 months of isoniazid
- 3 months of rifampicin and isoniazid
- Other : (free text box)

41. If you wish to, please comment on which treatment regime is planned for use in your organisation, and the reasons why

(Provide only one response)

(free text box)

Survey end

42. Thank you very much for completing this survey.

(Select only one)

- Please take me to the end of the survey so that I can submit my answers



Question 44

Survey end

43. Thank you very much for completing this survey.

(Select only one)

- Please take me to the end of the survey so that I can submit my answers

Comments

44. We welcome all comments about latent TB screening, either in your organisation, or in general. Please submit your responses. It may take a few seconds to register your responses.

(Provide only one response)

(free text box)