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TB screening of migrants to low TB burden nations: insights from evaluation of UK practice

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Abstract

Background: Tuberculosis(TB) primarily occurs in the foreign-born in European countries, such as the UK, where increasing notifications and the high proportion of foreign-born cases has refocused attention on immigrant(new-entrant) screening. We investigated how UK Primary Care Organisations(PCOs) screen new-entrants and whether this differs according to TB burden in the PCOs(incidence less than or greater than 20 cases/100,000 p.a.,respectively).

Methods: Anonymous, 20-point-questionnaire sent to all 192 UK PCOs asking which new-entrants are screened, who is screened for active TB/latent TB infection(LTBI) and methods used. Descriptive analyses undertaken. Categorical responses compared using χ^2-test.

Results: 177/192(92.2%) PCOs responded; all(177) undertook screening action in response to abnormal chest X-rays but only 107/177(60.4%) screened new-entrants for LTBI. Few new-entrants had active-TB diagnosed(median 0.0%,IQR 0.0-0.5%) but more were identified with LTBI(median 7.85%,IQR 4.30-13.50%). High-burden PCOs were significantly less likely to screen new-entrants for LTBI(OR:0.26,95% CI:0.12-0.54,$p<0.0001$). Among PCOs screening for LTBI, there was substantial deviation from national guidance in selection of new-entrant subgroups and screening method.

Conclusions: Considerable heterogeneity–and deviation from national guidance–exist throughout the UK new-entrant screening process with high-burden regions undertaking the least screening. Forming an accurate picture of current front-line practice will help to inform future development of European new-entrant screening policy.

Introduction

Tuberculosis(TB) in Europe remains a public health concern. Although TB incidence has fallen in most European nations there is increasing concern that these declines may not be sustained.[1] Whilst TB notifications among local-born nationals continue to fall, those from the foreign-born migrant population which are worrying as they continue to increase year on year.[1] As a result, foreign-born individuals, despite making up a minority of the general population in European countries, account for over 40% of TB cases in several Western European nations, including Germany, France, Italy, Denmark, Netherlands, Norway, Sweden and the United Kingdom(UK).[2]

The UK epitomises the impact that migration from high TB burden nations has on TB epidemiology in low burden European nations. TB notifications have increased by 40% between 1998 and 2008;[3] over the same period UK-born cases have fallen by 5% whilst those amongst foreign-born individuals have increased by 94%.[3] Thus, foreign-born individuals now account for 72% of all cases, and have a TB incidence over 20 times that of UK-born individuals(86 cases/100,000 p.a. vs. 4 cases/100,000 p.a. respectively).[3] This epidemiology is driven by the synergy between migration from the Indian Subcontinent and Sub-Saharan Africa, which have the highest TB burdens in the world,[4, 5] and the reactivation of latent TB infection(LTBI), acquired in the countries of birth,[6] soon after arrival in the UK. Consequently approximately 50% of foreign-born cases occur in the first 5 years after migration(known as new-entrants).[3]

This contrasting data has refocused attention and debate on new-entrant TB screening in Europe. Previous studies have found marked heterogeneity in the national guidelines followed by different European countries for TB screening of immigrants.[7, 8] Unfortunately, there is little work comparing these guidelines against actual practice in individual countries-particularly those, like the UK, where foreign-born individuals disproportionately bear the burden of disease.[3]

UK policy advocates identification, chest radiography(CXR) and medical examination by port-of-entry Health Control Units for all new arrivals intending to stay for more than 6 months

from countries with a TB incidence greater than 40 cases/100,000 p.a(figure 1).[9] The results(called port forms) are forwarded, via local Health Protection Units, to local NHS TB services covering the Primary Care Organisation(PCO) area where the new-entrant intends to settle to complete screening.[9] In 2006, the National Institute of Health and Clinical Excellence(NICE) issued new national guidelines for TB control and prevention with specific guidance on new-entrant screening by local TB services.[10] In addition to screening for active TB, NICE recommends that local TB services should identify LTBI in a select subset of new-entrants(all individuals <16 years old from countries with TB incidence >40 cases/100,000 p.a. and 16-35 year olds from countries with TB incidence >500 cases/100,000 p.a. or Sub-Saharan Africa).[10] NICE recommends step-wise diagnosis of LTBI beginning with a CXR which, if normal, is followed by a tuberculin skin test(TST) which, if positive requires a confirmatory test with interferon-gamma release assays(IGRAs) prior to chemoprophylaxis.[10] These guidelines, the first in Europe to incorporate IGRAs into diagnostic algorithms for LTBI, were subsequently adopted by most high-income countries in Europe and North America.[11, 12]

Given that the UK exemplifies the enormous impact that migration from high TB burden nations has on the rapidly-growing burden of TB among the foreign-born in low TB burden European nations, and has had guidelines for screening legal, documented, new-entrants in place for four years, it is an ideal European setting in which to undertake a nationwide study to evaluate the actual screening provision for legal, documented, new-entrants by local TB services, the level of adherence to national(NICE) guidance and how provision relates to the regional heterogeneity of the overall TB burden.

Methods

Areas of interest in questionnaire

A 20-point anonymous questionnaire was developed(online supplementary information) to ask which groups of new-entrants are routinely screened further(which port forms are acted on and

whether new-entrants identified through primary-care registrations are screened), the numbers of new-entrants screened and identified to have active TB or LTBI, which subgroups of new-entrants are screened for LTBI and the methods employed. The questionnaire was pre-piloted amongst TB nurses and Public Health specialists involved in new-entrant screening.

Sampling frame

All 192 UK primary care organisations(152 Primary Care Trusts in England, 22 Local Health Boards in Wales, 14 NHS Health Boards in Scotland and 4 Health and Social Care Trusts in Northern Ireland) were contacted by telephone to identify who had responsibility for screening new-entrants. If there was uncertainty, local Health Protection/Public Health Units in each PCO were also contacted to confirm to whom they forwarded the port forms. In most cases, local respiratory clinics/TB services undertook new-entrant screening(usually TB Clinical Nurse Specialists or Respiratory Physicians) although some areas delegated the task to specialist migrant nurses, health protection nurses, or health visitors.

Anonymous questionnaires were then emailed to those individuals who were most intimately involved in immigrant screening (usually in the local TB service), with a reminder email and telephone call 4 weeks after the initial mailing. To take account of the fact that immigrant screening is complex and often undertaken in multiple locations, the investigator (MP) ensured that the most knowledgeable individual completed the questionnaire to encompass all possible avenues of screening immigrants. If the completed questionnaire was returned electronically it was coded and the accompanying email destroyed. In some cases, the questionnaires were completed over the phone with the investigator(MP). At no point were any individual, person-specific data collected on the questionnaire.

Statistical analysis

PCOs were categorised as low- or high-TB-burden(incidence less than or greater than 20 TB cases/100,000 p.a.,respectively) according to their reported incidence in 2007.[13-18] Classification of port forms was in line with national guidance: port 103 - CXR abnormal, port 102 – CXR inconclusive/has not been undertaken, port 101 – CXR normal. PCOs which screened port 102 forms and/or port 101 forms/new-entrants identified through primary-care registrations and offered chemoprophylaxis if appropriate were defined as actively screening for LTBI. Adherence to NICE guidance on which new-entrants should be screened for LTBI and the methods by which LTBI should be identified was defined as following the guidelines without deviation.

Categorical responses from low- and high-burden regions were compared using Pearson's chi-square test(or Fishers exact test if appropriate) and unadjusted univariate odds ratios(with 95% confidence intervals). Continuous data were found to be non-normally distributed and therefore summarized with median and interquartile(IQR), and compared using non-parametric Mann-Whitney U test. Missing data were excluded on a question-by-question basis. Analyses used STATA 9.2(StataCorp,College Station,TX). A p-value <0.05 was considered significant.

Results

Response rate and TB burden of responding PCOs

Responses were received from 177/192(92.2%) of PCOs; 76.3%(135/177) were categorised as low-TB-burden areas. There was no significant difference between responders and non-responders in terms of TB incidence(χ^2 =0.06, p=0.79).

Selection of new-entrants for further screening action

Table 1 outlines which new-entrants are selected for further screening action. All responding PCOs(177/177) reported that they screened new-entrants issued with an abnormal CXR form.

Fewer PCOs screened new-entrants issued with inconclusive CXRs/CXRs not undertaken(134/177-75.7%), normal CXRs(96/177–54.2%) and those identified through new-patient registrations in primary-care(62/177–35.0%).

High-burden PCOs were significantly less likely to screen new-entrants where the CXR was inconclusive/not undertaken(61.9% vs. 80.0%; OR 0.41, 95% CI 0.19-0.86,p=0.019) and where the CXR was normal(28.6% vs. 62.2%; OR 0.24, 95% CI 0.11-0.52,p<0.0001). There was a trend towards high-burden PCOs being less likely to undertake further screening of new-entrants identified through primary care,(23.8% vs. 38.5%; OR 0.50, 95% CI 0.23-1.1,p=0.08).

Numbers of new-entrants screened and estimated yield for active TB

78/177(44.1%) PCOs provided estimates for the numbers of new-entrants screened annually. An average of 70.5 new-entrants(IQR 20-200) were screened annually with no significant difference between low-TB-burden areas(median 60.0,IQR 20-278) and high-TB-burden areas(median 100.0,IQR 25-200)(p=0.91).

Of the 65/177(36.7%) PCOs that provided details on the proportion of new-entrants identified with active TB(there was no significant difference in those providing versus not providing yield data for active TB in terms of TB incidence(p=1.0);see online supplementary information for numbers of active TB cases identified), the reported yield was very low with a median of 0.0% new-entrants(IQR 0.0-0.5%) eventually diagnosed with active disease. There was no significant difference between low(median 0.0%,IQR 0.0-0.9%) and high-TB-burden PCOs(median 0.0%,IQR 0.0-0.5%) in the yield for active TB(p=0.45).

Coverage of screening for latent TB infection and the estimated yield for LTBI

Only 107/177(60.4%) PCOs screened new-entrants for LTBI; high-burden PCOs were significantly less likely to screen new-entrants for LTBI(35.7% vs. 68.1%; OR 0.26, 95% CI

0.12-0.54,p<0.0001). 105/177(59.3%) PCOs screened those under 16 years of age, 104/177(58.8%) screened those aged 16-35 years and 6/177(3.4%) screened those over 35 years of age.

In the 40/107 PCOs(37.4%) that could provide details for the proportion of new-entrants identified with LTBI(there was no significant difference in those providing versus not providing yield data for latent TB in terms of TB incidence(p=1.0)), 7.85%(IQR 4.30-13.50%) of new-entrants were diagnosed with LTBI. Amongst the PCOs that screened for LTBI, low-burden PCOs identified a lower proportion of new-entrants with LTBI(median 6.70%,IQR 4.30-10.00%) than high-burden PCOs(median 15.00%, IQR 9.00-33.00%)(see online supplementary information for numbers of cases of latent TB identified).

Selection of new-entrants to screen for LTBI and adherence to NICE guidance

Table 2 documents which sub-groups of new-entrants, as defined by their country of origin, PCOs selected to screen for LTBI. In the 107 PCOs which screened for LTBI overall, 98/107(91.6%), 105/107(98.1%), 105/107(98.1%) and 4/107(3.7%) reported that they screened under 16 year-olds for LTBI arriving from: countries with TB incidence >40 cases/100,000 p.a., countries with TB incidence >500 cases/100,000 p.a., Sub-Saharan Africa and other countries respectively. Low TB burden and high TB burden PCOs did not significantly differ in which new-entrants under 16 years of age they selected to screen for LTBI.

PCOs displayed more variability in which new-entrants aged 16-35 years they screened. Whilst 47/105(data missing for 2 PCOs-44.8%) PCOs screened those from countries with a TB incidence >40/100,000 p.a., higher proportions(104/107–97.2%) screened those from countries with a TB incidence >500 cases/100,000 p.a. and those from Sub-Saharan Africa.

Fewer PCOs screened individuals over 35 years of age. 2/105(1.9%)(data missing for 2 PCOs) screened new-entrants from countries with TB incidence >40/100,000 p.a., 6/105(5.7%)

screened individuals from countries with a TB incidence >500/100,000 p.a. or Sub-Saharan Africa.

As a consequence, whilst a high proportion of PCOs adhered to NICE guidance on which under 16 and over 35 year-olds to screen for LTBI(91.6% and 94.3% respectively) far fewer(49.5%) followed NICE guidance on which 16-35 year-olds(who comprise the largest proportion of new-entrants) to screen. There was no significant difference found between high-burden and low-burden PCOs with respect to adherence to this aspect of NICE guidance.

Methods of screening new-entrants for LTBI and adherence to NICE guidance

Amongst the PCOs which screened for LTBI, the specific screening methods used are summarised in table 3.

In children(under 16 years-old) 75/105(71.4%) PCOs use the dual TST and confirmatory IGRA approach, 28/105(26.6%) still use TST alone, with 6/105(5.7%) using IGRA as a stand-alone test.

There is considerable variability in the current screening processes for adult new-entrants(table 3), which extends to the screening tools used(TST alone, dual TST + confirmatory IGRA or IGRA alone) and the sequence in which they are used. The most common screening protocol for adults is the step-wise TST and IGRA approach(73/104 PCOs–70.2%), although 29/104(27.9%) still use the TST alone. It was interesting to note that high-burden PCOs were more likely than low-burden PCOs to use the TST alone(42.9% vs 25.6%, p=0.18) but less likely to use the TST plus IGRA(50.0% vs 73.3%, p=0.08) with little difference in the proportions using the IGRA alone(5.0% vs 5.6%, p=0.60.)

77/107(72.0%) PCOs use IGRAs in screening new-entrants(children and adults) for LTBI with fewer high TB burden PCOs(60.0%) than low TB burden areas (73.9%)(OR 0.53, 95% CI 0.17-1.6, p=0.27) routinely using IGRA in new-entrant screening. The use of IGRAs is relatively similar in the under 16(75/105 – 71.4%), 16-35(75/104 – 72.1%) and over 35 age-groups(5/6 –

83.3%). Almost all PCOs which used the IGRA used it as a confirmatory test(76/77 – 98.7%) although a number of PCOs also appear to be using it as a stand-alone diagnostic tool(8/77 – 10.4%). Of the 2 commercially available IGRAs, 59/76(77.6% - 1 PCO did not know the name) use the Quantiferon-Gold(Cellestis, Australia) and 20/76 (26.3%) use T.SPOT.TB(Oxford Immunotec, UK).

Adherence to NICE guidance on the methods by which to screen adult(16-35 years old) and child(<16 years old) new-entrants occurred in 72/104 PCOs(69.2% - 71.1% in low-burden vs 57.1% in high-burden areas (p=0.29)) and 69/105 PCOs (65.7% - 67.0% in low-burden areas vs. 57.1% in high-burden areas (p=0.46)) respectively.

Discussion

This nationwide evaluation of the provision of new-entrant screening by local primary-care organisations in the UK has revealed that whilst screening for active TB is consistently undertaken, screening for LTBI is highly variable, deviates from national guidance and is inversely related to regional TB burden. Our work suggests that heterogeneity particularly exists in the selection of new-entrant subgroups to screen for LTBI and the specific methods used.

Migration and infectious diseases, particularly immigrant TB, are gaining increasing importance as a Europe-wide health policy issue[1] suggesting that our findings have wider implications for most European nations. Our study methodology provides a basic template from which European nations can evaluate their own new-entrant screening programmes to gain objective insights into how screening is undertaken at the front-line, whether national guidance is being adhered to and whether screening relates to regional heterogeneity of TB burden within and across EU member states.

We found that all PCOs screened new-entrants issued with an abnormal CXR form presumably as they are suspected to have active TB and thus perceived as the greatest threat to public health.[9] However, abnormal CXR forms comprise only a fraction of all port forms

issued. More often port forms indicate that the CXR is either inconclusive/has not been undertaken or normal, but our findings show that fewer PCOs, 75.7% and 54.2% respectively, attempt to undertake further screening action for these port notifications. Only 35% of PCOs reported routinely screening new-entrants identified through primary-care registrations. Therefore, the port-of-entry system remains the main method by which new-entrants are identified and referred for further assessment by local TB services.

Few cases of active TB were diagnosed through new-entrant screening(median 0.0%). Although only 65/177 PCOs provided these data, the yields are similar to previous UK Health Protection Agency(HPA) estimates(0.12%) and local experience from port screening.[19-21] This reinforces the view that there is little pulmonary TB to identify amongst new-entrants arriving in the UK, suggesting that the current emphasis on CXR for initial screening may be misplaced.[22] Indeed, a recent HPA review recommended urgently reassessing the benefits of continuing with the CXR as the initial diagnostic test for new-entrants.[19]

Low yields of active TB and the fact that TB in the foreign-born results largely from reactivation of LTBI[6, 23] reinforce the potential of tackling LTBI in new-entrants.[10, 24, 25] However, we found only 60.4% of PCOs screen new-entrants for LTBI, despite the yield being higher than for active TB. Thus, a substantial proportion of UK PCOs are not implementing NICE guidance on LTBI screening.[10]

In addition, our study has revealed, for the first time, that high-burden PCOs are significantly less likely to attempt to screen new-entrants with normal CXRs for LTBI. This important finding suggests that high TB burden areas in the UK, which account for most foreign-born TB, are the most ethnically-diverse(with individuals who have migrated from TB endemic regions such as the Indian Subcontinent and Sub-Saharan Africa) [26, 27] and also have the highest prevalence of LTBI, are actually following-up and screening the lowest proportion of new-entrants. This potentially undermines national policy. Remedying this disparity between current practice and actual need requires a regionally-targeted increase in resources.

Although it was beyond the scope of this study to identify reasons for the disparity in screening for LTBI, it is likely that PCOs determine which new-entrants to screen based on pragmatic considerations such as limited service capacity, a lack of dedicated funds for undertaking organised screening and a feeling that screening asymptomatic persons with normal CXRs provides little benefit in preventing TB.[19, 28] It is possible that auditing immigrant screening practices may reduce the heterogeneity that our study has uncovered.

Amongst PCOs which screen for LTBI, most were relatively consistent, and in line with NICE guidance, in which <16(from countries with TB incidence >40/100,000 p.a.) and >35(screening not recommended) new-entrant subgroups they screened. However, most immigrants are 16-35 years-old and in this group PCOs vary considerably in whom they screen for LTBI.[4] Whilst almost all PCOs screen individuals from countries with a TB incidence >500/100,000 p.a. and Sub-Saharan Africa, in accordance with NICE, nearly half of PCOs still screened individuals from countries with a TB incidence >40/100,000 p.a.[10] This heterogeneity likely reflects uncertainty about current NICE guidance which has resulted in targeting only immigrants from Sub-Saharan African countries even though over 60% of foreign-born cases occur in immigrants from non-Sub-Saharan African regions including the Indian Subcontinent, South-East Asia and Latin America where TB incidence is 40-500 cases/100,000.[3, 10, 29]

In addition, PCOs used variable screening methods for adult new-entrants. Although 72.2% of PCOs use IGRAs to identify LTBI, over a quarter still use TST alone. Amongst PCOs that do employ IGRAs, most still use them to confirm a positive TST as per NICE guidance, though a few areas have now moved to single-step IGRA testing. This shift may have been driven by recent evidence suggesting IGRAs are cost-effective and, if positive, can predict progression to active TB.[30, 31]

Previous work in this area has been small-scale, hampered by poor response-rates, not focused on comparing screening practices by TB burden and, often, conducted prior to NICE guidance. Nonetheless, a prior smaller-scale survey undertaken by the British Thoracic Society

found that a low proportion of TB clinicians undertook new-entrant screening.[32] A previous survey also found that less than half of Public Health Consultants would act on port forms which indicate the CXR is either inconclusive/has not been undertaken or normal-with areas receiving most notifications actually screening the fewest new-entrants.[33]

Our study has several limitations. The information was gathered through a questionnaire with the potential for recall/responder bias especially for the small proportions that provided estimates of the yield for active and latent TB. In addition, this cross-sectional survey only provides a snap-shot at one time-point. Although we focused on legal migrants, undocumented migrants are also a high-risk population who are likely to benefit from TB screening although they are often difficult to identify.

Future work should consider emergent data highlighting the high prevalence of LTBI in new-entrants and their elevated rate of progression to active TB[20, 30, 34, 35] to inform revised health-economic models. The resultant cost-effective analyses should, in turn, clarify the optimal threshold of TB incidence in immigrants' respective countries of origin at which to screen for LTBI and whether screening programmes should move from port-of-entry screening to a primary-care based model which may facilitate wider migrant health programmes such as blood-borne virus screening.[20, 24, 36] An urgent reappraisal of screening policy has recently been called for in the UK,[37] where the recently-initiated review of NICE guidance provides a timely opportunity to prioritise screening for LTBI in a wider spectrum of new-entrants to include those from the Indian Subcontinent, especially in high-burden regions.

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Conflict of Interest Statement

AL is inventor for patents underpinning T cell-based diagnosis. The ESAT-6/CFP-10 ELISpot was commercialised by an Oxford University spin-out company (Oxford Immunotec Ltd, Abingdon, UK) in which Oxford University and Professor Lalvani have a minority share of equity. MP, IA, PJW and GPG have no conflict of interest.

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Contributors

All authors jointly conceived of the report. AL conceived the need for nationwide evaluation of current screening practice and all authors designed the survey which was carried out and analysed by MP. MP produced the first draft of the manuscript which was reviewed and revised by all authors.

Ethical Approval

No patient-specific data or personal identifiers were used in the preparation of this report.

Figure Legend

Figure 1. Flow chart of pathway for TB screening of new-entrants to the United Kingdom (port referral flows in red, primary care flow in blue. The blue primary care flows are only activated when a new-entrant registers with primary care services after settling in a specific area; new-entrants are not directly referred to primary care services *for* TB screening on arrival in the UK.)
[1]CXR abnormal – port 103 form; [2]CXR inconclusive/has not been undertaken – port 102 form; [3]CXR normal – port 101 form

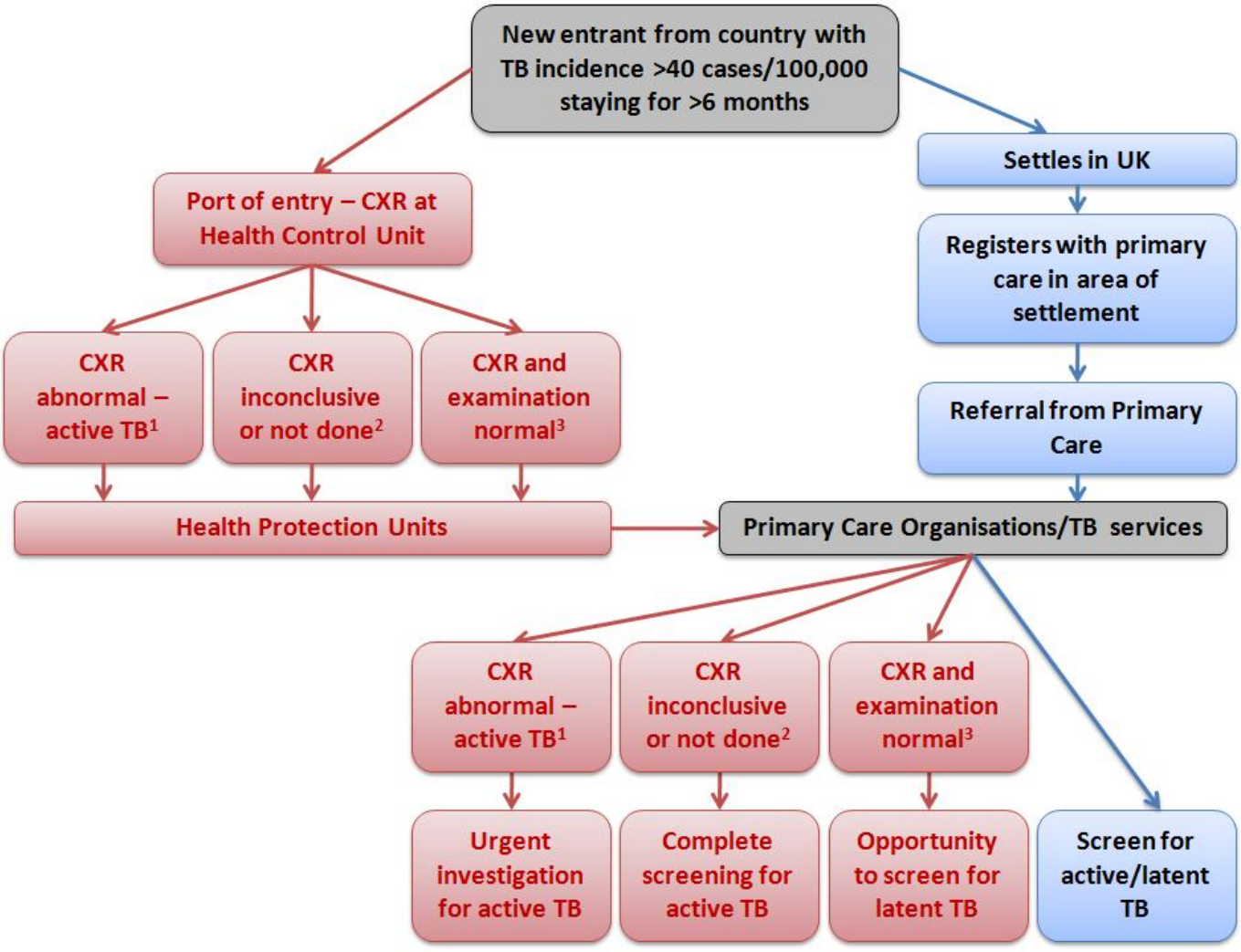
New entrant from country with TB incidence >40 cases/100,000 staying for >6 months
Port of entry – CXR at Health Control Unit
Settles in UK
Registers with primary care in area of settlement
Referral from Primary Care
CXR abnormal – active TB[1]
CXR inconclusive or not done[2]
CXR and examination normal[3]
Health Protection Units
Primary Care Organisations/TB services
CXR abnormal – active TB[1]
CXR inconclusive or not done[2]
CXR and examination normal[3]
Urgent investigation for active TB
Complete screening for active TB
Opportunity to screen for latent TB
Screen for active/latent TB

Table 1. Proportion of high and low TB burden Primary Care Organisations that undertake further screening action in new-entrants issued with different port notifications or referred from primary care
[1]CXR abnormal – port 103 form; [2]CXR inconclusive/has not been undertaken – port 102 form; [3]CXR normal – port 101 form

Method of Referral	Low TB burden PCO n=135(%)	High TB burden PCO n=42 (%)	OR (95% CI)	p value
CXR abnormal[1]	135 (100)	42 (100)	NA	NA
CXR inconclusive/has not been undertaken[2]	108 (80.0)	26 (61.9)	0.41 (0.19-0.86)	0.019
CXR normal[3]	84 (62.2)	12 (28.6)	0.24 (0.11-0.52)	<0.0001
Primary Care	52 (38.5)	10 (23.8)	0.50 (0.23-1.1)	0.08

Table 2. New-entrant sub-groups stratified by age and country of origin that are screened for latent TB infection amongst the subset of high and low TB burden Primary Care Organisations in the United Kingdom that actually undertake screening for latent TB in new-entrants

New-entrants aged under 16 years	Low TB burden PCO n=92 (%)	High TB burden PCO n=15 (%)	OR (95% CI)	p
>40 cases/100,000 p.a.	84 (91.3)	14 (93.3)	1.3 (0.16-11.5)	0.79
>500 cases/100,000 p.a.	91 (98.9)	14 (93.3)	0.15 (0.01-2.6)	0.20
Sub-Saharan Africa	91 (98.9)	14 (93.3)	0.15 (0.01-2.6)	0.20
Other countries	4 (4.3)	0 (0.0)	NA	1.00
New-entrants aged 16-35 years	**Low TB burden PCO n=92 (%)**	**High TB burden PCO n=15 (%)**	**OR (95% CI)**	**p**
>40 cases/100,000 p.a.	37 (41.1)*	10 (66.7)	2.9 (0.91-9.1)	0.07
>500 cases/100,000 p.a.	90 (97.8)	14 (93.3)	0.31 (0.03-3.7)	0.35
Sub-Saharan Africa	90 (97.8)	14 (93.3)	0.31 (0.03-3.7)	0.35
Other countries	4 (4.3)	0 (0.0)	NA	1.00
New-entrants aged over 35 years	**Low TB burden PCO n=90 (%)^**	**High TB burden PCO n=15 (%)**	**OR (95% CI)**	**p**
>40 cases/100,000 p.a.	1 (1.1)	1 (6.7)	6.4 (0.37-107.5)	0.20
>500 cases/100,000 p.a.	5 (5.6)	1 (6.7)	1.2 (0.13-11.2)	0.86
Sub-Saharan Africa	5 (5.6)	1 (6.7)	1.2 (0.13-11.2)	0.86
Other countries	0 (0.0)	0 (0.0)	NA	NA

***For the 16-35 age-group there were missing data for 2 PCOs for the >40/100,000 p.a. category and so the denominator was 90 not 92**

^ For the over 35 age-group there were missing data for 2 PCOs and so the denominator was 90 not 92 for all categories

Table 3. Heterogeneity in the protocols and tools (including the uptake of Interferon-gamma-release assays (IGRAs)) amongst those Primary Care Organisations (PCOs) that actually undertake screening for latent TB infection (<16 age-group – n=105 PCOs screened for LTBI, 16-35 age-group n=104 PCOs screened for LTBI; overall n=107 screened for LTBI).

Sequence of tests used	Low TB burden PCO n=91 (%)*	High TB burden PCO n=14 (%)*	OR (95% CI)	p-value
New-entrants aged under 16 years				
TST+CXR	23 (25.3)	5 (35.7)	1.6 (0.50-5.4)	0.41
TST+CXR+IGRA	66 (72.5)	9 (64.3)	0.68 (0.21-2.2)	0.52
IGRA+CXR	5 (5.5)	1 (7.1)	1.3 (0.14-12.2)	0.81
Other	2 (2.2)	0 (0.0)	NA	1.0
IGRA used	66 (72.5)	9 (64.3)	0.68 (0.21-2.2)	0.52
New-entrants aged 16-35 years	**Low TB burden PCO n=90 (%)[+]**	**High TB burden PCO n=14 (%)[+]**	**OR (95% CI)**	**p-value**
CXR+TST	5 (5.6)	0 (0.0)	NA	1.0
CXR+TST+IGRA	27 (30.0)	1 (7.1)	0.18 (0.02-1.4)	0.11
CXR+IGRA	3 (3.3)	0 (0.0)	NA	1.0
TST+CXR	18 (20.0)	6 (42.9)	3.0 (0.92-9.7)	0.07
TST+ IGRA+CXR	39 (43.3)	6 (42.9))	0.98 (0.3-3.1)	0.97
IGRA+CXR	2 (2.2)	1 (7.1)	3.4 (0.29-40.0)	0.33
IGRA used	67 (74.4)	8 (57.1)	0.45 (0.14-1.5)	0.19

***Numbers do not add up to total as 5 low burden PCOs and 1 high burden PCO use more than 1 method of screening**

[+]Numbers do not add up to total as 4 PCOs in low burden areas use more than one method of screening

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