UK pre-entry tuberculosis screening report 2015
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Published September 2016
PHE publications gateway number: 2016324
## Contents

Executive summary 4  
Acknowledgements 5  
1. Tuberculosis screening clinics 6  
2. Methods 9  
3. Demographics of all applicants 10  
4. Diagnostic tests and case detection 12  
5. Conclusion 22  
6. References 24  
7. Appendix 26
Executive summary

Following a successful pilot from 2005 to 2012, and global roll-out between 2012 and 2014, pre-entry TB screening for active pulmonary disease in all long-term visa applicants coming from high incidence countries to the UK has been fully operational in 101 countries since March 2014. The previous on-entry screening at UK airports was phased out and stopped in April 2014. Pre-entry screening is done in collaboration with the UK Home Office. Public Health England (PHE) provides advice, training, clinic audits, and data and information to support the quality assurance and evaluation of the programme.

The report is based on data from overseas clinics for the period October 2005 to December 2015. There has been considerable improvement in data quality and collection, although it is anticipated that data collection can be improved further by use of electronic data collection tools in the near future.

A total of 1,217,842 applicants were screened between October 2005 and December 2015, of which 256,115 were screened in 2015. The median age of applicants for the entire period was 24.7 years (interquartile range 21.0-30.2 years) and the largest proportion of applicants was in the 15-34 year age group (79.3%, 899,302/1,133,500) where age was known. The majority of applicants were male (57.3%). The largest screening volumes in 2015 were in China [27.3% (69,845/256,115)], India [16.6% (42,431/256,115)], Pakistan [8.6% (22,043/256,115)] and South Korea [6.1% (15,608/256,115)] reflecting current migration trends, showing a decrease in migrants from the Indian subcontinent and an increase in Chinese migrants.

In total, 382 TB cases were detected in 2015, giving an overall TB yield of 149.2 per 100,000 applicants. The TB detection rate has increased dramatically from 44.9 per 100,000 in 2006 to 149.2 per 100,000 in 2015, probably due to the increased use of sputum culture and improved overall quality of screening. In 2015, the TB detection rates were highest in the Indian subcontinent [199.2 per 100,000 (95% CI 167.6 – 235.1)] and lowest in Europe and the Commonwealth of Independent States (CIS) [25.9 per 100,000 (5.4 – 75.80). The TB screening yields of most countries were within the ranges which would be expected from UK surveillance of active TB cases. However, there are some exceptions, with some countries screening and detecting more or less active TB cases than expected.

In conclusion, this report provides a summary of pre-entry TB screening activities for the UK. The fully rolled out programme shows improved data quality and collection. The TB yield has also improved over time suggesting that screening is also improving.
Acknowledgements

We gratefully acknowledge the provision of data by the International Organisation for Migration (IOM), other overseas panel physicians, the Foreign and Commonwealth Office (FCO) posts and the Home Office.

We also acknowledge the help and support of Robert Sookoo, Dr Nicol Black, and Sophia Masud and Dr Graham Bickler (Port Health Unit at Heathrow).

We are thankful for support of TB Surveillance Unit for the provision of enhanced tuberculosis surveillance system (ETS) data and to Emily Newton for reviewing the report.

Authors

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1. Tuberculosis screening clinics

Introduction

Rates of tuberculosis (TB) and case numbers increased in the UK between 2000 and 2011. However, in the past four years the UK has experienced year-on-year decreases in the number of cases and rate of TB. The incidence is still high compared with other Western European countries such as Germany and France [1].

In 2015, 6,240 cases of TB were reported in the UK, an incidence of 9.6 per 100,000 [2]. TB in England is concentrated in urban areas and among specific risk groups, such as people with socio-economic risk factors and particularly those who were born in high TB incidence countries. The TB rate in the non-UK born population was 15 times higher than in the UK born population and 73% of all TB cases were non-UK born [3]. The impact of TB cases born abroad on UK TB numbers and the cost to the NHS means that pre-entry screening has a potential for reducing TB numbers with financial benefits for the NHS. Therefore, on-entry TB screening was phased out in favour of pre-entry screening for active pulmonary TB in 2012.

Aims and objectives of the report

The aim of this report is to present the current figures from the pre-entry screening programme for active pulmonary TB, show trends and provide a comparison by demographic and geographical characteristics, as well as to compare numbers detected overseas and domestically in the UK. Through data analysis and information, the report helps to inform quality assurance, identify issues associated with screening clinics and provide feedback for stakeholders.

Pre-entry screening

The UK pre-entry TB screening programme requires visa applicants from high TB incidence countries (≥40/100,000), who intend to stay in the UK for longer than six months to be certified free of pulmonary TB before they can apply for a visa. This is mandated by paragraph 2(2) to schedule 2 of the Immigration Act 1971 [4]. It was fully implemented and replaced the previous on-entry pulmonary TB screening programme at UK ports in March 2014.
The TB pre-entry screening programme was informed by and has close similarities with other TB pre-entry screening approaches, most notably those used by partner countries from the Five-Country Conference (5CC): Australia, Canada, New Zealand and USA. Pulmonary TB screening is based on chest x-rays (CXR) and symptom enquiry, followed by sputum smear and culture when TB is suspected. Applicants found to have pulmonary TB, are required to successfully complete treatment before they can proceed with visa application.

**Pilot and phases of pre-entry screening**

A successful pilot of the TB pre-entry screening scheme was jointly carried out by the Home Office and the International Organisation for Migration (IOM) between October 2005 and September 2012 in 15 countries (Bangladesh, Burkina Faso, Cambodia, Cote D'Ivoire, Eritrea, Ghana, Kenya, Laos, Niger, Pakistan, Somalia, Sudan, Tanzania, Thailand and Togo).

The pre-entry screening programme was thereafter rolled out in phases to 101 countries with World Health Organization (WHO) estimated TB incidence ≥40 per 100,000 population for 2012 [5], as outlined in Figure 1. The final phase of the roll-out (Phase 4) [6,7] was completed on 31 March 2014.
Figure 1: Map of countries and phase in which they joined the UK pre-entry TB screening programme
2. Methods

Data collection

Data was collected from two sources, IOM and non-IOM clinics. IOM data collected by IOM panel physicians was entered via a secure web-based IOM system, collated by the central IOM office in Manila and securely transferred to PHE. Data from non-IOM providers was collected by the clinics, collated via the overseas UK visa application centres and securely transferred to PHE. This report covers a ten-year period (2005–2015); comparisons between years and geographical areas may be affected by the roll-out process and policy changes. The report focuses on the 2015 data but also provides overall trends.

Data cleaning and analysis

Data was cleaned, validated and missing values completed where possible. IOM data was of good quality, but non-IOM data contained some missing variables and discrepant dates. Whenever possible, missing values were deduced from other variables. Variables from IOM and non-IOM data were harmonised and merged into a common dataset.

Clean data was imported into Stata v.13 (Statacorp LP, College Station, TX, USA) which was used for all statistical analyses. Graphs and tables were created with MS Excel 2010 and exported to MS Word (Microsoft Corp, Redmond, WA, USA).

Data was available for IOM screening activities between October 2005 and December 2015 and non-IOM providers between September 2012 and December 2015. Data up to December 2015, provided up to 15 May 2016, was included in this report.
3. Demographics of all applicants

In 2015, data was available from a total of 256,115 UK visa applicants. Of these 61.9% (158,407/256,115) were screened by non-IOM and 38.2% (97,708/256,115) by IOM clinics. This chapter provides data on all applicants (IOM and non-IOM), except where specifically noted.

Age and sex distribution of all applicants

Information on age and sex was available for all applicants screened in IOM clinics. Data on age and sex was missing for 24.0% (37,965/158,407) and 28.3% (44,854/158,407) of non-IOM applicants respectively. Of all applicants screened and where data was available, the median age for applicants was 23 years and the largest number of applicants was in the 15 to 24 year age group (47.6%, 64,169/218,150), followed by the 25 to 34 year group (29.4%, 64,169/218,150). Only 3.8% (8,378/218,150) of the applicants were aged 45 years and over (Figure 2). In all age groups, the number of female applicants exceeded males, except in the lowest age group (0–14 years).

Figure 2: Distribution of all applicants by age group and sex, 2015

Distribution of all applicants by screening provider, country and region

As of 31 March 2014, screening was implemented in approved clinics in 71 countries, which were screening for 101 countries (some countries have no clinics and applicants have to go to other countries for screening, for example, Somalians are screened in
Kenya). However, in 2015, data was only available from 58 (out of 71) of the countries. Countries where data was missing comprised just 0.2% (748/310,178) of the total number of persons entering the UK who require pre-entry screening. This was due to better data returns in 2015.

In 2015, more than half of all recorded screens [52.1% (133,391/256,115)] took place in South East Asia and just over a fifth [27.4% (69,845/256,115)] were screened in China. A total of 27.4% (70,277/256,115) of applicants were from the Indian subcontinent and 15% (38,025/256,115) were from Africa (Figure 3). Only a small number of applicants were from Europe and the Commonwealth of Independent States\(^1\) [CIS; (4.5% (11,567/256,115)], Middle East [0.9% (2,323/256,115) and South and Central America [0.2% (532/256,115)]. This is explained by visa regulations, regional migration trends and the clinic timeline for roll-out. No data was received from the Caribbean.

\(^1\) Europe and CIS includes data from: Belarus, Kazakhstan, Moldova, Russia and the Ukraine.
4. Diagnostic tests and case detection

Because of limitations in data quality and the proportion of missing data in the non-IOM returns (7.5% (11,832/158,407) of the non-IOM applicants had missing data on CXR), the following paragraphs and flow-chart (Figure 4) are restricted to IOM data only.

Chest X-Rays (CXR)

The TB screening flowchart (Figure 4) shows that out of 97,708 applicants from IOM clinics, 88,016 (90.1%) had a CXR taken. Reasons for not obtaining a CXR were known for 9,677 (99.9%) of the 9,686 individuals where CXRs were not done. A total of 162 did not have a CXR because they were pregnant and 9,515 were children under 11 years old.

Among individuals who underwent CXR examination, 2.3% (1,859/80,016) had lesions consistent with TB and were referred for sputum collection, as recommended by UK technical instructions [6]. A total of 1,969 applicants had sputum samples taken for tests (these included 110 individuals that did not undergo CXR examinations). A total of 66 applicants had no culture confirmation, but were diagnosed according to the clinical case definition (page 17), were not issued a clearance certificate and were referred for TB treatment. Of these, 57 (86.4%) had TB-related CXR changes, and for the remainder, TB was diagnosed based on the medical assessment. Including the 143 culture confirmed cases, the total number of TB cases was 209.

Of the 88,016 individuals that had CXR examinations, 85,156 had normal CXR and 1,859 individuals had abnormalities that were consistent with TB-related abnormalities (data on abnormalities consistent with TB was missing for 1 individual).
Sputum tests

For CXRs with abnormalities consistent with TB, the UK Technical Instructions [8] require three sputum samples to be submitted for smear and culture.

The overall sputum test results for IOM data, which combined the smear and culture results, are summarised in Table 1. Between January and December 2015, a total of 1,969 individuals had sputum samples taken, including 101 samples for persons who did not undergo CXR screening. In addition, as of 15 May 2016, 35 sputum tests were pending. Sputum smears and culture are mandatory because smears alone have reduced sensitivity [8].

a. Sputum smears

Of the 1,967 individuals that had sputum smears, 2.2% (43/1,967) were positive and 0.2% (4/1,967) were inconclusive. The majority [96.5% (1,898/1,967)] were sputum smear negative but 1.1% (22/1,967) results were pending. All individuals with positive sputum smears had undergone CXR examination first. One hundred and ten individuals
(76.9%, 110/143) were smear negative but culture positive and would not have been detected by screening under the previous protocol.

b. Sputum cultures

Overall, 7.3% (143/1,969) of visa applicants who had sputum cultures performed were positive in 2015. The majority [91.0% (1,731/1,969)] were negative although 35 cultures (1.8%) were pending (Table 1).

Table 1: Sputum test results for individuals tested between January and December 2015 by IOM clinics. The table gives combined results for smear and culture

<table>
<thead>
<tr>
<th>Sputum test results</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>1,791 (91.0)</td>
</tr>
<tr>
<td>Positive</td>
<td>143 (7.3)</td>
</tr>
<tr>
<td>Pending</td>
<td>35 (1.8)</td>
</tr>
<tr>
<td>Total</td>
<td>1,969 (100.0)</td>
</tr>
</tbody>
</table>

Descriptive analysis of CXR and sputum test positivity by country

For countries which had screened more than 3,000 applicants, the proportion of positive CXRs and the TB detection rate of the programme are shown in Figure 5. There was variation between CXR positivity and TB detection rate. The reasons for this are complex and may be related to the quality and interpretation of CXRs or sputum samples.

Figure 5: CXR positivity and TB rate by country, January to December 2015*

*For countries which had screened more than 3,000 applicants.
Sputum cultures as a proportion of sputum smears by year

The ratio of sputum cultures to smears (a proxy for estimating the proportion of sputum cultures among all sputum tests) has increased significantly over the years. Figure 6 shows this proportion and the TB rates over the years from IOM clinics. There has been a significant increase of TB detection over the years (Chi-square for trends \(p<0.001\)). Increasing TB detection rates may in part be explained by the increasing proportion of sputum cultures taken (Figure 6).

**Figure 6: Sputum cultures as a proportion of sputum smears\(^5\) by screening year (IOM data only)**

![Graph showing sputum cultures as a proportion of smears by screening year](image)

*As of May 2016, 35 sputum samples are pending and the rate may increase when final results are available.

\(^5\)As a proxy for the proportion of cultures amongst all sputum tests done.

**Tuberculosis case definition**

A TB case was defined as outlined in the enhanced tuberculosis surveillance system (ETS) data dictionary and using the following criteria:

- TB confirmed by microbiological tests (eg sputum tests, including culture and/or smear tests)

- In the absence of sputum test confirmation, a case that met the following criteria:
  - a clinician’s judgement that the patient’s clinical and/or radiological signs and/or symptoms are compatible with tuberculosis, AND
  - a clinician’s decision to treat the patient with a full course of anti-tuberculosis therapy
Descriptive analysis of TB cases

A total of 382 cases of TB were detected and notified through the screening programme in 2015. Just over half of the cases [54.7% (209/382)] were reported from IOM clinics. Non-IOM clinics reported fewer cases (45.3% (173/382)) but had more pending sputum culture results (478 and 35 for non-IOM and IOM, respectively). Figure 7 shows the number of TB cases and detection rates by year of screening. TB detection rates have increased significantly from 2006 to 2015, but stabilised in the last three years. TB cases may increase after pending sputum results become available. The screening year was missing for 1,860 records and four TB cases.

Of all the TB cases in 2015 where sex was known, 56.6% (154/272) were female and the TB rates were similar for males and females (127.0 and 130.2 per 100,000, respectively). Figure 8 shows the distribution of TB cases and TB rates by age group in 2015. The largest number of TB cases was found among 24 to 34-year-olds followed by 15 to 24-year-olds, but the highest case detection rates occurred among the oldest age group (≥55 years). Age was missing for 65.9% (114/173) of the TB cases screened by the non-IOM clinics.

Figure 7: Yearly number of TB cases and detection rates data, January 2006 to December 2015

*As of May 2016, 513 sputum samples are pending and the rate may increase when final results are available. We also improved operationalising the case definition in 2015, in keeping with improved data completion.
The regional distribution of TB cases and rates is shown in Figure 9. Most cases detected by pre-entry screening were either from East and South East Asia [52.6% (201/382)] or the Indian subcontinent [36.6% (140/382)]. The rate was highest in the Indian subcontinent (199.2 per 100,000). The rate was also high in South and Central America (188.0 per 100,000) but only a few screens were carried out there (532, and thus the wider 95% CI). The rate in South East Asia (150.7 per 100,000) was higher than Africa (92.0 per 100,000). The rates were lowest in Europe and the CIS (25.9 per 100,000) and the Middle East (86.1 per 100,000) although both regions had performed fewer screens. No data was submitted from the Caribbean in 2015.
Figure 10 shows the distribution of cases and rates of TB in 10 countries with the highest screening volumes in 2015. The overall yield among these countries was 112.7 per 100,000, (range 20.4; CI 2.5 – 73.9 to 322.9; CI 199.9 – 493.6). These countries detected more than half of all TB cases in 2015 [59.4% (227/382)].

TB detection rates in China, South Korea, Hong Kong, Russia and Kazakhstan were comparable to 2014 WHO prevalence rates; they were lower than 2014 WHO prevalence rates in Pakistan, Nigeria, Malaysia, Bangladesh, South Africa, Ghana, Indonesia and Kenya but higher than WHO prevalence estimates in India, Thailand, Philippines, Nepal and Vietnam, among countries that had screened more than 2,000 applicants.

Figure 10: Number of TB cases and detection rates in the 10 countries with the largest number of applicants, January to December 2015

Figure 11 shows the number of TB cases and TB detection rates by visa category. Where visa category was known, 9.6% (26/272) had applied under Family Reunion, 47.4% (129/272) had applied under Settlement and Dependents, 20.6% (56/272) had applied under Students, 14.7% (40/272) had applied under Work, 1.5% (4/272) had applied under Working Holiday Maker and 6.3% (17/272) had applied under Other.

The TB rates (per 100,000) per category were Family Reunion (152.0), Settlement and Dependents (255.2), Students (52.0), work (160.5), Working Holiday Maker (65.4) and Other (161.5). Visa category was missing for 28.8% (110/382) of TB cases, all of whom were screened by non-IOM providers. Almost a quarter of all screens carried out by the non-IOM providers [24.8% (39,209/158,407)] had visa information missing.
Drug susceptibility testing of positive TB cultures

Analysis of drug susceptibility was limited to IOM clinics; the magnitude of missing data made analysis of non-IOM returns difficult. Within IOM clinics, a total of 537 positive sputum cultures had drug susceptibility (DST) testing done between January 2007 and December 2015. Figure 12 shows the number of positive sputum cultures and the proportion that had DST performed. The proportion of cultures with DST ranged between 57% and 98% and there was no linear increase. TB culture and DST is a mandatory requirement under the UK technical instructions, and important to allow appropriate treatment for TB cases.

Figure 13 summarises the overall DST results. During this period the majority of TB cultures were sensitive to all first-line drugs [84.5% (454/537)]. Of the 15.5% with drug resistance, 8.6% (46/537) had isoniazid monoresistance and 3.4% (18/537) were classified as poly-drug resistant (resistant to more than one first-line drug, but not MDR). Nine [1.7% (9/537)] multi-drug resistant TB (MDR) and one [0.2% (1/537)] extensively-drug resistant (XDR) TB case were detected in 2015. Rifampicin mono-resistance was detected in one culture (0.2%) and a further eight cultures (1.5%) showed monoresistance to one of the other three first-line drugs, most commonly isoniazid, ethambutol and pyrazinamide. Drug susceptibility terms are defined in the Appendix (page 29).
Comparison of screening yields with ETS and pre-entry screening data

Overall, TB numbers detected through pre-entry TB screening programme have increased significantly from 14 in 2006 to 382 in 2015. During the same period the total number of UK pulmonary TB cases (as reported to national surveillance, ETS) identified within the year of entry from the 101 countries [9] in the screening programme has decreased from 380 in 2006 to 88 in 2015 (Figure 14). The decreasing number of TB
cases diagnosed within the first year of entry to the UK may be due in part to pre-entry screening and changes in migration trends.

**Figure 14: Number of TB cases diagnosed by pre-entry screening in the 101 programme countries and those identified within one year of UK entry**, 2006 to 2015

*The number of pulmonary TB cases identified within one year of entry into the UK was from all 101 high incidence countries but the number of TB cases diagnosed by pre-entry screening were from an increasing number of countries as screening was rolled out; 5 pilot countries (2006), 15 pilot countries (2007 and 2012), 101 countries (by 2014).

**As of May 2016, 513 sputum samples are pending and the rate may increase when final results are available.

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2 For countries, which only became part of pre-entry screening during the global roll-out in 2012–13, there is a possibility of under-ascertainment, as clinics were establishing reporting systems during this transition phase.
5. Conclusion

This is the third annual report of the pre-entry screening programme and reports on UK TB pre-entry screening activities and outcomes until the end of 2015.

This report covers the first full year since global roll out to 101 countries (screening in 71) was completed in March 2014. The throughput, case numbers and rates appear to have stabilised. In 2015, just over 250,000 screens were recorded and 382 TB cases detected at a rate of 149.2 per 100,000. After a significant increase in throughput and case detection during the pilot and roll-out phases, these figures are very similar to those for 2014.

Throughput figures follow migration patterns. In 2015, the vast majority of applicants came from South East Asia, the Indian subcontinent and sub-Saharan Africa, with much smaller proportions from other regions. As in previous years, most visa applicants were young adults (often students) but this is the first time there were slightly more females than men. Case numbers and detection rates were fairly high among people from South East Asia and the Indian subcontinent; conversely, numbers and rates were lower in sub-Saharan Africa. For the first time, this report provides data on drug resistance proportions detected between 2007 and 2015 among the IOM applicants, confirming any first-line drug resistance in 83 of 537 persons (15.5%) where culture results were available. Of these, nine (1.7%) had multi-drug resistant TB of which one was a case of extensively-drug resistant TB.

Data quality remains of concern, particularly in the non-IOM data. However, further significant improvements around data quality were made in 2015, not least through close collaboration and communication with providers overseas and greater teaching and training activities remotely and in person. More work remains to be done, particularly in low throughput areas, and further improvements are expected with the ongoing development of the global web-based data solution.

In conclusion, this report indicates that pre-entry screening has been successfully rolled out and after significant improvement of screening operations in previous years, including near-universal sputum culture confirmation among IOM applicants [10, 11], appears to be performing at a stable level. Quality assurance has played an important role in ensuring successful and appropriate screening overseas. However, TB detection rates still vary significantly between countries and sites, different age groups and visa types. The reasons for this are not always clear [9]. Improved case ascertainment and maintaining a high quality of screening procedures may potentially increase case detection rates further as does the collaboration with, and learning from, settings and countries with higher detection rates [10].
Notwithstanding the need for a multi-dimensional TB strategy for England [14], it is clear that pre-entry screening has an impact and the potential to reduce the number of prevalent cases notified in the UK. Ongoing and sustained efforts to maintain quality assurance alongside well designed and relevant research work is needed to guide and inform the shape and direction of the programme.
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7. Appendix

Definitions of drug susceptibility terms:

**Extensively-drug resistant TB (XDR TB)**
Extensively-drug resistant is defined as resistance to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (that is, amikacin, kanamycin or capreomycin).

**Multi-drug resistant TB (MDR TB)**
Multi-drug resistant TB (MDR TB) is defined as resistance to at least isoniazid and rifampin, with or without resistance to other drugs.

**INH resistant**
TB that is resistant to isoniazid, a first-line anti-TB drug and not other drugs.

**Monoresistant to a drug other then INH**
Resistance to a first-line treatment drug other than INH, for example, ethambutol.

**Pansusceptible**
Susceptible to all first line drugs, for example, isoniazid.

**Poly-drug resistant**
Poly-drug resistance refers to resistance to two or more first-line drugs but not to both isoniazid and rifampicin.

**Rif monoresistance**
Resistance to rifampicin, a first-line drug and not other drugs.