UK pre-entry tuberculosis screening report 2014
About Public Health England

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Executive summary

Pre-entry TB screening for active pulmonary disease in all long-term visa applicants coming from high incidence countries to the UK was successfully piloted from October 2005 to May 2012 and implemented in 101 countries between September 2012 and March 2014. The previous on-entry screening at UK airports was phased out and was 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 between October 2005 and December 2014. Despite considerable improvement in data quality and collection, some concerns remain. It is anticipated that data collection will be improved by use of advanced of electronic data collection tools in the near future.

A total of 961,725 applications were screened between October 2005 and December 2014 of which 233,251 were screened in 2014. The median age was 25 years (interquartile range: 9.2 years) and the largest proportion of applicants was aged 15 to 34 years. The majority of applicants were male (60.5%). The largest screening volumes were in Pakistan (40.5% (389,509/961,725)), Bangladesh (19.5% (187,157/961,725)) and Thailand (7.1% (68,608/961,725)) although these do not reflect current migration trends.

In total, 983 TB cases were detected between October 2005 and December 2014, giving an overall TB yield of 102.5 per 100,000 applications. In 2014, 224 TB cases were detected. The TB rate was higher among females than males, and the majority of TB cases were found among applicants aged 15 to 34 years (618/983) although older age groups had higher TB rates. The TB detection rate in 2006, the first full year of screening, was 44.9 per 100,000. In 2014 when the full roll-out was completed, the detection rate increased to 149.8 per 100,000, suggesting that detection rates have improved markedly. This is probably due to use of sputum culture for most smears in line with UK technical instructions changes. In 2014 the TB detection rates were highest in East and South East Asia (228.5 per 100,000 (95% CI 207.9 to 250.6)), with no cases detected in the Caribbean and the Middle East with 155 and 3,387 applications, respectively. The TB screening yields of most countries were within the ranges which would be expected from UK surveillance. 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 with time suggesting that screening is getting better.
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1. Tuberculosis screening clinics

Introduction

Tuberculosis (TB) rates have been increasing during the last decade in the UK although there has been a small decrease over the past two years; the incidence is still high compared with other Western European countries. In 2013, there were 7,892 TB cases reported in the UK, an incidence of 12.3/100,000. TB in the UK is concentrated in urban areas and among specific risk groups, such as people with socio-economic risk factors and particularly those who were born or spent significant time in high TB incidence countries. The high levels of TB in the UK among non-UK born individuals have raised the interest in pre-entry screening for active pulmonary TB.

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 the trends over the years, provide a comparison by demographic and geographical characteristics, and compare the numbers detected overseas and domestically in the UK. The report informs quality assurance of the programme and feedback to 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. It has been fully implemented and replaced the previous on-entry pulmonary TB screening programme at UK ports in April 2014.

The TB pre-entry screening programme has been informed by and has close similarities with other TB pre-entry screening approaches, most notably those used by other partner countries from the five-country conference (5CC): Australia, Canada, New Zealand and the 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 Organisation (WHO) estimated TB incidence ≥ 40 per 100,000 population as outlined in Figure 1. The final phase of the roll out (Phase 4) 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 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 UK visa application centres and securely transferred to PHE. This report covers a nine year (2005 to 2014) period and comparisons between years and geographical areas may be affected by the roll-out process and policy changes.

Data cleaning and analysis

Data was cleaned and validated, and missing values were 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 2014 and non-IOM providers between September 2012 and December 2014. Data up to December 2014, correct as of 3 February 2015, was included in this report.

The observed TB detection rates from overseas screening were compared to what the expected yields would be in the UK surveillance data for the funnel plot. The 95% and 99% confidence intervals (CIs) were calculated and plotted using the expected pulmonary TB rate from ETS.
3. Demographics of applicants

Data was available from a total of 961,725 UK visa applications. Of these 84.4% (810,628/961,725) were screened by IOM and 15.6% (151,097/961,725) by non-IOM clinics. In 2014, of the 233,251 applications, 128,198 (55.0%) were screened by non-IOM clinics.

Age and sex distribution of applicants

Information on age and sex was available for all applications screened in IOM clinics. The median age for these applicants was 24.5 years and the largest number of applications was in the 15 to 24 year age group (48.8%) followed by the 25 to 34 year olds (35.6%). Only 3.3% of the applications were aged 45 years and over (Figure 2). There were more male than female applicants in all age groups except for those aged 55 years and over.

Age and sex were missing for 30.7% (46,377/151,097) and 41.1% (62,085/151,097) of non-IOM applications, respectively. Non-IOM data was therefore excluded from Figure 2.

Figure 2: Distribution of IOM applications by age group and sex
Applications distribution by screening provider, country and region

As of 31 March 2014, screening was implemented in approved clinics in 71 countries; the clinics screened for 101 countries (some countries have no clinics and have to go to other countries for screening eg Somalisians are screened in Kenya). However data was only available from 48 (out of 71) of the countries. Countries that did not provide data accounted for only 2.5% of the total number of people entering the UK on visas that require a TB certificate. IOM-led clinics screened 84.4% of all recorded applications.

From 2005 to 2014, approximately 40.5% of all recorded screens (389,509) took place in Pakistan and just under a fifth (19.5%) in Bangladesh. Figure 3 shows that in 2014 almost two thirds (64.5%) of the applications were from the Indian sub-continent with one fifth from East and South East Asia. Africa accounted for 13.4% of the applications and there were only a small number of applications from Europe and the Commonwealth of Independent States ¹ (CIS; 1.2%), Middle East (0.4%) and the Caribbean (<0.1%). This is explained by visa regulations, regional migration trends and the clinic roll out timeline.

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

Chest X-rays

Data on chest X-rays (CXR) was near complete from IOM clinics but there was missing data for 35.3% of the non-IOM applications.

The TB screening flowchart (Figure 4) shows that amongst a total of 810,628 applications from IOM clinics, 791,501 (97.6%) had a CXR taken. Reasons for not obtaining a CXR were known for 19,120 (99.9%) of the 19,123 such cases. A total of 3,806 did not undergo CXR because they were pregnant and 15,314 were children under 11 years old.

Among individuals who underwent a CXR, 3.9% (31,093/791,501) had lesions consistent with TB and were referred for sputum collection, as recommended by the UK technical instructions.\(^5\)

Figure 4: Flow-through of IOM data, October 2005 to December 2014
Sputum tests

For CXRs with abnormalities consistent with TB, the UK technical instructions\textsuperscript{5} require three sputum samples be submitted for smear and culture.

The overall sputum test results for both IOM and non-IOM, which combine the smear and culture results, are summarised in Table 2. Since October 2005 among all applications a total of 37,488 individuals had sputum taken, including 4,027 for people who did not undergo CXR screening. Of these, 1.8% (672/37,488) were positive for tuberculosis (laboratory confirmed TB, Table 1). In addition, as of 31 December 2014, 45 sputum tests were inconclusive and 913 were pending. Seventy-five cases were diagnosed clinically and 983 TB cases were found in total between October 2005 and December 2014.

a. sputum smears

Of the 37,488 individuals who had sputum taken, all had a sputum smear test. Of the sputum smear tests, 1.1% (422/37,488) were positive and 0.1% (49/37,488) were inconclusive. Eight (1.9% (8/422)) of the individuals with positive smears did not have a CXR first.

b. sputum cultures

Overall, 26.2% (9,816/37,488) of visa applicants who had sputum samples taken had sputum cultures done. This figure is an overall average over the years and has significantly improved with newer versions of the United Kingdom tuberculosis technical instructions (UKTBTIs). In 2014, 53.6% (2,497/4,659) of all sputum samples had cultures done.

Of all individuals who had sputum cultures done, 5.7% (558/9,816) were positive for tuberculosis and 12 had inconclusive results. Of these, 98.0% of (547/558) positive cultures were from IOM clinics. All but one of the 558 individuals had undergone CXR examination before submitting sputum.
Table 1: Sputum test results for individuals tested between October 2005 and December 2014. 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>35,858 (95.7)</td>
</tr>
<tr>
<td>Positive</td>
<td>672 (1.8)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>45 (0.1)</td>
</tr>
<tr>
<td>Pending</td>
<td>913 (2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>37,488 (100)</td>
</tr>
</tbody>
</table>

Descriptive analysis of CXR and sputum test positivity by country

For countries which had screened more than 5,000 applications, the proportion of positive CXRs and the TB detection rates 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* (2005 to 2014)

Sputum cultures as a proportion of sputum smears by year

The ratio of sputum cultures to smears (as a proxy of all tests) has increased significantly over the years. Figure 6 shows this proportion and the TB rates over the years from IOM clinics only. The probability of diagnosing TB increased with increasing year (Chi-square for trends p<0.001). This would imply that the increasing TB detection rates could in part be explained by the increase in the proportion of sputum cultures improving the chances of detecting a case of TB.
Figure 6: Sputum cultures as a proportion of sputum smears by screening year (IOM data only).

* As of February 2015, 644 sputum samples are pending and the rate may increase when final results are available.

Figure 7 shows a statistical control chart of the difference between cumulative TB rate detected by pre-entry screening (observed) and the rate of pulmonary TB cases detected by the enhanced TB surveillance system (ETS) in the UK within one year of entry among the cohort who entered that year (expected). Two countries in Sub-Saharan Africa (SSA) and two in the Indian subcontinent (ISC) were below the lower 99% CI suggesting that they detected less TB cases than would be expected from UK observational data.

Three countries in East and South East Asia had yields higher than expected as they were above the upper 99% CI. The rest of the countries were within the lower and upper 99% CI, with nine countries very close to the expected line.

The funnel plot was based on cumulative screening yields over the years (2005 to 2013) and may overestimate or underestimate the differences if detection rates improved or worsened in recent years respectively. The overall expected rate was an average of all countries, which assumes uniform rate per country and does not take into account the different TB incident rates in different countries. The detection of cases from screening may have improved over the years as policy changes were implemented. While cases were detected by active surveillance during screening, the expected cases were from passive surveillance. Some TB cases in the UK among migrants are due to transmission of disease within the UK. The plot must therefore be interpreted with caution.
Figure 7: Funnel plot of TB detected by pre-entry screening less TB detected in the UK by country

ESEA=East and South East Asia, ISC=Indian Sub-continent and SSA=Sub-Saharan Africa.

* The expected rate is calculated as the pulmonary TB cases diagnosed within 1 year of entering the UK for period 2009 to 2011 over inbound migrants who entered the UK during that year, stratified by country and compared with the observed rate (detected by UKTB pre-entry screening programme) between 2006 and 2014.

** The confidence intervals were based on an estimation of the standard error of the expected proportion.
Tuberculosis cases

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 (e.g. sputum tests, including culture and/or smear tests).
- In the absence of culture confirmation, a case that meets 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 983 cases of TB were detected and notified through the screening programme between October 2005 and 31 December 2014. The majority of the cases (74.9% (736/983)) were reported from IOM clinics. Figure 8 shows the number of TB cases and detection rates by year of screening. TB detection rates have increased from 2006 to 2013. There was a 2.4% (153.4 to 149.8 per 100,000) decrease in the TB detection rate last year mainly because of the 913 pending sputum tests results. The rate may increase when the final results are available.

Of all the TB cases where sex was known, 52.1% (455/874) were male; however, the TB rate in males (83.7 per 100,000) was lower than that of females (117.8 per 100,000). Figure 9 shows the distribution of TB case numbers and TB rates by age group. The largest number of TB cases was found among the 15 to 24 year olds followed by the 25 to 34 year olds, but the highest case detection rates were found among the oldest age group (≥55 years).
Figure 8: Yearly number of TB cases and rates data, January 2006 to December 2014

* As of February 2015, 913 sputum samples are pending and the rate may increase**** when final results are available.

Figure 9: Distribution TB cases and rates by age group, October 2005 to December 2014

The regional distribution of TB cases and rates is shown in Figure 10. Most cases detected by pre-entry screening were either from East and South East Asia (45.9% (451/983)) or the Indian sub-continent (45.1% (443/983)). The rate was highest in East and South East Asia (228.5 per 100,000). Rates detected in the Indian subcontinent and Africa were lower (71.5 and 67.0 per 100,000 respectively). No cases were detected from the Caribbean or the Middle East but the numbers screened were low (155 and 3,387 respectively).
Figure 10: Regional distribution TB cases and rates, October 2005 to 31 December 2014

Figure 11 outlines the distribution of the cases and rates of TB in 10 countries with the highest screening volumes. The overall yield among these countries was 98.8 per 100,000, (Range 11.2; CI 0.3–62.6 to 260.9; CI 221.9–304.7).

Figure 11: Number of TB cases and rates in the 10 countries with the largest number of applications, October 2005 to 31 December 2014*

*Excludes Hong Kong and Malaysia where clinical data was missing
Figure 12 shows the number of TB cases and TB detection rates by type of visa category. Most of the cases occurred among students (402 cases) but the rate was moderate (81.7 per 100,000). Conversely fewer cases occurred among those on family reunion visas (19 cases), but TB detection rates in this category were the highest (159.5 per 100,000).

**Figure 12: Distribution of number of TB cases and rates by visa type**

Comparison of screening yields with ETS and Pre-entry screening Pilot data

Overall, TB numbers and yields detected through screening in the 15 IOM pilot countries have increased significantly between 2006 and 2013. During the same period the total number and rates of UK TB cases (as reported to national surveillance, ETS) within the year of entry from these pilot countries has decreased (Figure 13). The increasing yield in the pre-entry screening programme and the decreasing numbers of early TB reports post entry appear related. This would suggest that pre-entry TB screening is having a positive impact on UK tuberculosis cases among migrants detected within the first year of entry.
**Figure 13**: Comparison between of pulmonary TB cases detected by pre-entry screening and cases notified in the UK within one year of entry from the 15 Pilot pre-entry screening countries

*This figure compares the number of pulmonary TB cases and rate (per 100,000) detected by the 15 pilot countries for the pre-entry screening programme by year, to TB cases and rate notified in ETS in patients from those same 15 countries.

¥ Cases diagnosed by pilot screening result from active surveillance while those from ETS are obtained from passive surveillance.
5. Conclusion

This report provides an overview on UK TB pre-entry screening activities and outcomes between 2005 and 2014.

In keeping with the expansion of the programme, the overall number of screened applicants has increased considerably between 2006 and 2014, although the number of applicants from the initial pilot countries has decreased. Between October 2005 and December 2014, most screens were recorded by IOM providers. This corresponds to the nature of the global roll-out and, to a lesser extent, missing data from non-IOM providers. The vast majority of applicants were screened in the Indian sub-continent and this reflects both migration trends and the timeline of clinic establishment. Most visa applicants were young male adults and the majority of these were students.

The data quality in 2014 has significantly improved compared with previous years, although further improvements are needed and expected with the development of a single global web-based data collection tool. The quality of screening itself also appears to be improving. Almost all applicants receive chest X-rays with the exception of those who were either pregnant or children aged less than 11 years old. The overall rate of CXR abnormalities is about 4%; however, there is significant variation of these rates between sites and countries and this warrants further investigation.

The overall yield of TB cases among applicants was 102.3 per 100,000 applications, although this also varied significantly between countries and sites, different age groups and visa types. Nevertheless, TB detection rates have increased over the last eight years, possibly as a result of improved practice, including the near complete implementation of culture confirmation. Evidence from other countries demonstrates the effect of culture confirmation and supports current UK policy in this respect. It is possible, however, that TB detection rates could be improved further. It is encouraging to see that TB notification rates among migrants occurring soon after arrival to the UK have significantly decreased, while overseas detection rates have increased during the same period. This indicates a possible effect of pre-entry screening.

In conclusion, this report demonstrates the feasibility of overseas screening and shows early descriptive evidence of its effect. Much remains to be done, including further improvement of data completion and quality, improvement of understanding of unexplained variations in CXR referral rates and yield. Meanwhile, work with overseas providers to improve the quality of this programme continues. Monitoring the effects and evaluating the cost effectiveness of this programme to inform future clinical and policy changes in the programme is in progress.
6. References


