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UK pre-entry tuberculosis screening report 2017

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Executive summary

The tuberculosis pre-entry screening programme has been operational in 101 countries since replacing on-entry screening at UK airports in March 2014. The programme is delivered in collaboration with the UK Home Office. Public Health England provides advice, training, clinic audits, and data and information to support the quality assurance and evaluation of the programme.

This report presents data from 170 overseas clinics for the period between October 2005 and December 2017. Since programme roll out, there have been significant improvements in data quality and collection. We are still working with partners to improve data quality and expect that the uptake of electronic data collection tools will contribute further to this improvement.

Since October 2005, we have received 1,712,561 applications which represents 1,279,026 individual applicants. The median age of applicants for the entire period was 24 years (interquartile range 20.0-30.0 years) and the largest proportion of applications where age was known, were adolescents and young adults aged 15-34 years (78.4%, 1,194,433 / 1,712,561). Where sex was known, 54.0% of applicants were male.

In total, 255,510 applicants were screened in 2017. The largest screening volumes in 2017 were in China [33.1% (84,559 / 255,510)], India [23.7% (60,477 / 255,510)], Pakistan [8.3% (21,129 / 255,510)] and Nigeria [4.2% (10,834 / 255,510)] reflecting current migration trends.

During 2017, there were 298 active tuberculosis cases detected through pre-entry screening, giving an overall tuberculosis yield of 116.6 per 100,000 applicants. The tuberculosis detection rate has increased dramatically from 44.9 per 100,000 in 2006 to 168.4 per 100,000 in 2014, in keeping with an increased use of sputum culture and improved overall quality of screening. There was a decrease in rate between 2015 and 2016 with but the rate increased again in 2017. The tuberculosis screening yields of most countries were within the ranges which would be expected from UK surveillance of active tuberculosis cases. There are exceptions to this, where some countries are screening and detecting more or less active tuberculosis cases than expected.

This report provides a summary of pre-entry tuberculosis screening activities for the UK during 2017. The programme continues to monitor tuberculosis trends overseas of which we see an overall increase in detected TB over time (with the exception in 2016).

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Authors

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1. Tuberculosis screening clinics

Introduction

The UK experienced an increase in rates of tuberculosis (TB) and case numbers between 2000 and 2011. Rates peaked in 2011, and since then have decreased by approximately one third. Despite these reductions, the UK still has the third highest TB rate in Western Europe [1].

The high percentage of non-UK born cases and the cost to the NHS means that pre-entry screening of migrants has the potential to reduce TB numbers with financial benefits for the NHS. Pre-entry screening for active pulmonary TB was rolled out from 2012 to replace on-entry TB screening in the ports and can help decrease prevalent TB cases in non-UK born individuals in the UK [4].

5,567 cases of TB were reported during 2017 in the UK (8.4 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. During 2017, 70% of UK TB cases were among non-UK born persons, a rate 15 times higher than UK born cases [3].

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. A comparison of numbers detected overseas and domestically in the UK will also be presented. Through data analysis and information, the report helps to inform quality assurance, identify issues associated with individual screening clinics and provide feedback for stakeholders.

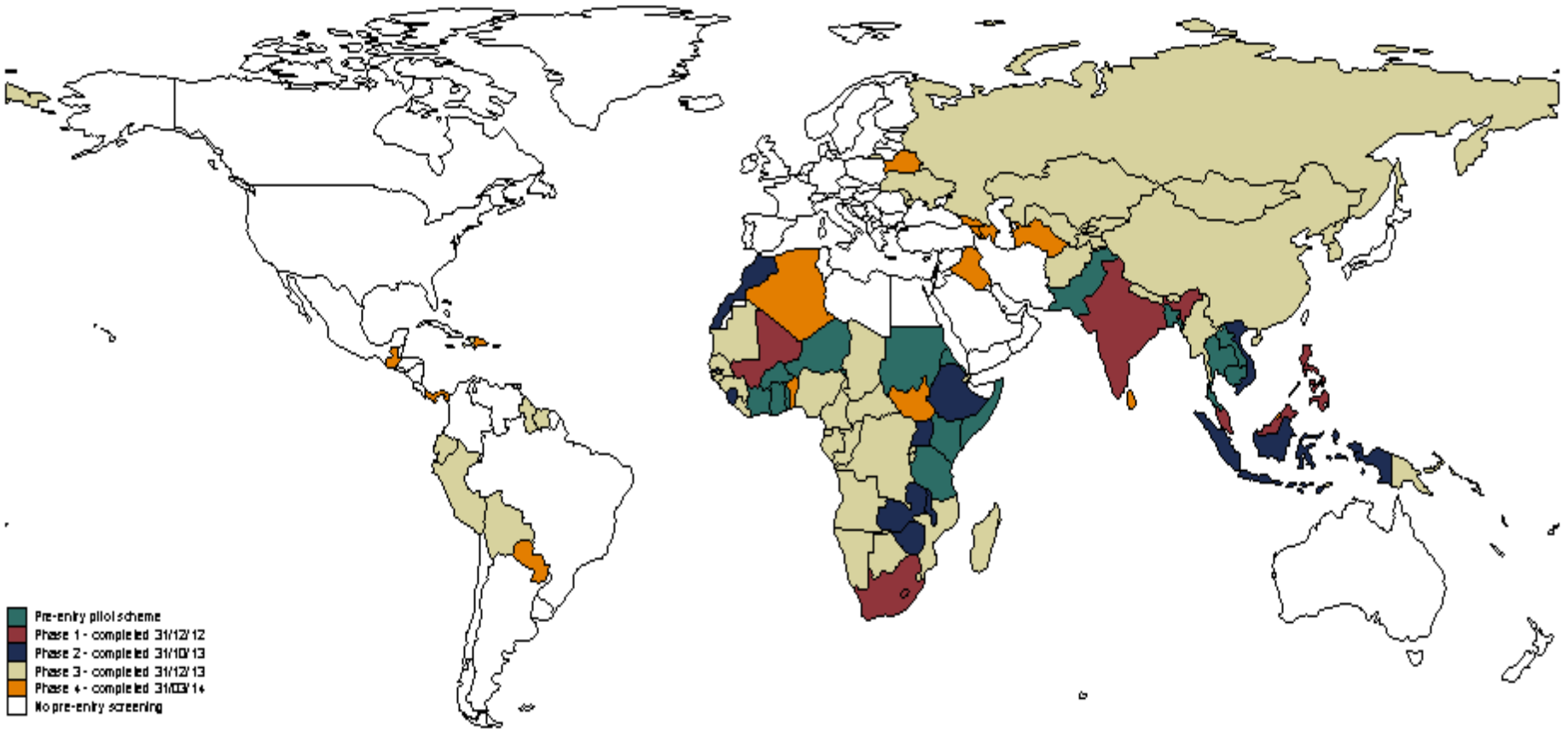
Pre-entry screening

Visa applicants who intend to stay in the UK for longer than six months and who reside in a high TB incidence country (>40/100,000), are required to take part in the UK pre-entry TB screening programme. This is mandated by the UK Immigration Act 1971, paragraph 2(2), schedule 2 [5] and was based on a successful pilot jointly carried out by the Home Office and the International Organisation for Migration (IOM). This pilot took place 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 programme was globally rolled out by March 2014 to 101 countries [6,7] with World Health Organization (WHO)

estimated TB incidence >40 per 100,000 population for 2012 [8] (Figure 1). TB pre-entry screening is now carried out by both the IOM and non-IOM panel physicians.

The UK TB pre-entry screening programme reflects the screening programmes used by other countries. Most notably, the UK partners with countries from the Migration-5: 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 [9]. Applicants with pulmonary TB are required to successfully complete treatment before they can proceed with visa application.

Figure 1: Map of the countries in the UK pre-entry screening programme and the phase in which each country joined



2. Methods

Data collection

This report presents data collected from IOM and non-IOM clinics. IOM data was collected by IOM panel physicians, entered via a secure web-based IOM system and collated by the central IOM office in Manila. This data was then 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. During 2017, the TB screening team conducted an audit of culture updates from all non-IOM clinics for the period between 2012 and 2017. Clinics were required to provide the clinical details of all patients that had culture confirmed TB during this time period. We received complete culture updates from 63% (107/170) of clinics, including all the high throughput clinics. This increased the number of culture confirmed cases and included cases not originally identified by screening. This report focuses on the 2017 data but also provides overall trends using data from 2006 from this programme. Comparisons between years and geographical areas may be affected by the roll-out process and policy changes. The data trends presented this year have taken into account the updated case numbers following the sputum culture updates from non-IOM providers for the years 2012 to 2017.

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 2017 and non-IOM providers between September 2012 and December 2017. Data up to 31 December 2017, as received by 1 May 2018, was included in this report.

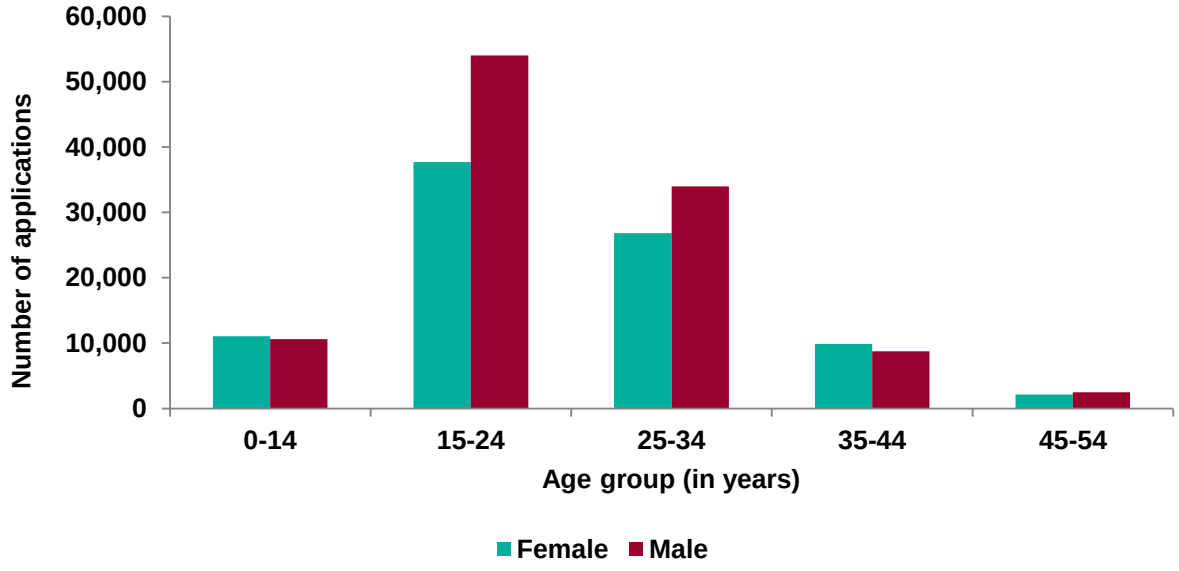
3. Demographics of all applicants

Pre-entry screening data for 2017 was available for 255,510 UK visa applicants. Screening by non-IOM clinics accounted for 62.8% (160,466 / 255,510) of applicants and 37.2% (95,044 / 255,510) by IOM clinics. Data from non-IOM and IOM clinics is presented together throughout this chapter, except where noted otherwise.

Age and sex distribution of all applicants

Information on age and sex was available for all applicants screened in IOM clinics, but missing for 33.3% (53,499 / 160,466) of non-IOM applicants. 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 (45.5%, 91,864 / 202,011), followed by the 25 to 34 year group (31.7%, 60,953 / 201,011). Only 4.3% (8,763 / 201,011) of the applicants were aged 45 years and over (Figure 2). There were more female applicants in all age groups except the 0-14 and 35-44 years age groups.

Figure 2: Distribution of all applicants by age group and sex, 2017



Distribution of all applicants by screening provider, country and region

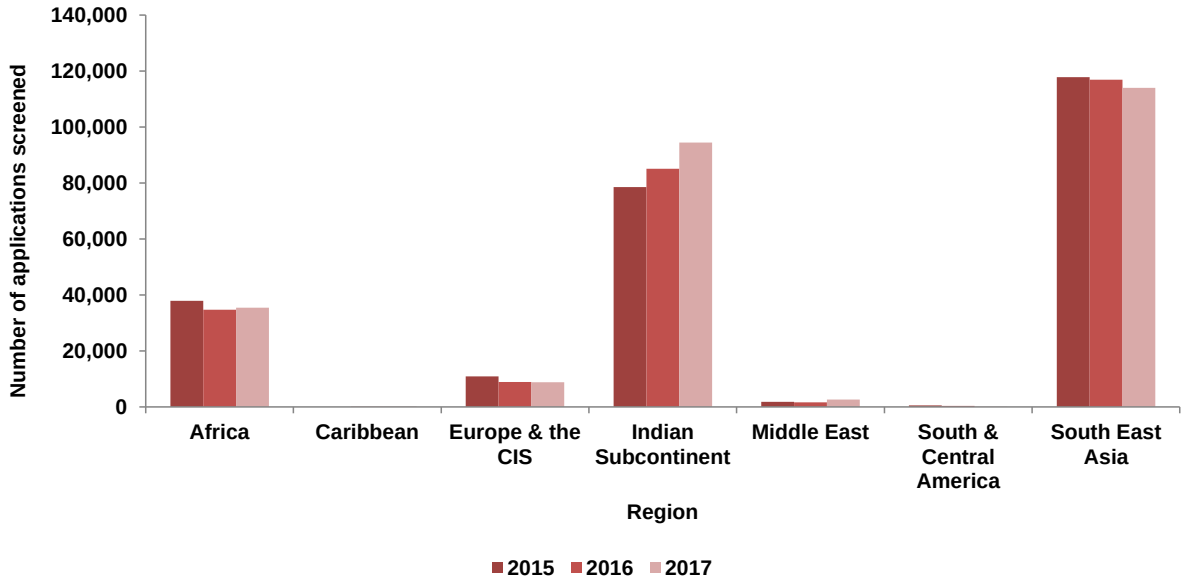
As of 31 March 2014, screening was being conducted in approved clinics in 67 countries on behalf of 101 countries. Some countries do not have screening clinics and applicants are screened in neighbouring countries. For example applicants from Somali are screened in Kenya. Data was available for 86 out of the 101 countries in 2017. We

estimate that the remaining 15 countries from which data was missing screened only 0.4% (1,017 / 255,510) of the total UK visa applicants received for 2017 [10].

Of the applications that underwent screening in 2017, almost half of recorded screens [44.6% (114,014 / 255,510)] took place in South East Asia. A third [33.1% (84,559 / 255,510) were screened in China and just over a third (36.9% (94,403 / 255,510) of applicants were from the Indian subcontinent. 14.0% (35,410 / 255,510)] were from Africa and a small number of applicants were from Europe and the Commonwealth of Independent States[1] [CIS; (3.5% (8,847 / 255,510)], Middle East [1.0% (2,632 / 255,510) and the Carribean [0.1% (143 / 255,510)]. 60 applicants were from the South & Central America.

The number of applicants by region between 2015 and 2017 is shown in figure 3. The number of applicants from Africa and Europe and the CIS reduced by 6.5% and 18.8% repectively between 2015 and 2017. By contrast, applicants from the Indian subcontinent and the Middle East increased by 20.2% and 44.4%, repectively, over the same period. The number of applicants from South East Asia was stable with only a modest decrease of 3.2% between 2015 and 2017. The number of applicants from the Carribean and South and Central America remained low over the same period. Regional distribution of TB screening largely reflects overall migration trends to the UK.

Figure 3: Number of applicants by region for the last 3 years, 2015-2017*



* Data for from some non-IOM providers was missing

[1] Europe and CIS includes data from: Belarus, Kazakhstan, Moldova, Russia and the Ukraine.

4. Diagnostic tests and case detection

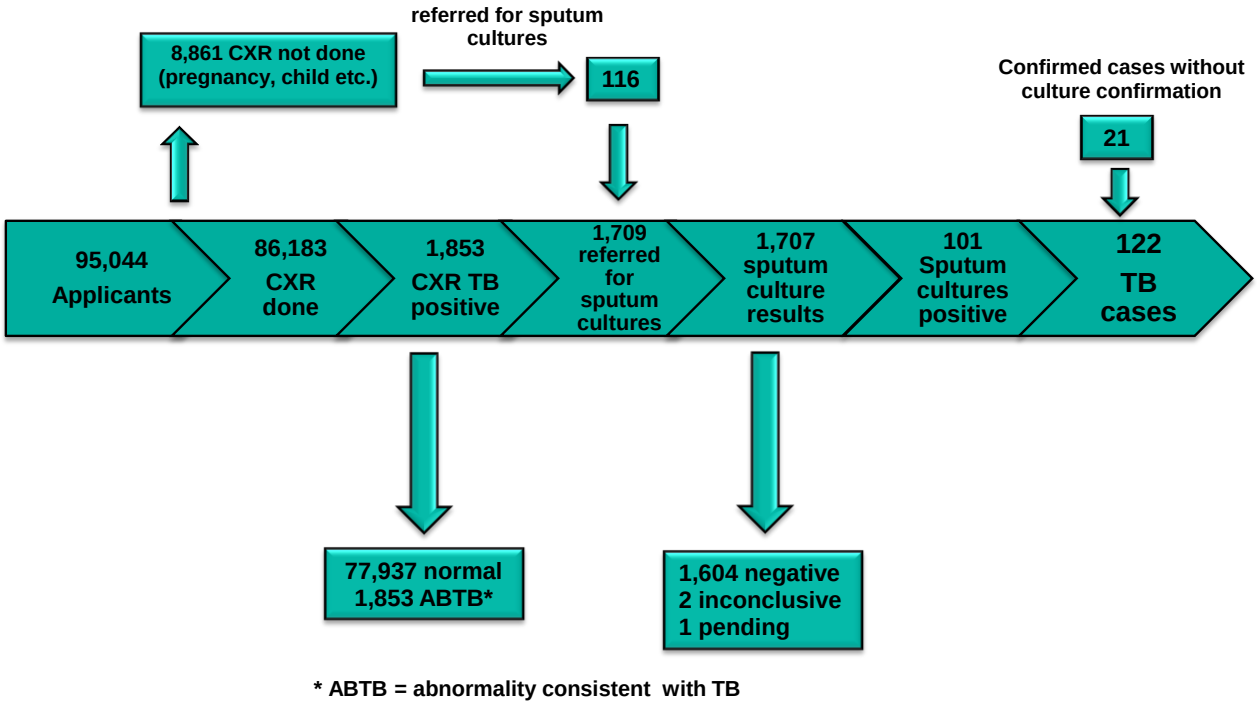
Due to the issues in data quality received from non-IOM clinics, the following paragraphs and flow-chart (Figure 4) are restricted to IOM data only. Non-IOM data quality issues include missing data for applicant flows and missing data on sputum culture results (3.8%, 6,168 / 160,466).

Chest X-Rays (CXR)

Of the 95,044 applicants from IOM, 86,183 (90.7%) had a CXR taken (Figure 4). Reasons for not obtaining a CXR were known for 8,853 (99.9%) of the 8,861 individuals where CXRs were not done. A total of 114 people did not have a CXR because they were pregnant and 8,739 were children under 11 years old.

Of the 86,183 individuals that had CXR examinations, 90.4% (77,937 / 86,183) had normal CXR and 2.2% (1,853 / 86,183) individuals had abnormalities that were consistent with TB. The total number of sputum cultures results available was 1,707 including the 116 that didn't undergo chest x-ray screening because they were pregnant (114) and 2 with suspected pregnacies. Only one sputum culture result was pending at the time of writing. Of the 1,707, 101 cases were culture confirmed and an additional 21 applicants were diagnosed according to the clinical case definition (see Appendix 7.1). All of these 122 TB cases were not issued with clearance certificates and were instead referred for TB treatment. Twenty of the 21 clinically diagnosed cases had TB-related CXR changes. Including the 101 culture confirmed cases, the total number of TB cases diagnosed by IOM was 122; this represents a increase of 27.1% from 2016 (n=96). Of the remaining 146 cases with abnormalities consistent with TB, two were among the clinically diagnosed cases but 143 were classified as old TB.

Figure 4: Flow-through of IOM data, January to December 2017



Sputum tests

The UK tuberculosis technical instructions (UKTBTI) mandate sputum culture for the diagnosis of active TB because of the low sensitivity of smears [9]. For this reason, sputum smear results are not included in Figure 4.

For CXRs with TB-related abnormalities, the UK Technical Instructions [9] require three sputum samples to be submitted for smear and culture.

a. Sputum smears and cultures

Of the 1,705 individuals who had sputum smear results, 1.7% (29/1,705) were smear positive and 0.1% (1/1,705) were inconclusive. The majority [98.2% (1,675/1,705)] were sputum smear negative. All individuals with positive sputum smears had undergone CXR examination first (Table 1).

Overall, 5.9% (101/1,707) of visa applicants with sputum cultures tested positive for *Mycobacterium tuberculosis complex* in 2017. The majority [94.0% (1,604/1,707)] were

negative and one gave inconclusive results. 81 individuals (82.2%, 81/101) were smear negative but culture positive and would not have been detected by screening under the previous protocol (Table 1). Twenty individuals were culture and smear positive while nine individuals were smear positive but culture negative.

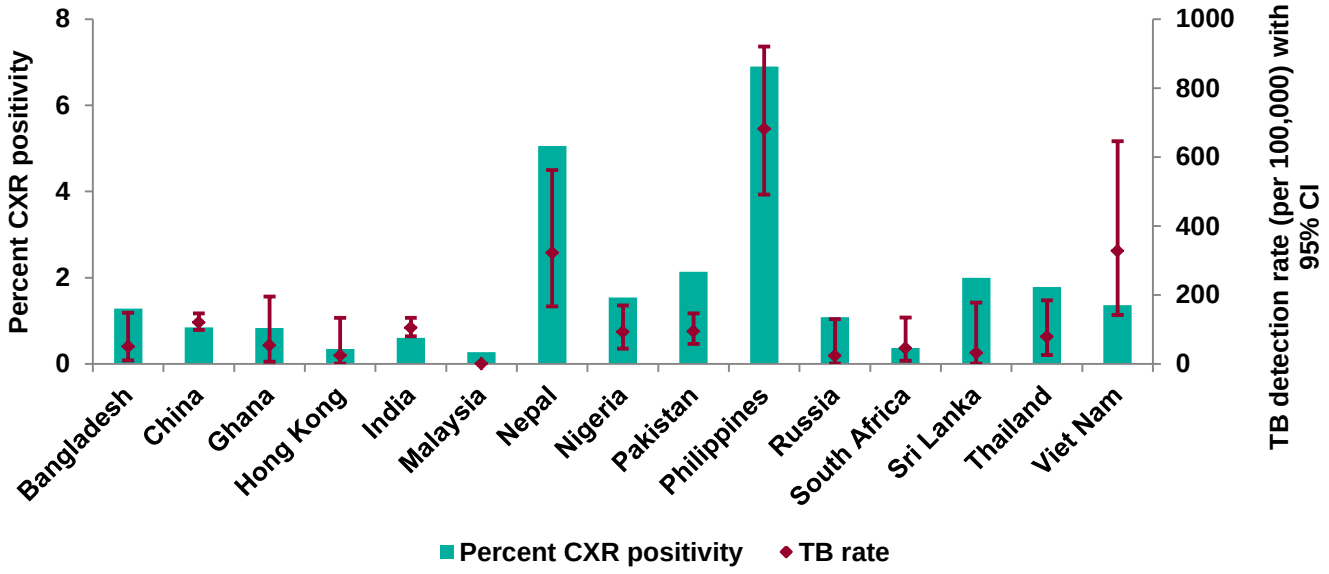
Table 1: Sputum smears and culture test results for individuals tested between January and December 2017 by IOM clinics.

Sputum test	Smear [n, (%)]	Culture [n, (%)]
Negative	1,675 (98.1)	1,604 (93.9)
Positive	29 (1.7)	101 (5.9)
Inconclusive	1 (0.1)	2 (0.1)
Pending	1 (0.1)	1 (0.1)
Total	1,706 (100.0)	1,708 (100.0)

Descriptive analysis of CXR and sputum test positivity by country

Figure 5 shows the the proportion of positive CXRs and the TB detection rate for top 15 throughput countries which screened more than 2,400 applicants in 2017. There was no consistent relationship 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 applicants' TB detection rate by country, January to December 2017*

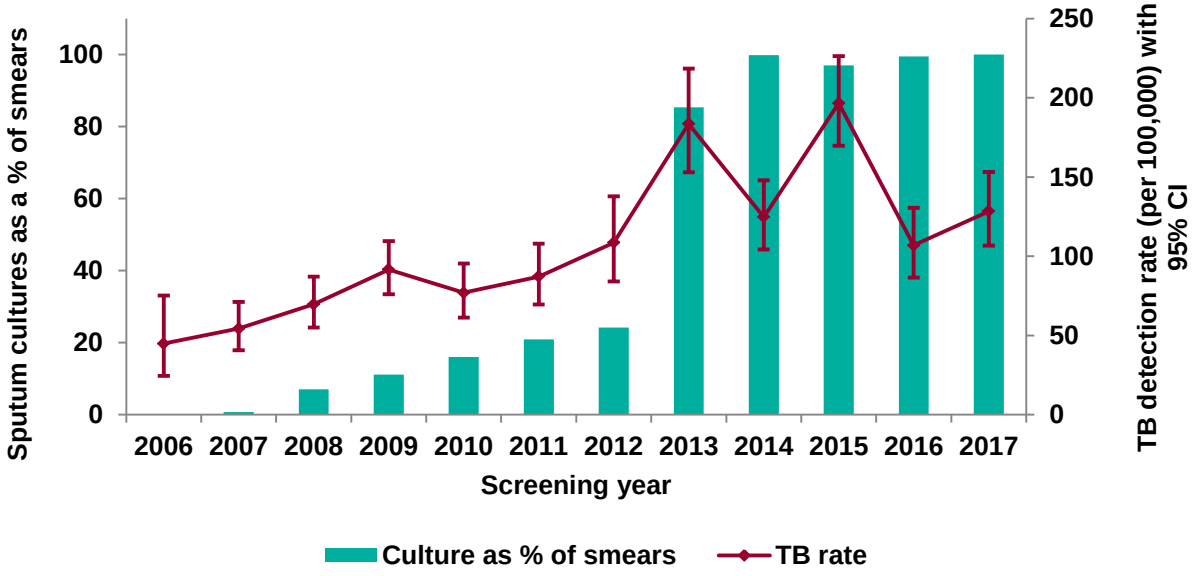


*For countries which had screened more the 2,400 applicants.

Sputum cultures as a proportion of sputum smears by year

The ratio of sputum cultures to smears, a measure of the extent to which the culture confirmation policy of UKTBTIs is adhered to, has increased significantly over the years. Figure 6 shows this proportion and the yearly TB rates from IOM clinics. There has been a significant increase in TB detection over the years (chi-square for trends $p<0.001$) between 2006 and 2017. Increasing TB detection rates during this period may in part be explained by the increasing use of sputum cultures taken (Figure 6). There was a decrease in the number of cases detected in 2016 despite a good sputum culture to smear ratio but an increase was observed in 2017.

Figure 6: IOM sputum cultures as a proportion of sputum smears[$] by screening year



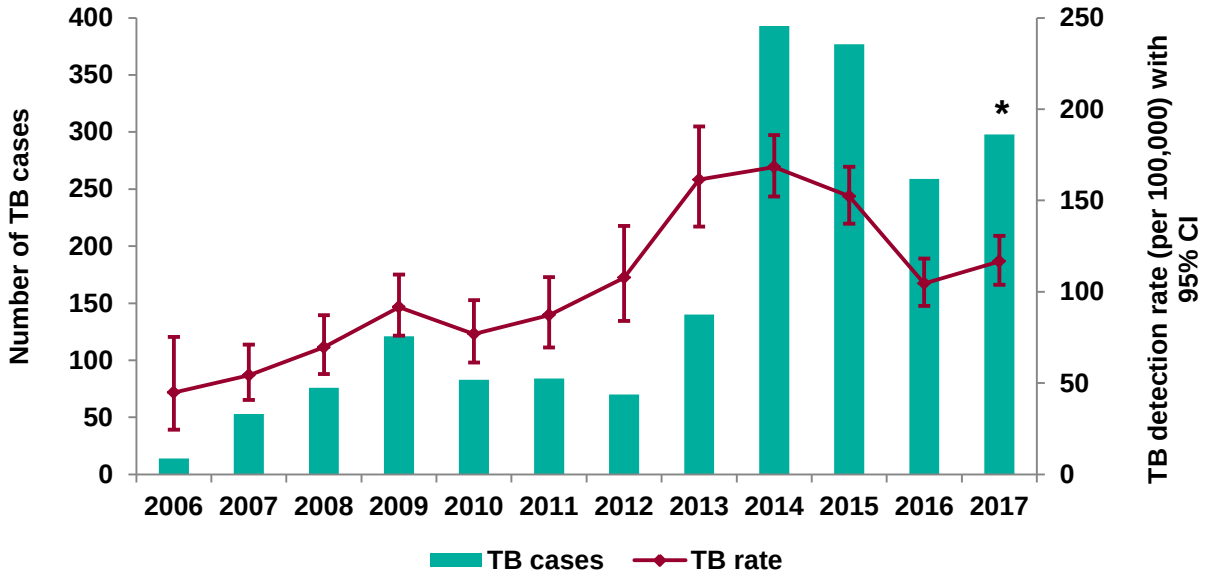
[$]As a proxy for proportion of cultures in amongst all sputum tests done

Descriptive analysis of TB cases

In 2017, 298 cases of active TB were detected and notified through the entire screening programme (IOM and non-IOM), giving an overall tuberculosis yield of 116.6 per 100,000 visa applicants. 59.1% of the cases (176/298) were reported from non-IOM clinics. The TB detection rate in IOM clinics was higher than that in non-IOM clinics (128.4 (95%CI 106.7-153.3 versus 109.7 (95% CI 94.1-127.1 per 100,000). As of 1 May 2018, a total of 794 sputum culture results from 2017 were still pending (compared to 759 in 2016) and the number of cases may increase when these are available. Figure 7 shows the number of TB cases and detection rates by year of screening. TB detection rates increased significantly between 2006 and 2014, then decreased in 2016 and increased again in 2017.

Females accounted for 58.3% (126/216) of all the TB cases in 2017 where sex was known. The TB rates were slightly higher in females compared to males (112.3 and 100.5 per 100,000, respectively).The sex distribution of 2017 applicants was similar compared with 2016 (55.6% & 56.3% females, respectively). Figure 8 shows TB detection rates by age group for the years 2015, 2016 and 2017. The highest case detection rates occurred among the oldest age group (≥55 years).

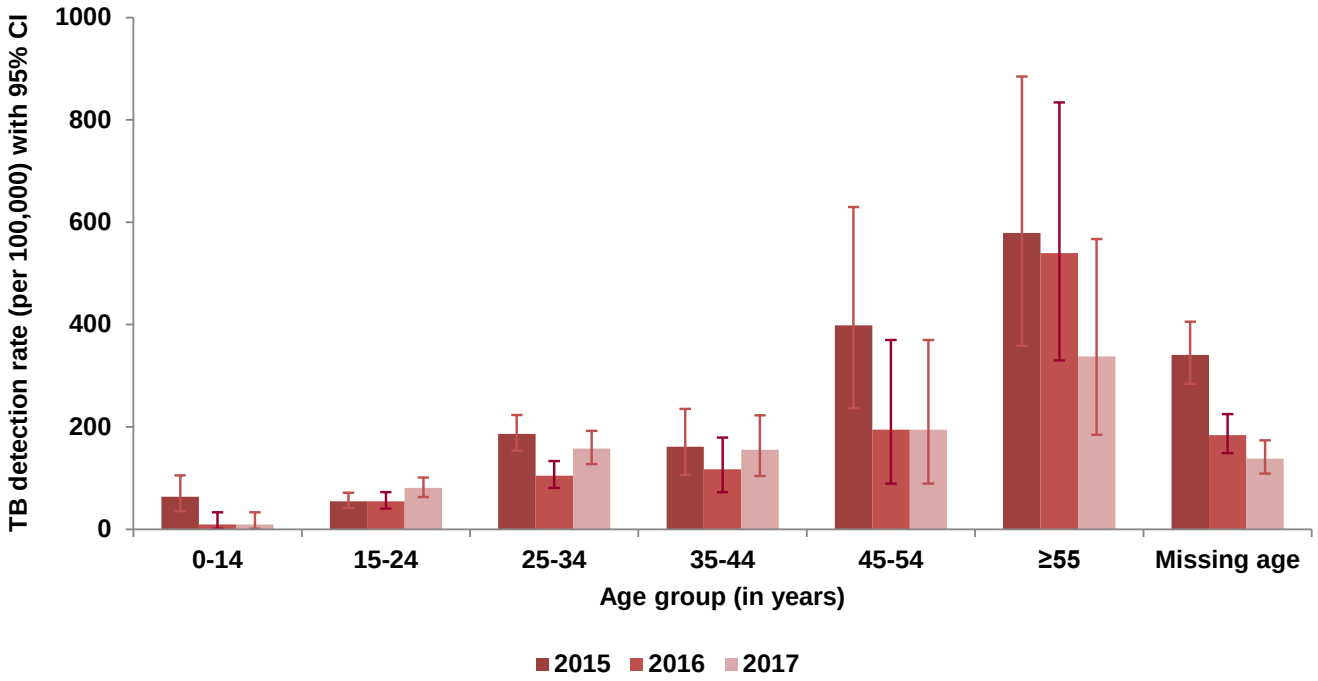
Figure 7: Annual number of TB cases and detection rates, January 2006 to December 2017



*As of 1 May 2017, 794 sputum culture results were pending and the rate may increase when final results are available.

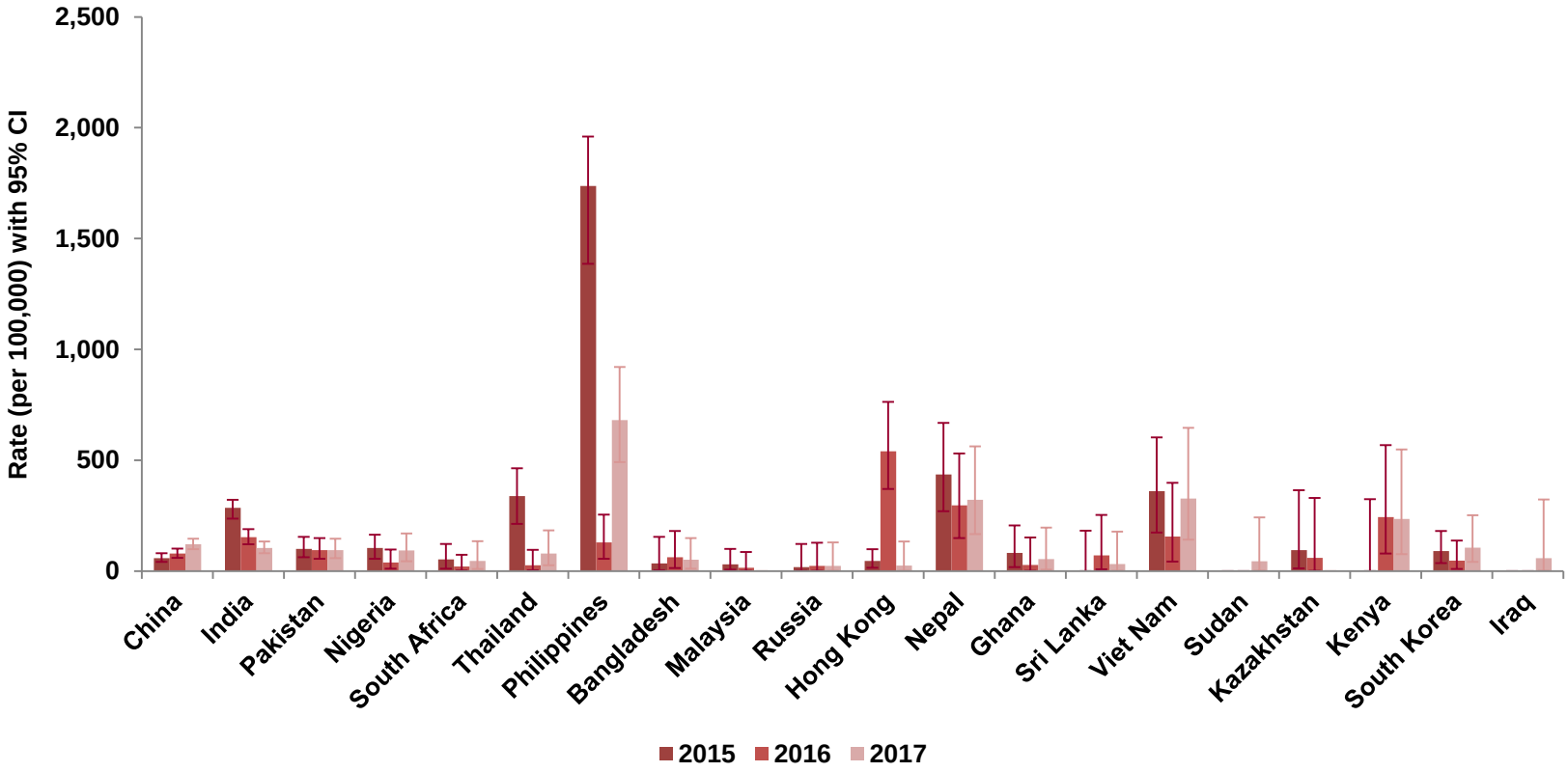
Figure 8 shows that the TB rates were stable in all age groups except for those aged 0-14 and age groups over 45 which decreased between 2015 and 2017.

Figure 8: TB detection rates by age group by year, 2015-2017



The TB detection rates (with 95% CI) between 2015 and 2017 in 20 countries with the highest throughput are shown in figure 9. The TB rates were stable in most countries with non-significant changes in the period 2015 to 2017. However, significant changes were observed in India, Philippines, Thailand and Hong Kong. The fluctuations in rates affected both IOM and non IOM providers. IOM cases increased by 27.1% from 96 in 2016 to 122 in 2017 and non-IOM cases by 8.0% from 163 in 2016 to 176 in 2017.

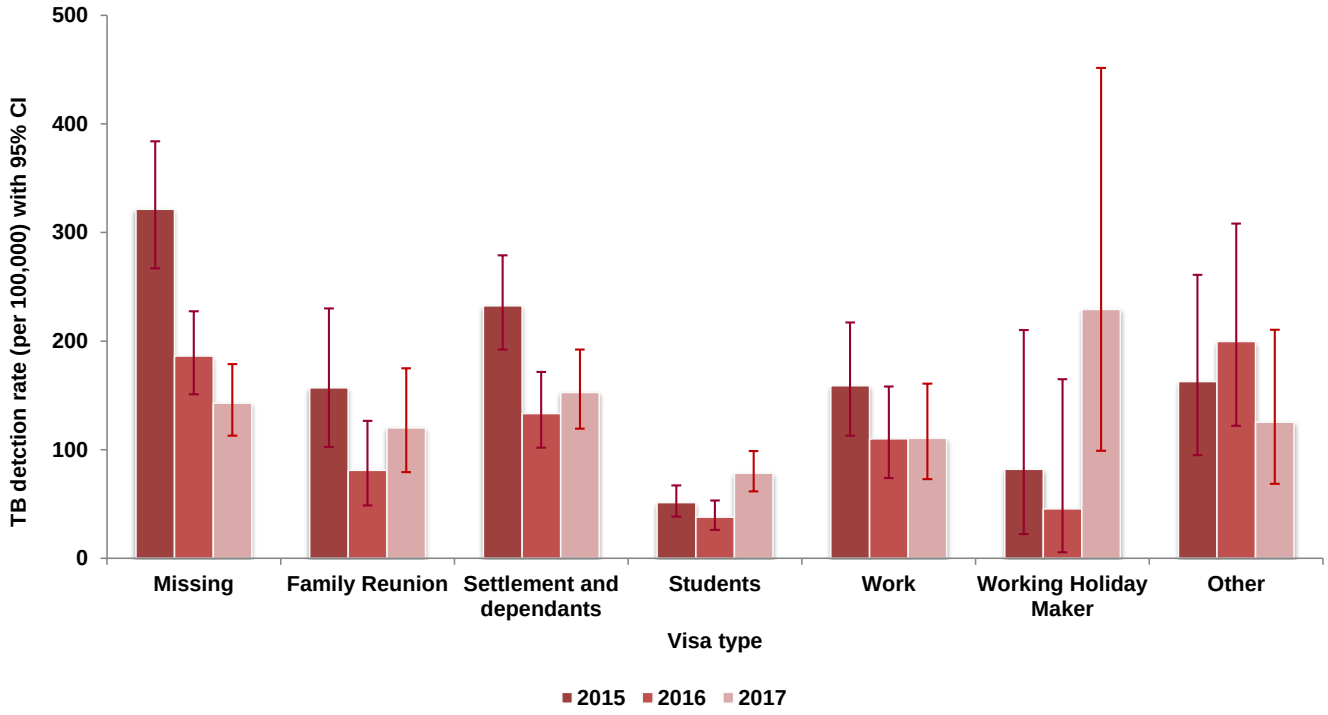
Figure 9: TB detection rates in the 20 countries with the largest number of applicants for years 2015-2017.



*As of 1 May 2017, 794 sputum samples are pending and the rates for 2017 may increase when final results are available.

TB detection rates by visa category for years 2015 to 2017 are shown in figure 10. For the cases that visa category was known, there were decreases in detection rates between 2015 and 2016 for “Family Reunion”, “Students”, “Settlements and dependants” and “Working Holiday Maker” with varying increases in rates in 2017. For those applying for “Work” visas, the detection rates decreased bween 2015 and 2016 but were stable between 2016 and 2017. Under the “Other” visa category, the detection rate increased between 2015 and 2016 but decreased in 2017 (Figure 10).

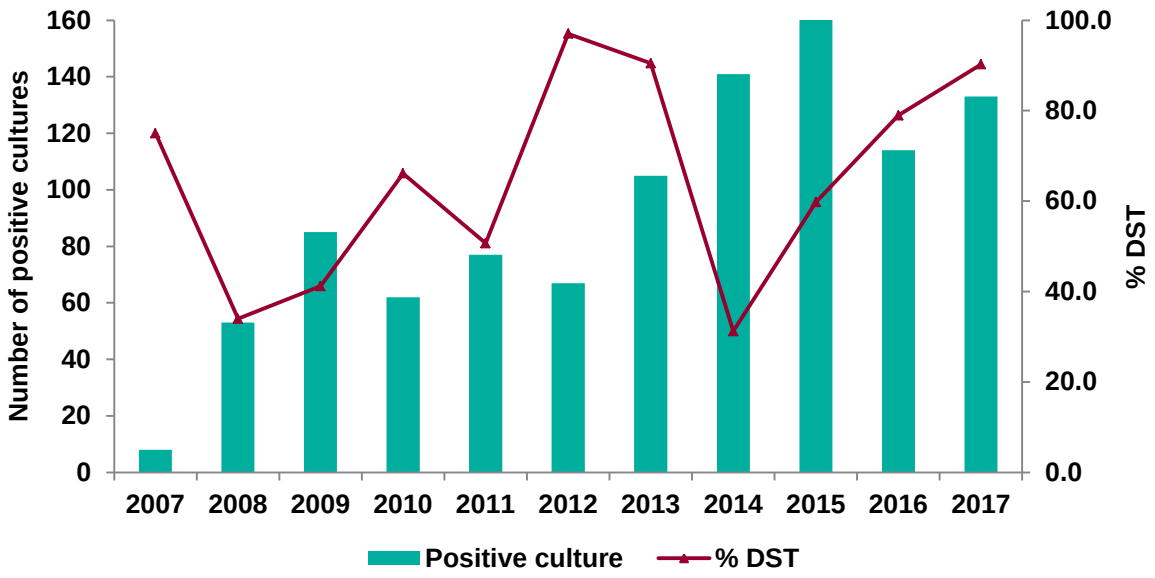
Figure 10: TB detection rates by applicant visa type, 2015-2017.



Drug susceptibility testing of positive TB cultures

TB culture and drug sucepitibility testing (DST) is a mandatory requirement under the UKTBTIs, and important to allow appropriate treatment for TB cases. Figure 11 shows the number of positive sputum cultures and the proportion that have had DST performed. The proportion of cultures with DST ranged between 33.3% and 100% and there was no linear increase.

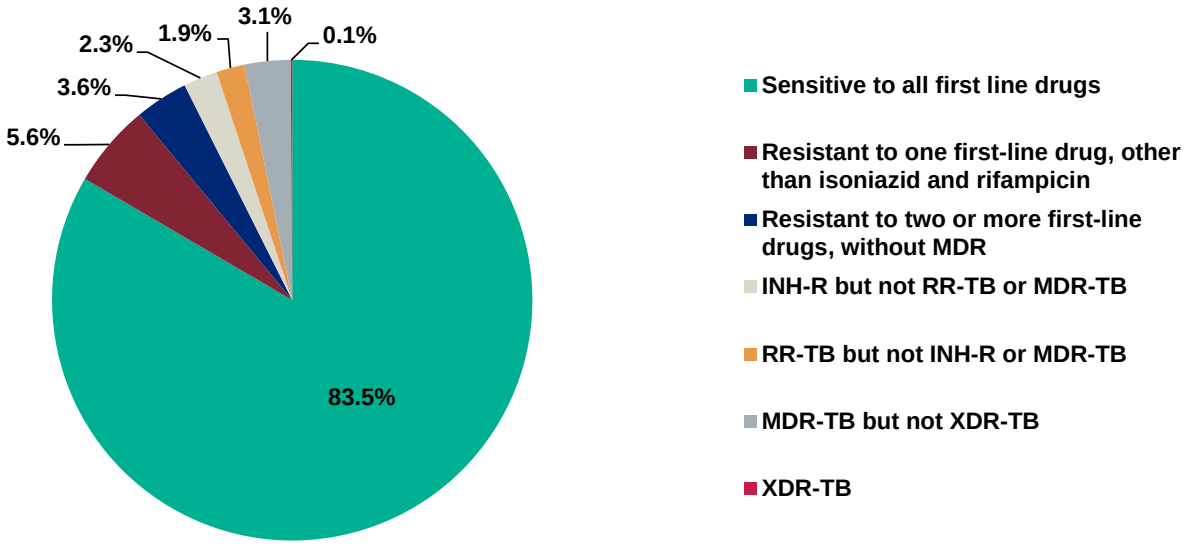
Figure 11: Trends in drug susceptibility testing, 2007 to 2017*



*The graph partially reflects low but increasing drug sensitivity testing as it was rolled out among IOM clinics (2007 to 2011) and low drug sensitivity testing among non-IOM clinics (2012 to 2017).

Figure 12 summarises the overall DST for both IOM and non-IOM providers' results between 2007 and 2017. During this period the majority of TB cultures were sensitive to all first-line drugs [83.5% (586/702)]. Of the 16.5% with drug resistance, 2.3% (16/702) had isoniazid monoresistance and 3.6% (25/702) were classified as poly-drug resistant (resistant to two or more first-line drugs, but not MDR). Twenty-two [3.1% (22/702)] multi-drug resistant TB (MDR) and one [0.1% (1/702) extensively-drug resistant (XDR) TB case were detected. Rifampicin monoresistance (RR-TB) was detected in 13 cultures (1.9%) and a further 39 cultures (5.6%) showed monoresistance to one of the other three first-line drugs (ethambutol, pyrazinamide and streptomycin). Drug susceptibility terms are defined in the Appendix 7.2.

Figure 12: Summary of drug susceptibility patterns for the 702 positive TB cultures, 2007 to 2017

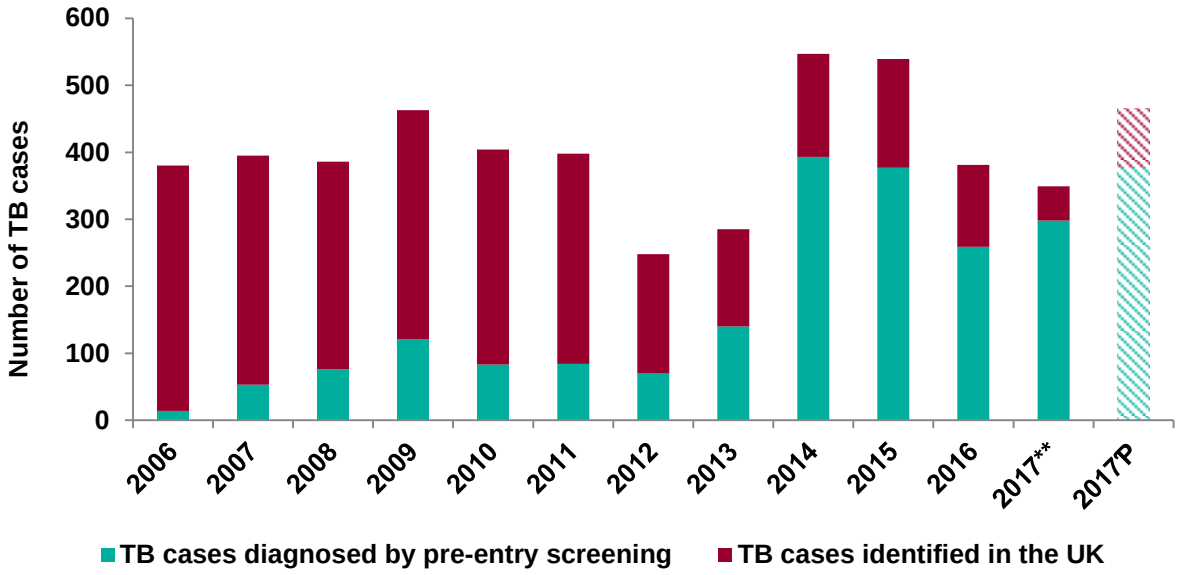


XDR= Extensively drug resistance, MDR=Multiple drug resistance, INH=Isoniazid & RIF=Rifampicin.

Comparison of screening yields between ETS and pre-entry screening data

Overall, TB numbers detected through the pre-entry TB screening programme increased significantly from 14 in 2006 to 393 in 2014, then decreased to 259 in 2016 and increased again to 298 in 2017. 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 [10] in the screening programme decreased from 416 in 2006 to 84 in 2017 (figure 13). 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 [4].

Figure 13: 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 2017[2]



*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 1 May 2018, 794 sputum culture results were pending and the number of cases may increase when final results are available.

ᴾProjected number of TB cases detected based on pending sputum samples (pre-entry screening) and lag in detection for final year in graph for ETS cases.

[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 report is the fifth annual report and it presents data from the UK TB pre-entry screening programme until the end of 2017. This year represents the third year of operation since full roll out among 101 countries.

For the last few years, the screening throughput has remained stable at about a quarter million assessments annually, and the demography of applicants, a relatively young cohort with a slight female preponderance, has also remained similar.There is, however a marked change in the geographical distribution of applications with an increase of applicants from China and India and a decrease in applicants from South East Asia and Sub-Saharan Africa. Most visa applicants continue to be young adults (often students).

In 2017, 298 TB cases were detected in the pre-entry screening programme – a detection rate of 116.6 per 100,000. This is an increase from 2016 which had a case detection rate of 104.6 per 100,000 with 259 cases. Case numbers and detection rates were fairly high among people from the Indian subcontinent and South East Asia and numbers and rates were lower in sub-Saharan Africa. The increase in rates and numbers in 2017 was mainly due to increased cases detected in South and South East Asia and in Africa.

For the first time, we also report on drug resistance data for the entire programme (IOM and non-IOM) for the period 2007 to 2017. The majority of the people with culture confirmed TB were sensitive to all first-line drugs (83.5%, 586/702), 2.3% (16/702) were isoniazid resistant, 1.9% (13/702) were rifampicin resistant, 3.1% (22/702) had multi-drug resistant TB and 0.1% (1/702) had extensively-drug resistant TB. The drug-resistant cohort is larger than the one reported through the domestic ETS and the early detection and treatment of drug resistant cases pre-departure may yield some benefits for domestic TB control in the UK.

Although data quality particularly in the non-IOM data remains of concern, significant improvements around data quality were made in 2017, including a culture confirmation audit leading to improved sputum culture results returns. This resulted in an additional identification of 83 culture confirmed TB cases between 2006 and 2017, and our data has been updated accordingly. We continue to closely collaborate and ensure significant teaching and training activities remotely and in person to support the ongoing quest of data quality improvement. More work remains to be done, particularly in low throughput areas, and further improvements are expected with the ongoing development of a global web-based data solution.

There was a 15% increase in the number of cases detected through pre-entry screening in 2017 compared to 2016. This is reassuring and could suggest that the drop in TB

cases identified in 2016 (which was universally affecting most global regions, many visa types and IOM as well as non-IOM clincs), may have been an isolated phenomenon. Although we received late notifications and culture updates from the culture confirmation audit, these data did not completely resolve the decrease. It is most likely that this decrease was a combination of the improved TB control and decreasing rates in many sender countries, as well as a change of the socioeconomic composition of UK-bound migrants.

In conclusion, our report shows that after successful roll out of pre-entry screening a number of significant improvements have been made, including near-universal sputum culture confirmation among IOM applicants [11-16], and improved procedures in non-IOM clinics. We have been able to better quantify this through our recent culture confirmation audit. Quality assurance has played an important role in ensuring successful and appropriate screening overseas. Notwithstanding the need for a multi-dimensional TB strategy for England [17], it is clear that pre-entry screening has an impact and the potential to reduce the number of prevalent cases notified in the UK. For the first time, we were recently able to quantify the approximate 11.4% contribution of pre-entry screening to the significant reductions of TB cases in the UK [4]. We could also demonstrate that pre-entry screening facilities, such as new laboratories can contribute to sender countries' capacity building [18] and therefore indirectly support the sustainable development goal 3 aim of universal health coverage [19, 20].

As in previous years, TB detection rates continue to vary significantly between countries and sites, different age groups and visa types. Further work is required to better understand these variations and to mitigate against modifiable risks within the system. We continue to sustain efforts in maintaining quality assurance. This includes panel physician training and outreach alongside well designed and relevant research work.

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7. Appendices

7.1 Case definition

Tuberculosis case definition

A TB case was defined as outlined in the enhanced (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

7.2. Definitions of drug susceptibility terms

Extensively-drug resistant TB (XDR TB)
Extensively-drug resistant is defined as resistance to isoniazid and rifampicin, 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 rifampicin, 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.