UK pre-entry tuberculosis screening report 2016
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Executive summary

Following a successful pilot, 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 and replaced on-entry screening at UK airports since March 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 2016. There has been considerable improvement in data quality and collection during this time, although data collection is still done manually in many countries and it is expected that it will be significantly improved by use of electronic data collection tools in the near future.

A total of 1,465,622 applications representing 1,314,828 individual applicants were screened between October 2005 and December 2016. In total, 247,780 applicants were screened in 2016. The median age of applicants for the entire period was 25.9 years (interquartile range 20.0-30.0 years) and the largest proportion of applicants were adolescents and young adults aged 15-34 years (74.1%, 984,799/1,329,588). The majority of applicants were male (55.5%). The largest screening volumes in 2016 were in China [29.3% (72,694/247,780)], India [22.0% (54,606/247,780)], Pakistan [7.7% (19,097/247,780)] and Nigeria [4.2% (10,513/247,780)] reflecting current migration trends, showing a decrease in migrants from the Indian subcontinent and an increase in Chinese migrants.

In total, 249 TB cases were detected in 2016, giving an overall TB yield of 100.5 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, in keeping with increased use of sputum culture and improved overall quality of screening, but the number and rate decreased in the last year. The decrease affects many countries and affects cases with and without culture confirmation similarly. In 2016, the TB detection rates were highest in the Indian subcontinent [128.0 per 100,000 (95% CI 105.1 – 154.5)] and lowest in Europe and the Commonwealth of Independent States (CIS) [33.5 per 100,000 (95%CI 6.9 – 98.0)]. No cases were detected in the Caribbean, South and Central America and the Middle East although there were low numbers of applicants screened in these regions. The TB screening yields of most countries were within the ranges which would be expected from within 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, with reasonable TB yields which have overall increased over time albeit with a decrease last year.
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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 but have then levelled off and more recently decreased by about one third from a peak in 2011. However, the incidence is still the second highest in Western Europe [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. In 2015, 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 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. We now report on the second full year since roll out was completed on 31st March 2014.

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 the UK Immigration Act 1971, paragraph 2(2), schedule 2 [4] and was based on a successful pilot 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) and globally rolled out by March 2014 to 101 countries with World Health Organization (WHO) estimated TB incidence ≥ 40 per 100,000 population for 2012 [5] (Figure 1). TB pre-entry screening is now carried out by both the IOM and non-IOM panel physicians.

The TB pre-entry screening programme was informed by and has close similarities with other countries TB pre-entry screening approaches, most notably those used by partner countries from the Migration-5 (M5): 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 with pulmonary TB are required to successfully complete treatment before they can proceed with visa application.
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 an eleven-year period (2005–2016); comparisons between years and geographical areas may be affected by the roll-out process and policy changes. The report focuses on the 2016 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 2016 and non-IOM providers between September 2012 and December 2016. Data up to 31 December 2016, as received by 10 June 2017, was included in this report.
3. Demographics of all applicants

In 2016, data was available from a total of 247,780 UK visa applicants. Of these 63.7% (157,936/247,780) were screened by non-IOM and 36.3% (89,844/247,780) by IOM clinics. This chapter provides data on all applicants (IOM and non-IOM), 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 32.7% (51,692/157,936) of non-IOM applicants. Of all applicants screened and where data was available, the median age for applicants was 24 years and the largest number of applicants was in the 15 to 24 year age group (43.9%, 86,032/196,088), followed by the 25 to 34 year group (31.7%, 62,159/196,088). Only 4.3% (8,322/196,088) 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). These observations are similar compared with last year.

Figure 2: Distribution of all applicants by age group and sex, 2016

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. In 2016, data was available from 60 out of 71 countries, a slight improvement
from 2015 when 58 countries provided data. We estimate that the remaining 11 countries from which data was missing screened only 0.4% (1,270/283,402) of the total number of persons entering the UK who applied for visas and would have undergone TB screening [8].

In 2016, more than half of all recorded screens [46.9% (116,168/247,780)] took place in South East Asia and almost one third [29.3% (72,694/247,780) were screened in China. Just over a third (34.4% (85,179/247,780) of applicants were from the Indian subcontinent and 14.1% (34,801/247,780)] were from Africa. Only a small number of applicants were from Europe and the Commonwealth of Independent States\(^1\) [CIS; (3.6% (8,949/247,780)], Middle East [1.0% (2,345/247,780) and South and Central America [0.2% (389/247,780)]. Only 14 applicants were from the Caribbean.

Figure 3 shows that number of applicants reduced by 4.3% and 1.2% between 2014 and 2015 from Africa and Europe & the CIS respectively. By contrast, the number of applications increased by 14.2% and 15.8% over the same period for South East Asia and the Indian subcontinent respectively. Between 2015 and 2016, the number of applicants decreased by 8.5%, 12.9% and 22.6% for applicants from Africa, South East Asia and Europe & the CIS but increased by 21.1% for applicants from the Indian Subcontinent. Regional distribution of TB screening largely reflects overall migration trends to the UK.

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

There are significant data quality issues in non-IOM clinics including missing data for some of the items needed to present the applicant flows below, including the missing data on CXRs (3.6%, 5,689/157,936). Therefore, the following paragraphs and flowchart (Figure 4) are restricted to IOM data only.

Chest X-Rays (CXR)

The TB screening flowchart (Figure 4) shows that out of 89,844 applicants from IOM clinics, 81,264 (90.5%) had a CXR taken. Reasons for not obtaining a CXR were known for 8,574 (99.9%) of the 8,580 individuals where CXRs were not done. A total of 114 did not have a CXR because they were pregnant and 8,460 were children under 11 years old.

Of the 81,264 individuals that had CXR examinations, 91.5% (74,326/81,264) had normal CXR and 1.9% (1,542/81,264) individuals had abnormalities that were consistent with TB-related abnormalities. The total number of sputum cultures results available was 1,424 including the 108 that didn’t undergo chest x-ray screening. At least 226 sputum results were still pending at the time of writing. Of these 82 cases were culture confirmed and an additional 14 applicants were diagnosed according to the clinical case definition (See 7.1) and were not issued with clearance certificates but were referred for TB treatment. All 14 clinically diagnosed cases had TB-related CXR changes. Including the 82 culture confirmed cases, the total number of TB cases was 96; this represents a decrease of 54.1% (from 209 in 2015).
Sputum tests

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

Sputum cultures are mandatory according to the UKTIs because of the low sensitivity of smears [9]. For this reason, sputum smear results are not included in figure 4.

a. Sputum smears and cultures

Of the 1,432 individuals who had sputum smear results, 2.5% (36/1,432) were positive and 0.1% (2/1,432) were inconclusive. The majority [97.3% (1,394/1,432)] were sputum smear negative. All individuals with positive sputum smears had undergone CXR examination first (Table 1).

Overall, 5.8% (82/1,424) of visa applicants with sputum cultures tested positive for *Mycobacterium tuberculosis complex* in 2016. The majority [94.2% (1,341/1,424)] were negative and 1 gave inconclusive results.
61 individuals (74.4%, 61/82) were smear negative but culture positive and would not have been detected by screening under the previous protocol (Table 1). 21 individuals were culture and smear positive while 15 individuals were smear positive but culture negative.

Table 1: Sputum smears and culture test results for individuals tested between January and December 2016 by IOM clinics.

<table>
<thead>
<tr>
<th>Sputum test</th>
<th>Smear [n, (%)]</th>
<th>Culture [n, (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>1,394 (97.3)</td>
<td>1,341 (94.2)</td>
</tr>
<tr>
<td>Positive</td>
<td>36 (2.5)</td>
<td>82 (5.2)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>2 (0.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Total</td>
<td>1,432 (100.0)</td>
<td>1,424 (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 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 2016*

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

The ratio of sputum cultures to smears (a measure for the extent to which UKTIIs are adhered to) 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 $p<0.001$) between 2006 and 2015. 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.

Figure 6: Sputum cultures as a proportion of sputum smears$^\text{§}$ by screening year (IOM data only)

$^\text{§}$As a proxy for the proportion of cultures amongst all sputum tests done.

Descriptive analysis of TB cases

A total of 249 cases of TB were detected and notified through the entire screening programme (IOM and non-IOM) in 2016. Just over 60% of the cases [61.4% (153/249)] were reported from non-IOM clinics. As of 10th June 2017, a total of 759 sputum culture results were pending (compared to 513 last year) 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 2015, but a marked decrease was observed in 2016.

Of all the TB cases in 2016 where sex was known, 52.1% (75/144) were female though the TB rates were higher in males compared to females (89.5 and 75.7 per 100,000,
respectively. The 2016 data consisted of 56.3% females and 43.7% males; this distribution was similar to that of 2015. Figure 8 shows TB detection rates by age group for the years 2014, 2015 and 2016. The highest case detection rates occurred among the oldest age group (≥55 years).

**Figure 7: Annual number of TB cases and detection rates data, January 2006 to December 2016**

![Graph showing annual number of TB cases and detection rates](graph.png)

*As of 10 June 2017, 759 sputum culture results were pending and the rate may increase when final results are available.

Between 2014 and 2016, there was a year-on-year decrease in the TB detection rate among 0-14 year olds (Figure 8). For 15-24 year olds, TB rates decreased significantly from 158.6 per 100,000 to 54.2 per 100,000 between 2014 and 2015 but rates were similar between 2015 and 2016 (54.2 versus 54.6 per 100,000). TB detection rates for age groups 25-34 and 35-44 years increased significantly between 2014 and 2015 but decreased between 2015 and 2016. The rates for the higher age groups (45-54 and 55 and above years) also increased significantly between 2014 and 2015 before decreasing between 2015 and 2016 (Figure 8).
Figure 8: TB detection rates by age group by year, 2014-2016

Figure 9 shows the TB detection rates (with 95% CI) between 2014 and 2016 in 20 countries with the highest throughput. The rates in 2016 were lower than those of 2015 for almost all large throughput countries but the decrease was significant only in India and the Philippines. The decrease in cases detected affected both IOM and non-IOM providers. IOM cases decreased by 54.1% from 209 in 2015 to 96 in 2016 and non-IOM cases by 11.6% from 173 in 2015 to 153 in 2016.
Figure 9: TB detection rates in the 20 countries with the largest number of applicants for years 2014-2016.

*As of 10th June 2017, 759 sputum samples are pending and the rates for 2016 may increase when final results are available.
Figure 10 shows TB detection rates by visa category for years 2014 to 2016. Among those with known visa category, there were decreases in detection rates between 2014 and 2015 for “Family Reunion”, “Students”, “Working Holiday Maker” and “Other”; with increase in detection rates for “Settlements and dependants” and “Work”. Between 2015 and 2016, there were decreases in detection rates for all visa categories. However, the only significant change was the decrease in TB detection rate amongst “Students” between 2014 and 2015 (Figure 10).

Figure 10: TB detection rates by applicant visa type, 2014-2016.
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 621 positive sputum cultures had drug susceptibility (DST) testing done between January 2007 and December 2016. Figure 11 shows the number of positive sputum cultures and the proportion that had DST performed. The proportion of cultures with DST ranged between 48.8% and 100% 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 11: Trends in drug susceptibility testing by IOM, 2007 to 2016**

![Graph showing trends in drug susceptibility testing by IOM, 2007 to 2016.](image)

Figure 12 summarises the overall DST results between 2007 and 2016. During this period the majority of TB cultures were sensitive to all first-line drugs [84.7% (526/621)]. Of the 15.3% with drug resistance, 8.7% (54/621) had isoniazid monoresistance and 3.2% (20/621) were classified as poly-drug resistant (resistant to two or more first-line drug, but not MDR). Eleven [1.8% (11/621)] multi-drug resistant TB (MDR) and one [0.2% (1/621)] extensively-drug resistant (XDR) TB case were detected in 2015. Rifampicin monoresistance (RR-TB) was detected in one culture (0.2%) and a further eight cultures (1.3%) showed monoresistance to one of the other three first-line drugs, most commonly isoniazid, ethambutol and pyrazinamide. There were two additional MDR cases, 8 additional cases of isoniazid resistance and 2 additional polydrug resistance strains detected in 2016. Drug susceptibility terms are defined in the Appendix 7.2.
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 382 in 2015, but there was a decrease to 249 in 2016. 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 also decreased from 380 in 2006 to 57 in 2016 (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.
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 2016²

*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 10th June 2017, 759 sputum culture results were pending and the number of cases may increase when final results are available.

²Projected number of TB cases detected based on pending sputum samples (per-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 is the fourth annual report of the pre-entry screening programme and reports on UK TB pre-entry screening activities and outcomes in the second full year since roll out until the end of 2016.

The screening throughput was similar compared with 2015, with just under 250,000 assessments. The demography, including age and sex of applicants was also similar. The geographical distribution of applications continues to change with an increase of applicants from China and India and a decrease in applicants from South East Asia and Sub-Saharan Africa. As in previous years, most visa applicants were young adults (often students) and for the second year running there were slightly more females than men.

A total of 249 TB cases were detected overseas – giving a detection rate of 100.5 per 100,000 a decrease from 382 cases (149.2 per 100,000). 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, however the decrease in 2016 is geographically widespread, including in South and South East Asia and in Africa. This report also provides data on drug resistance proportions detected between 2007 and 2016 among the IOM applicants, confirming any first-line drug resistance in 93 of 621 persons (15.0%) where culture results were available. Of these, eleven (1.8%) 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 2016, 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.

The reasons for the decrease in numbers and rates for 2016 are not clear. It affects IOM-led and non-IOM led clinics and culture confirmed and non-culture confirmed cases. It can be seen in most regions and countries, and affects all visa categories. Whilst we cannot entirely rule out ascertainment bias not least because of incomplete data from non-IOM providers (with more cultures pending than last year), it is unlikely that these changes can be explained by artefacts alone. There was no change in the case definition and the decrease in cases affect areas with good and less good data. This pattern is also reflected in culture and non-culture confirmed cases. It is possible that reduced screening quality or applicant-related behaviours may be contributing to case underascertainment at provider level. However, one would expect a more discreet
geographical distribution for these concerns. Nevertheless these factors may contribute to the picture and will be subject to further scrutiny of the data, for example through matching of pre-entry data to the UK Notification system (ETS) to detect any such ‘missed’ cases.

It is possible that the improved TB control and decreasing rates in many sender countries may in part explain some of these decreases, although one would have expected these changes to be more gradual and less pronounced. Conversely, it is possible that some refugees from very high risk areas which may have been notified through the UKTB system are increasingly notified through other routes.

Lastly, an important consideration is whether the socioeconomic composition of UK-bound migrants changed. This is possible, since the total upfront cost of visas for applicants has dramatically increased recently, not least because of the introduction of the ‘health levy’ after April 2015.

It is quite possible, that not one single factor, but a combination of above has contributed to these observations, and further work to explore these is anticipated through the ETS matching.

In conclusion, our report shows that after successful roll out of pre-entry screening a number of significant improvement had been made, including near-universal sputum culture confirmation among IOM applicants [11-15]. 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 [16], it is clear that pre-entry screening has an impact and the potential to reduce the number of prevalent cases notified in the UK. A recent study has also demonstrated that pre-entry screening facilities, such as new laboratories can contribute to sender countries’ capacity building [17] and therefore indirectly support the sustainable development goal 3 aim of universal health coverage [18, 19].

However, TB detection rates vary significantly between countries and sites, different age groups and visa types and we observed a significant decrease in numbers and yield of TB cases detected overseas. Further work is required, both to understand but also to mitigate against modifiable risks within the system. Ongoing and sustained efforts are required to maintain quality assurance. This includes panel physician training and outreach alongside well designed and relevant research work.
6. References

1. ECDC Tuberculosis surveillance and monitoring in Europe 2016.  


7. New phase of tuberculosis screening launched as part of Immigration rules changes.  


10. UK pre-entry tuberculosis screening brief report: 2013


7. Appendices

7.1 Case definition

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 (e.g. 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.

Mono-resistant 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.