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Tuberculosis in the East Midlands: Annual review

Data from 2000 to 2017

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Data in this report

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Executive summary

This is the 2018 East Midlands tuberculosis (TB) annual report for data on patients with TB up to the end of 2017.

Since the year 2000, the peak incidence of new TB notifications in England was at 8,280 new patients in 2011. Since then the number of people notified with TB has fallen by nearly 40% to 5,102 people in 2017. At 9.2 per 100,000, this was the lowest rate of TB ever recorded in England and, for the first time, it is considered to be a low incidence country under current World Health Organisation (WHO) definitions (fewer than 10 people diagnosed with TB per 100,000 of the population) [1].

In the East Midlands, 351 tuberculosis (TB) cases were reported among residents in 2017. This is an increase of 10 on the previous year. The incidence rate of 7.4 persons per 100,000 population for the East Midlands remains below the national incidence of 9.2 per 100,000 [(2)]. Although there was a slight increase in 2017 in the number of new notifications in the East Midlands, there has been a substantial decline since 2012 until 2016. The increase in 2017 will need monitoring to ensure this doesn't become a sustained reversal in the trend.

There continues to be variation in the incidence of TB across the East Midlands with the highest incidence rates reported for residents of the city of Leicester (38.8 / 100,000 persons). Since the year 2000 the TB incidence in most areas of the East Midlands has decreased, with the most notable decline in Leicester. The increase in new notifications for the East Midlands overall in 2017 was driven by increases in Derby, Derbyshire, Leicester, Leicestershire, and Nottinghamshire.

There are now also 12 Local Authorities in England that have a 3-year average TB incidence of less than 1.0 per 100,000 – the WHO End TB pre-elimination target rate. None of the local authority areas in the East Midlands have reached that low level yet, although Derbyshire is close (1.1 / 100,000 in 2016 and 1.3 / 100,000 in 2017).

The incidence rate of TB was 13 times higher in those born outside the UK (37.6 patients per 100,000) compared to the UK-born population (2.8 patients per 100,000). The number of patients and the incidence rate of TB in the non-UK born population have seen a year-on-year decline since 2008. Approximately 45% of TB patients that were not born in the UK, and were diagnosed in 2017, entered the UK 11 or more years previously. The most common country of birth of non-UK born TB patients in 2017 was India (38.9%). However, the incidence of TB in UK-born persons is broadly static and therefore strategies to target this group are needed.

Unlike in previous recent years, where the most common ethnicity for newly diagnosed TB patients in the East Midlands was Indian, in 2017 the most common ethnicity was in people whom identify as white, (129 persons), whereas for Indian the corresponding figure was 114 persons. Although the white ethnic group accounted for 37.4% of all TB patients in 2017, the incidence remains low (3.1 patients per 100,000) in this group.

In 2017, more than half (55.3%) of TB patients had pulmonary disease of which 73.1% were confirmed by culture. The proportion of all new patients experiencing a delay of more than 4 months from onset of symptoms to starting treatment was 40% and for pulmonary TB new patients, this was 33%. The longest delay was found to be between presentation to healthcare and diagnosis with a median of 33 days (pulmonary patients).

The incidence rate of TB in UK-born children under 15 years of age in East Midlands (1.4 patients per 100,000) is an indirect indicator of recent transmission. In December 2016, whole genome sequencing (WGS) was introduced in the East Midlands and 90.2% of culture-confirmed patients in 2017 had a WGS result which could be used to report relatedness.

There was a fourth consecutive annual decrease in the proportion of rifampicin-sensitive TB patients completing treatment within 12 months, 305 (74.8%), from a peak of 317 (88.1%) in 2013, (excluding those with CNS, spinal, miliary or cryptic disseminated disease). This was also below the proportion completing treatment for England as a whole (84.4%) [2]. Treatment completion for 2016 varied by upper tier local authority (UTLA) ranging from 62.1% (Lincolnshire) to 85.7% (Derby). The most common reason for not completing treatment at 12 months was still being on treatment.

The proportion of patients with multiple drug resistance (MDR)/rifampicin resistance (RR) in 2017 (3.8%, 8 patients) has remained similar to 2016 (3.9%, 8 patients), but is higher than the proportion of MDR/RR TB patients in England (1.7%).

There is a clear association in the East Midlands between the incidence rate of TB and deprivation. Social risk factors (histories of alcohol/drug misuse, homelessness, or imprisonment) were noted in 19.1% of TB patients over the age of 15 years, which was an increase from 11.3% in 2016. These risk factors are more commonly reported in UK-born patients. Those with social risk factors were statistically more likely to have pulmonary disease and require directly observed therapy (DOT). Treatment completion at 12 months was lower in those with social risk factors compared to those with none (53.6% vs 80%).

In 2017, 91.6% of TB patients in East Midlands were offered and received an HIV test (293 patients) although there was variation by UTLA, age and place of birth. TB notifications are matched annually with HIV surveillance data and for 2017, it is estimated that 3% of TB patients aged 15 years and over in the East Midlands are co-infected with HIV.

Although there was a substantial decline in TB incidence in the East Midlands between 2012 and 2016, there was a slight increase in the number of TB patients in 2017. This trend will require monitoring as we are halfway through the implementation period of the Collaborative TB strategy 2015-2020, which aims for a year-on-year reduction in TB incidences [3]. Certain risk groups continue to be more likely to be affected than others within the East Midlands. This underlines the need for services to work collaboratively, across the range of health and social care issues, to strive towards effective and sustained TB control to achieve a marked reduction in TB and in health inequalities associated with the disease.

Recommendations

Recommendations for local partners and PHE can be found in full on page 66 in line with the strategy areas for action (AfA). They include:

Improve access to services and ensure early diagnosis (AfA1):

TB Networks to reduce the delay in TB diagnosis through raising awareness of TB among local communities affected by the disease, other service providers and primary care. This includes utilising the resources available from TB Alert (http://www.thetruthabouttb.org/professionals/professional-education/)

East Midlands TB Control Board and TB Networks to encourage the use of the RCGP TB e-learning module. http://elearning.rcgp.org.uk/course/info.php?id=107

Provide universal access to high-quality diagnostics (AfA2)

TB Networks to increase the proportion of patients that have a diagnostic laboratory result, particularly culture results to ensure prompt identification of drug resistance and allow WGS to identify clusters.

Improve treatment and care services (AfA3)

TB Networks to continue their supportive case management of complex TB patients, offer DOT where indicated and consider the use of innovative approaches such as Virtually Observed Treatment (VOT) to improve case management.

TB Networks to implement or continue cohort review as a tool to improve local TB control and as a measure of treatment outcomes and contact tracing activity working towards the key performance indicators (KPIs) agreed by the East Midlands TB Control Board.

TB Networks to ensure information is completed accurately on the PHE Enhanced Tuberculosis Surveillance system, particularly with respect to dates of onset of symptoms, evaluation of treatment completion and TB relationship with death.

To reduce drug-resistant TB (AfA6)

TB Networks to continue supporting patients to complete treatment, using DOT or VOT where indicated, and to have plans in place to minimise patients being lost to follow-up.

TB Networks to use the British Thoracic Society (BTS) MDR-TB Clinical Advice Service to support MDR-TB case management.

To tackle TB in under-served populations (AfA7)

East Midlands TB Control Board and TB Networks to encourage the use of the resource ‘Tackling TB in under-served populations (USPs)’ [4] to take appropriate local action and better meet the needs of USPs.

TB Networks, to ensure appropriate access to services, treatment and support to enable patients to complete treatment.

TB Networks are encouraged to use ‘Tackling TB - local government's public health role’ [(5)], a joint publication from PHE and the Local Government Association to help support USPs with TB

To implement new entrant latent TB screening (AfA8)

Clinical Commissioning Groups (CCGs) to sustain the roll out of the new migrant LTBI screening programme within the 4 high-burden CCGs identified within East Midlands.

TB notifications and incidence

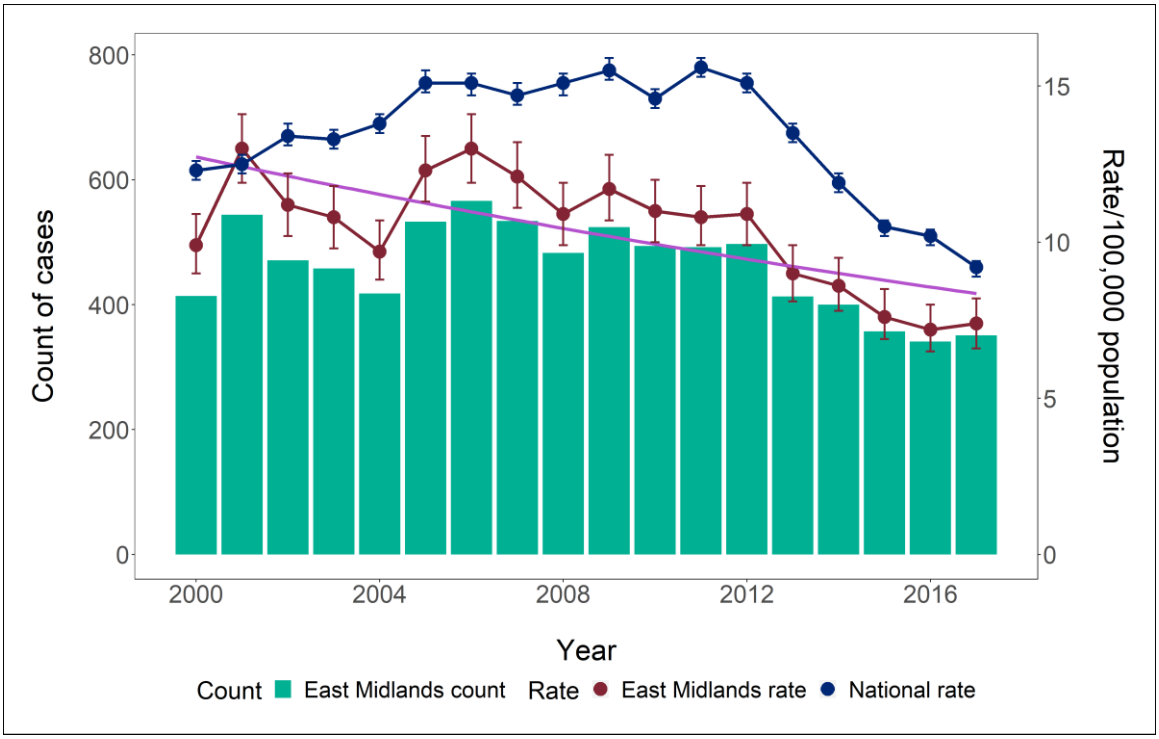
Overall numbers, rates and geographical distribution

In 2017, 351 TB patients were reported among East Midlands residents, an incidence of 7.4/100,000 population (95% CI 6.6–8.2). This represents a slight (but not statistically significant) increase of 10 persons from 2016 (Figure 1). Overall, despite this slight increase in 2017, the incidence (count and rates) of TB has declined substantially in the East Midlands, since the early to mid-2000s. Apart from the increase in 2017, the East Midlands trend otherwise mirrors the national trend.

The TB incidence of 7.4/100,000 in the East Midlands is statistically significantly lower than the England incidence rate of 9.2 per 100,000 population (95% CI 8.9-9.4). Patients reported in the East Midlands in 2017 accounted for 6.9% of the 5,102 patients reported in England [2].

TB Monitoring Indicator 1: Overall TB incidence per 100,000 population

Figure 1: TB case reports and rates, for the East Midlands, 2000 to 2017



As in previous years, the highest incidence rate of TB for East Midlands UTLAs was in Leicester (38.8/100,000). This rate is a further increase from the low point reached in 2015 (36.3/100,000). The increase in Leicester since 2015 is not however significant and as the difference in actual numbers of new notifications between 2015 and 2017 is

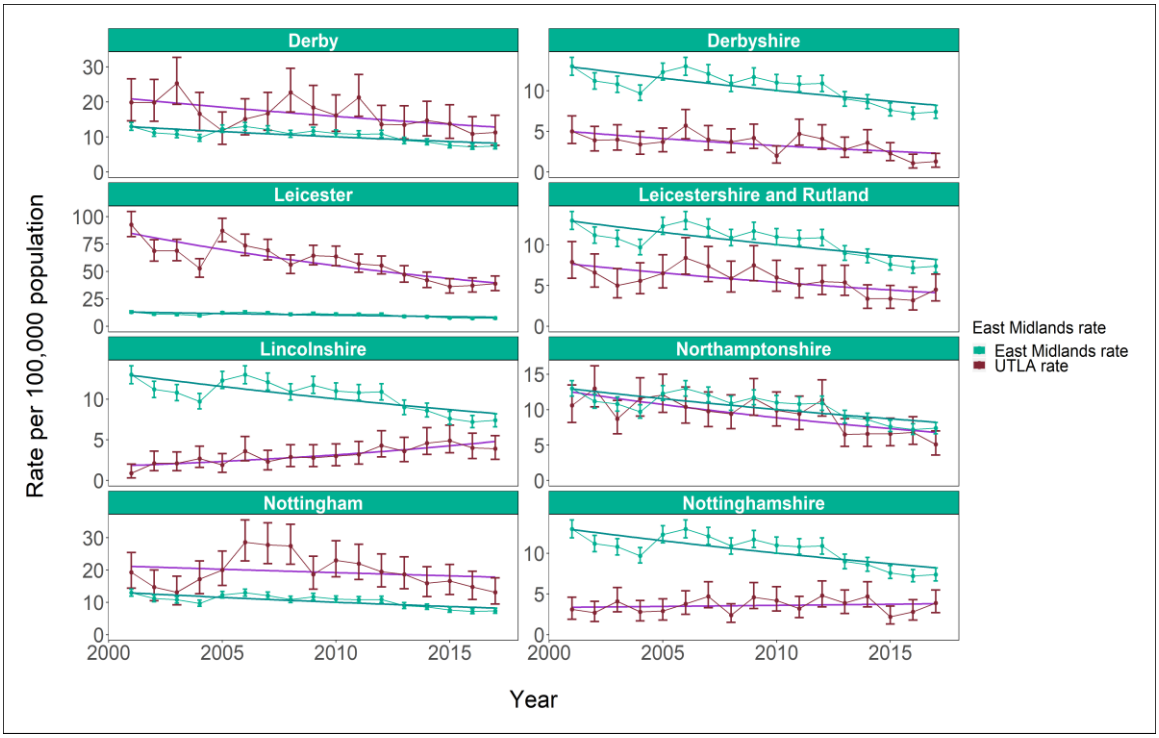
small, this increase may simply reflect year-to-year fluctuations. However, it does suggest that the long-term downward trend may have now plateaued for Leicester. Therefore, if the goal of TB eradication is to be achieved, then renewed efforts to reestablish the downward trend in Leicester are required. Particular focus may be required in the areas (for example, middle super output areas) with high incidence rates of TB.

The lowest incidence rate of TB new notifications was in Derbyshire (1.3/ 100,000) which was a slight (but not significant) increase from 2016 (1.1/100,000).

Overall, Nottingham, Lincolnshire and Northamptonshire had further decreases in the number and incidence of new patients with TB reported in 2017 compared with 2016, although in none was the reduction statistically significant, whereas Derby, Derbyshire, Leicester, Leicestershire and Rutland and Nottinghamshire all increased for the same period, but again none of these increases were statistically significant.

The trends of TB incidence (rate) for the UTLA areas in the East Midlands are shown in figure 2 below. These count and rate data for the East Midlands and UTLA areas are tabulated in tables C1a, C1b, C2a, C2b in the appendix.

Figure 2: TB case rates by sector/UTLA of residence and the East Midlands, 2001 to 2017

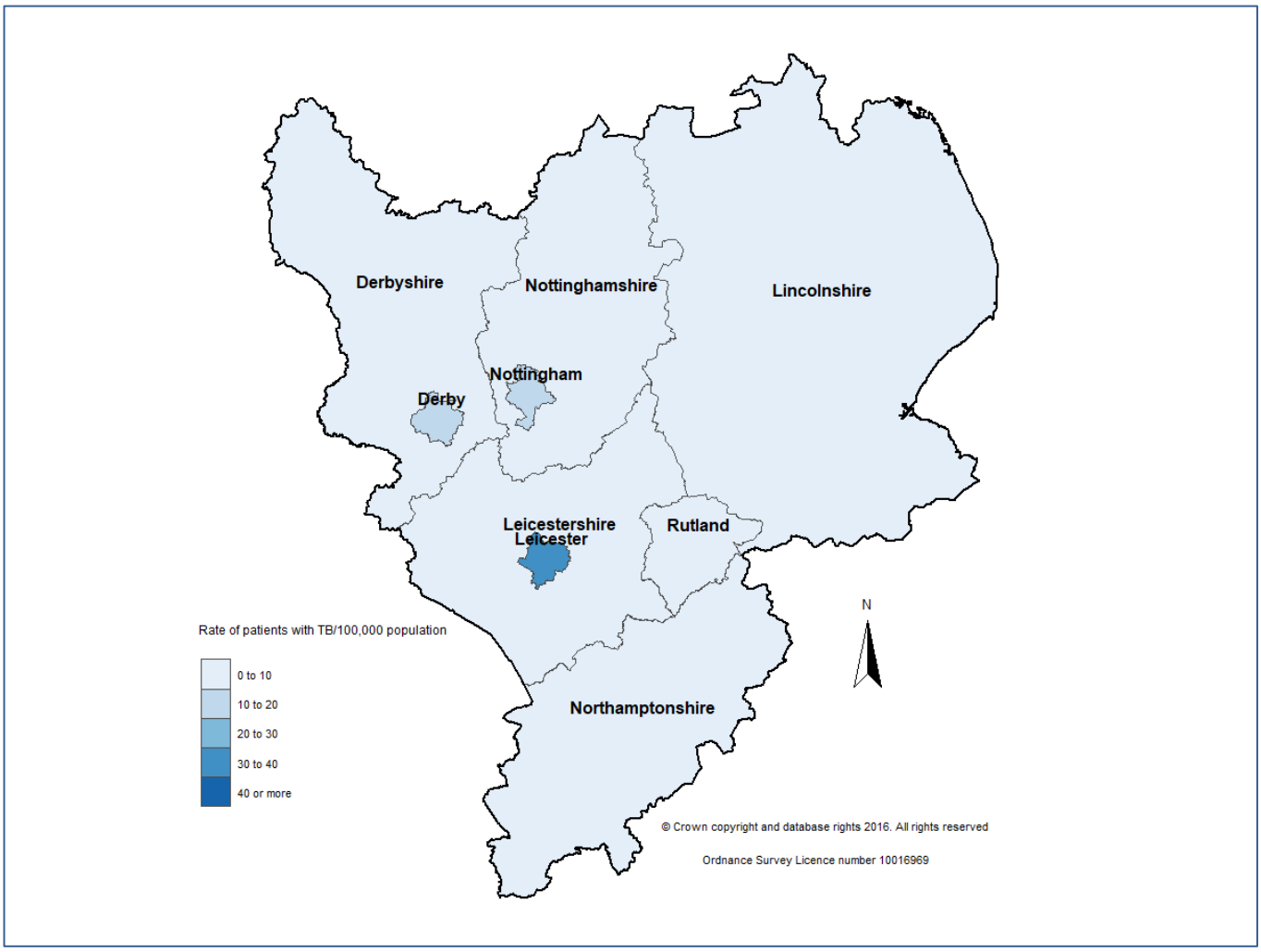


Note: Differing y scale for each UTLA

The mapping figures 3a and 3b below demonstrate that the overall East Midlands incidence rate of TB masks areas with higher incidence. As outlined previously the highest incidence rate of TB occurred within the city of Leicester, with other urban areas also dominating the highest incidence areas.

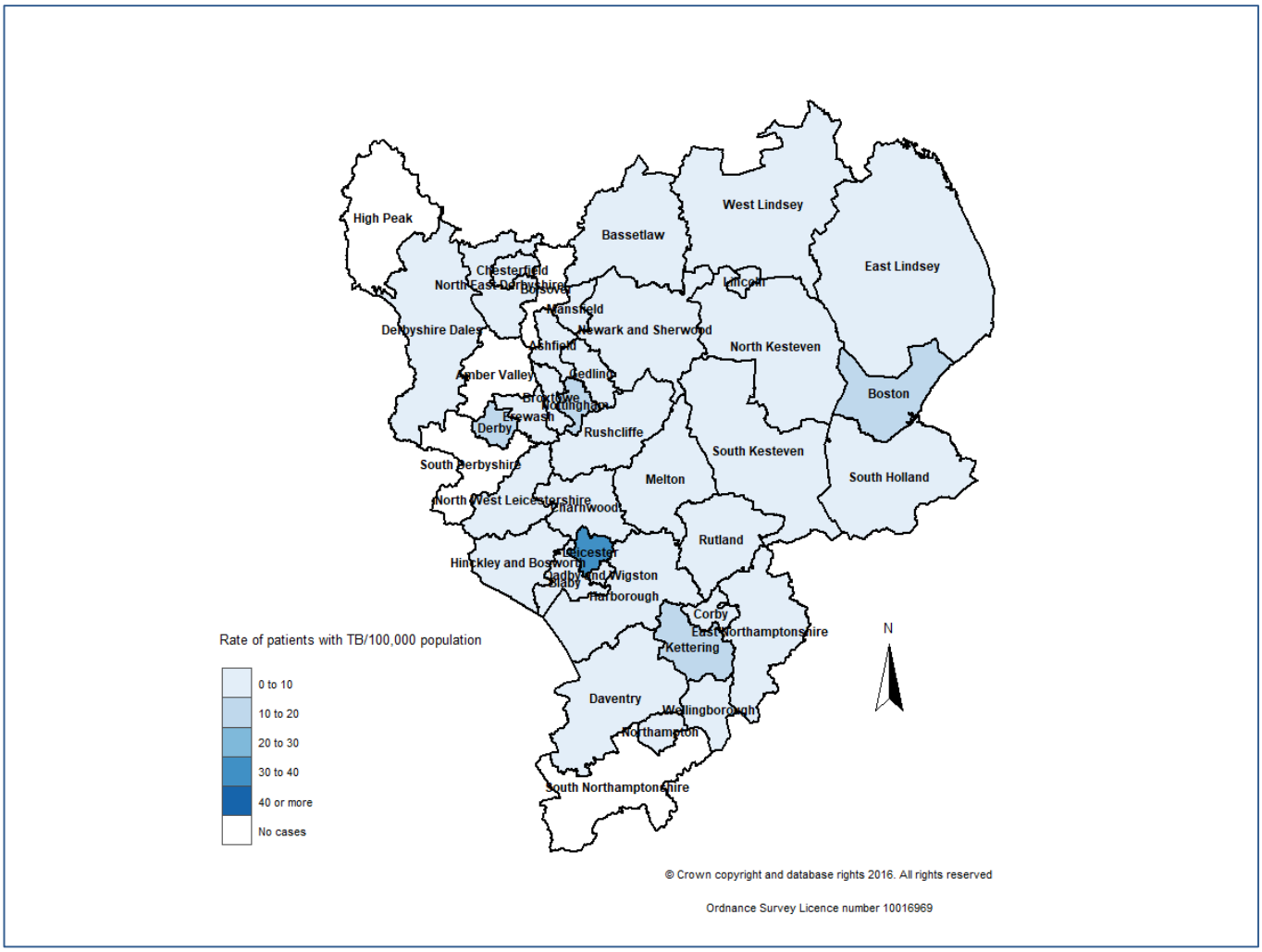
The majority of CCGs in the East Midlands had a 3-year average annual incidence rate of fewer than 10 patients per 100,000 population between 2015 and 2017. The exceptions were: NHS Leicester City CCG which had 3-year average annual incidence rates of 37.7/ 100,000 and NHS Nottingham City CCG, 14.9 / 100,000). The incidence rates by CCG are shown in the table C3 in the appendix.

Figure 3a: TB case rate by UTLA of residence, East Midlands, 2017



The incidence rates by middle layer super output area (MSOA), which are geographical areas with a minimum population of 5,000 (national mean is population of 7,200), show that 14 areas in the East Midlands had a 3-year average annual rate of more than 40 patients per 100,000 population between 2015 and 2017. Of these, 10 MSOAs were within Leicester (Leicester 004: E02002830, 005: E02002831, 006: E02002832 , 007: E02002833 , 010: E02002836 , 011: E02002837, 017: E02002843 , 018: E02002844 , 021: E02002847 and 022: E02002848, mainly North East/East of City), 1 in Lincolnshire (Boston 003: E02005419, within Boston town), 1 in Nottingham (Nottingham 018: E02002885, North East of City) and 2 in Derby (Derby 016: E02002811 and 020: E02002815, South of City). These high incidence MSOA areas could be good target areas for proactive work on reducing the burden of disease.

Figure 3b: TB rate per 100,000 population by local authority of residence, East Midlands, 2017



Demographic characteristics

Age and sex

As with previous years, the incidence rate of TB in 2017 for all patients with TB was statistically significantly higher in males; 8.9 patients per 100,000 population (95% CI 7.7 – 10.2) compared to females (5.8 patients per 100,000 population, 95% CI 4.9–6.9). Males accounted for 59.8% (210) of new TB notifications.

The incidence and rate of TB in the East Midlands is greatest in the age band 30 to 39 years (15.2/100,000 in men and 12.0/100,000 in women), with TB in men dominating females in almost all age groups except in the youngest age group – the 0-9 years age band. In this group the number of children diagnosed with TB each year is small [figure 4]. This pattern is also demonstrated in the longer-term trends, where the incidence in males dominates the incidence in females in most years and age bands [figure 5].

The trends by 10-year age bands since the year 2000 show a variable picture by sex and age. For example, the incidence rate of TB in young adult men (aged 20 -29 years) varied from a peak of 29.8 / 100,000 in 2008 down to 11.5 / 100,000 in 2015, rising then slightly to 12.4 / 100,000 in 2017. For older adult men aged 70 years or more the rate has declined from 22.6/100,000 in 2001, to 9.3 / 100,000 in 2017. By contrast, for men aged 30-39 years the rate was 12.6/100,000 in 2000 but has then remained consistently above that baseline in all years since. The pattern is similar for female persons, although less marked, except in young adult females age 20 – 29 years, where the decline has been more notable (peak of 27.0 / 100,000 in 2006 down to 5.6 / 100,000 in 2017).

Figure 4: TB case reports and rate by age and sex, for the East Midlands, 2017

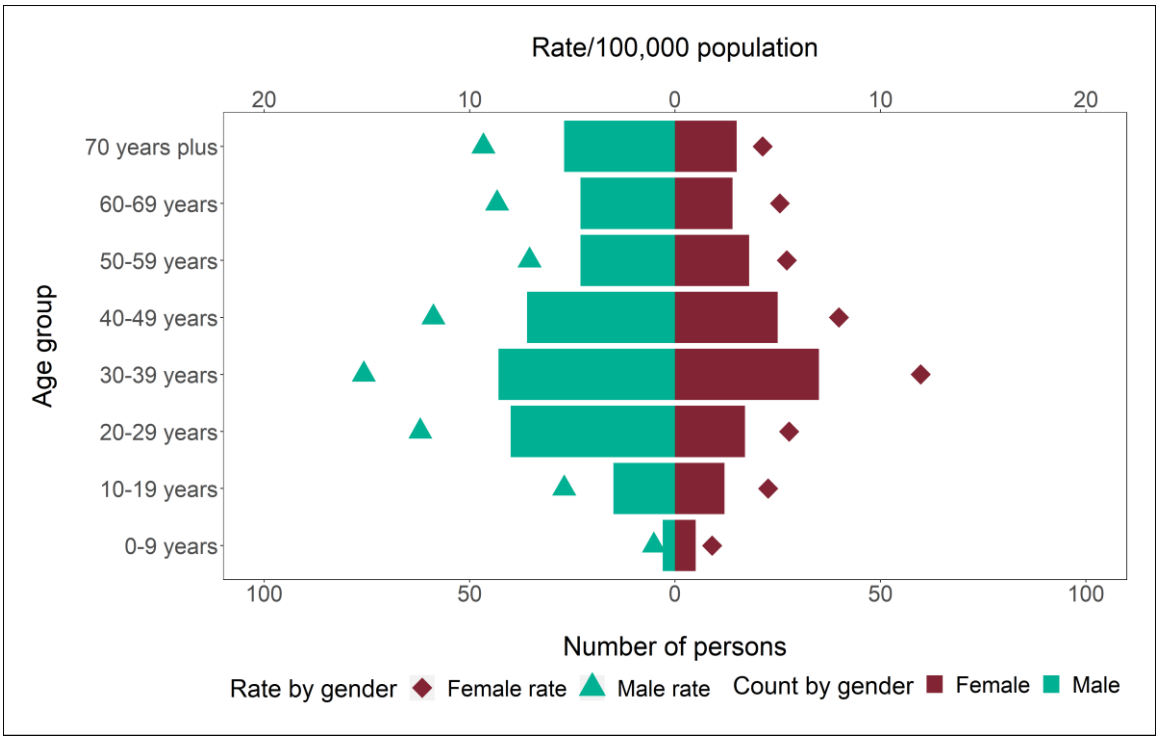
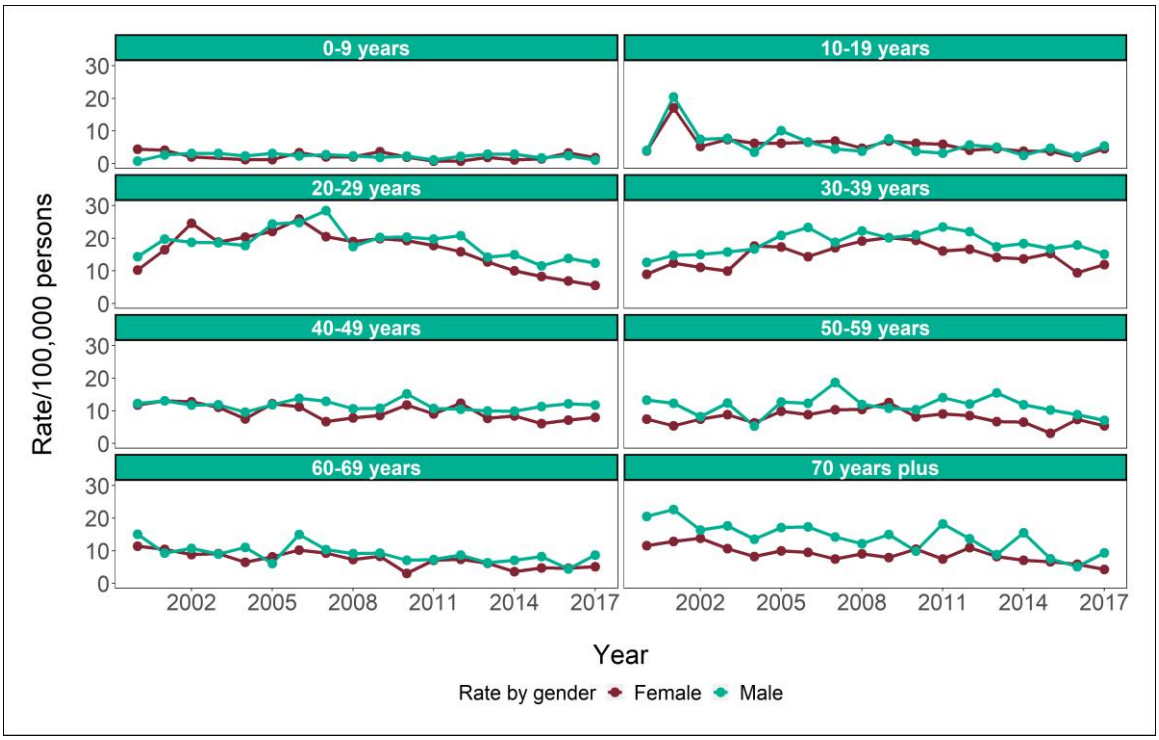


Figure 5: TB case rates by age group and sex, for the East Midlands, 2000 to 2017



In 2017, the rate of TB in all children under 15 years of age within the East Midlands was 2.0 per 100,000 population (17 patients), of which 64.7% were born in the UK. This is a decrease from 2.6/100,000 population in 2016 (21 patients – UK and not UK-born). Further information on TB in children for the UK-born population can be found on page 29. In 2017, there were 8 children with TB aged less than 5 years which was a decrease from 11 children in 2016. All of these 8 children aged under 5 who were diagnosed with TB in 2017 were born in the UK.

Place of birth and time since entry

In 2017, country of birth information was recorded for 339 patients (96.6% of all new notifications). Of these, 66.7% of all East Midlands TB patients were born outside the UK (226 new notifications as compared to 242 in 2016)

Using East Midlands residents who were non-UK born as a denominator, this is an incidence rate of 37.6 new notifications per 100,000 population. Although this rate is approximately 13-times higher than the incidence rate in those born in the UK (2.8 per 100,000 population), the rates within non-UK born population have been steadily decreasing since 2005 when the rate was 99.4/100,000. (Figure 6). By contrast, the TB incidence within the UK-born population has remained unchanged over previous years. In 2005, the rate for UK-born persons was 2.4/100,000. This rose to a peak of 3.6/100,000 in 2009, before falling back to the present rate of 2.8/100,000.

In 2017, information on the time between entry to the UK and TB diagnosis was recorded for 97.4% of non-UK born patients (220 patients). Among those reported in 2017 that were non-UK born and for whom information on time between entry and TB diagnosis was available, 15.5% were notified within 2 years of entering the UK and 40% within 6 years. There was a further increase in the proportion of patients notified 11 or more years after entry from the UK from 40% (94 patients) in 2016 to 45% (99 patients) in 2017. In numerical terms, the low point for this group was in 2004, when only 23 patients were notified, however this increased to 113 in 2011, before falling back a little to 99 in 2017. All the recent numbers have fallen back, the trend is concerning as it suggests that either patients are developing active TB from latent TB due to exposures a long time ago or that they are being exposed in the UK or from travel abroad, (however improved recording of these data may explain some of the increasing trend). It may be appropriate to consider what strategies could help address the TB incidence in this group.

The data on time between entry to the UK and TB diagnosis are displayed in Figure 7 (as a stacked bar chart). Some of the data fluctuations noted may reflect improved coding/recording of data over time.

TB Monitoring Indicator 2: TB incidence in UK-born and non UK-born populations

Figure 6: TB case reports and rate by place of birth and year of onset, East Midlands, 2000 to 2017

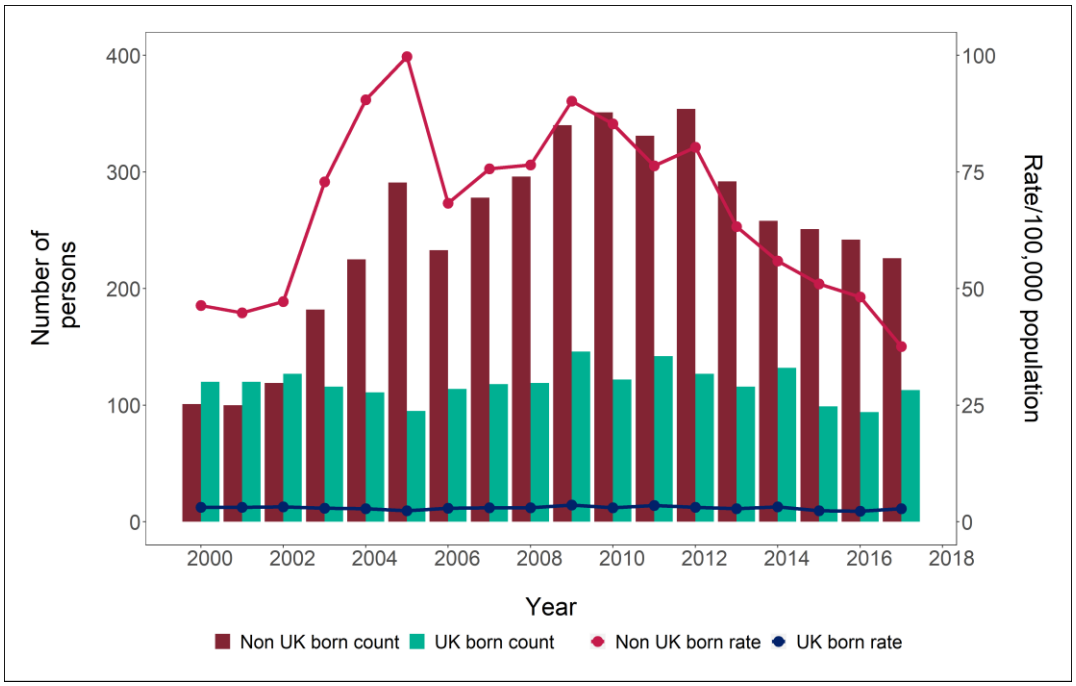
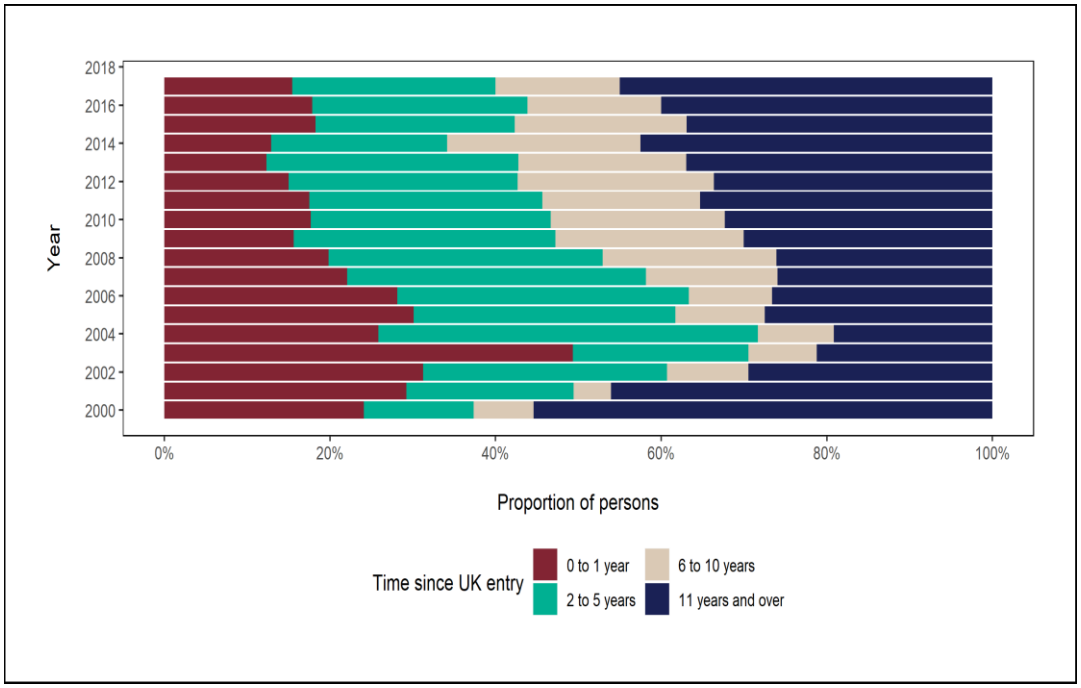


Figure 7: Time between entry to the UK and TB notification for non UK-born patients by year, East Midlands, 2000 to 2017



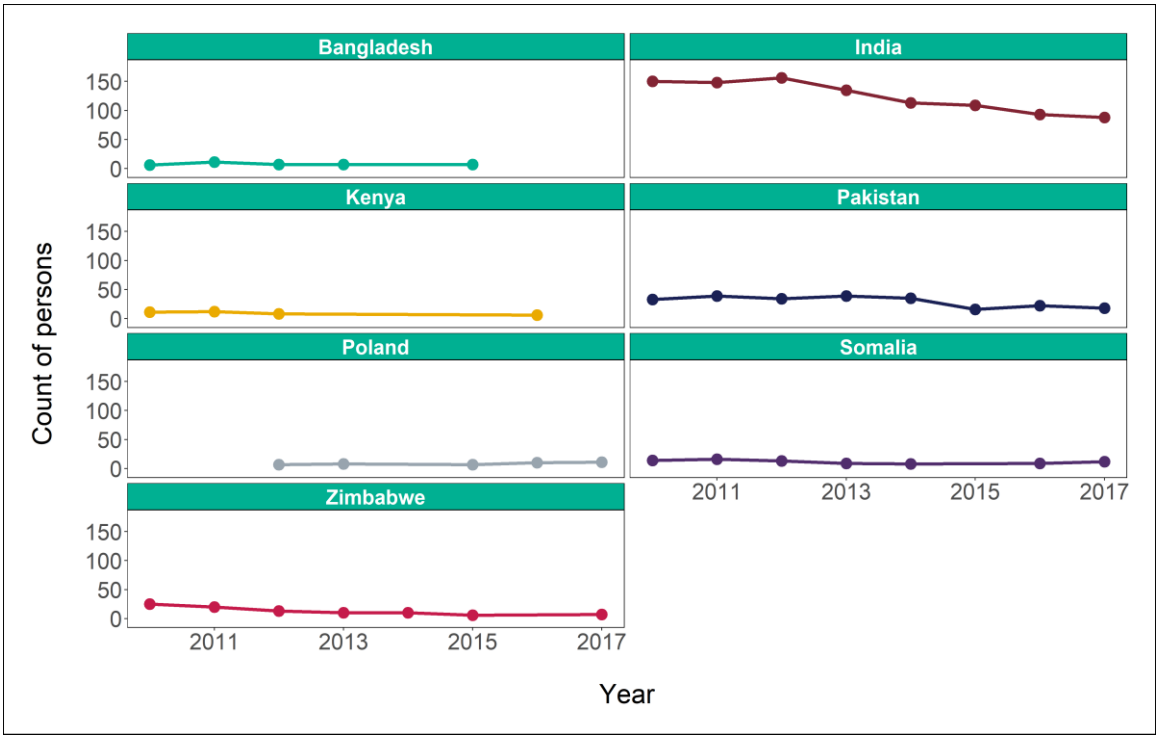
In 2017, the most commonly reported country of birth for non-UK born patients was India (38.9%), (Table 1) followed by Africa Other (13.7%) and Pakistan (8.0%), which was similar to 2016.

Table 1: The most common countries of birth of non UK born TB patients, East Midlands, 2017

Country of birth	Number of new TB notifications	%
India	88	38.9
Africa Other	31	13.7
Pakistan	18	8
Asia Other	15	6.6
Romania	14	6.2
Somalia	12	5.3
Poland	11	4.9
Europe Other	10	4.4
Sudan	9	4
Zimbabwe	7	3.1
Lithuania	5	2.2

Figure 8 below describes the trend in incidence of TB in persons born outside of the UK, by the most common countries of birth in 2017, from 2010 to 2017.

Figure 8: Trend in TB case numbers in the 7 most common countries of birth, East Midlands, 2010 to 2017



* Note: data are only displayed where there are more than 5 persons diagnosed with TB from the relevant country in that year.

Ethnicity

Ethnicity data was available for 345 patients (98.2% of notifications). The majority of TB patients are identified in people who describe their ethnicity as white, 37.4%, 129 patients, which is a rise from 30.9%, 105 patients in 2016 (Figure 9a), followed by those of Indian ethnicity, 33.0%, 114 patients – a drop from 34.7%, 118 patients in 2016. The trend is slightly upward in recent years for white ethnicity and markedly downward for those of South Asian ethnicity since 2010 (Figure 9b). The number of UK-born patients recording Black ethnicity (Black-Caribbean, Black-African and Black-Other combined) has also decreased compared to 2016.

Figure 9a: TB incidence count and rate per 100,000 population by ethnic group, East Midlands, 2017

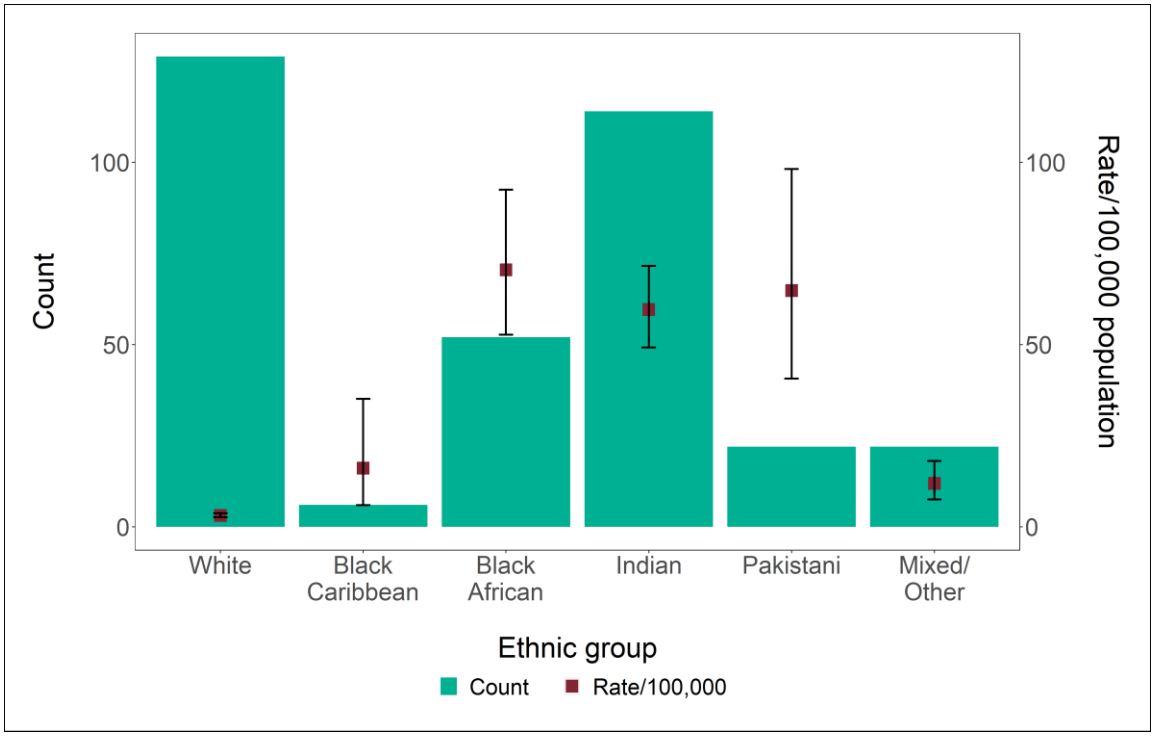
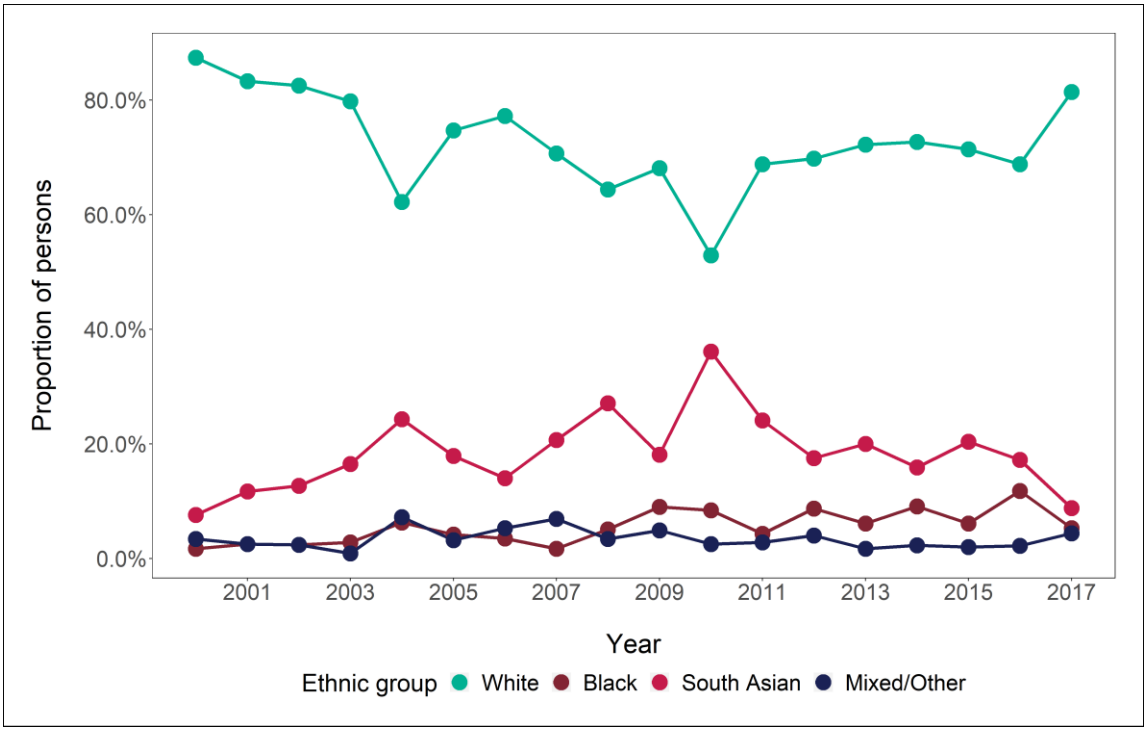


Figure 9b: Proportional TB case numbers by ethnic group for UK born patients, East Midlands, 2000 to 2017

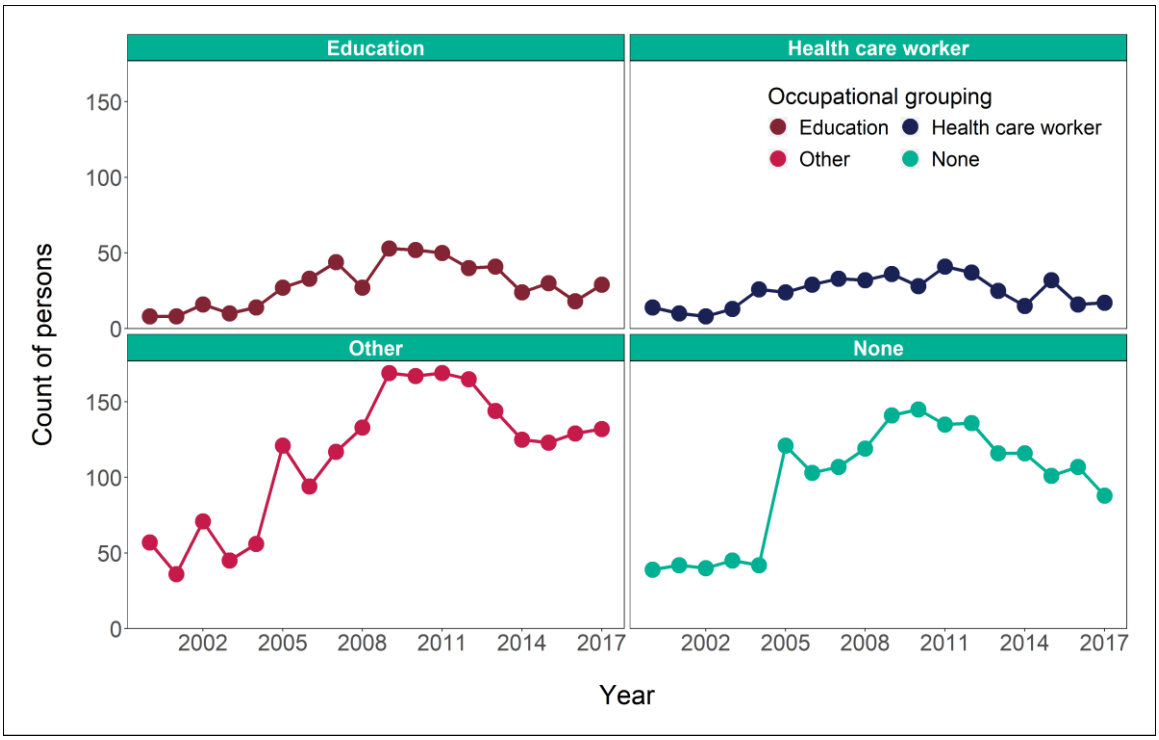


* Patients with Black-Caribbean, Black-African and Black-Other ethnic groups were grouped as 'Black'
** Patients with Indian, Pakistani and Bangladeshi ethnic groups were grouped as 'South Asian'
$ Patients with Mixed/Other and Chinese ethnic groups were grouped as 'Mixed/other'

Occupation

It is very striking that a substantial proportion (33.1%) of those diagnosed with TB in 2017 (aged ≥ 16 and ≤ 65 years) describe themselves as having no current occupation (ETS classification) (figure 10a). This group includes the retired, unemployed, prisoners, immigration detainees, asylum seekers and home makers. It has previously been recognised that prisoners, for example, have a higher incidence of TB compared to other individuals; however, the data serves as a useful reminder that TB prevention work is critical within subpopulations within the group that describe themselves as having no occupation. The increase in those who have an occupation described as other, reflects improvements in the recording of occupational categories.

Figure 10a: Trends in occupational category of TB patients aged 16 to 65 years, East Midlands, 2000 to 2017

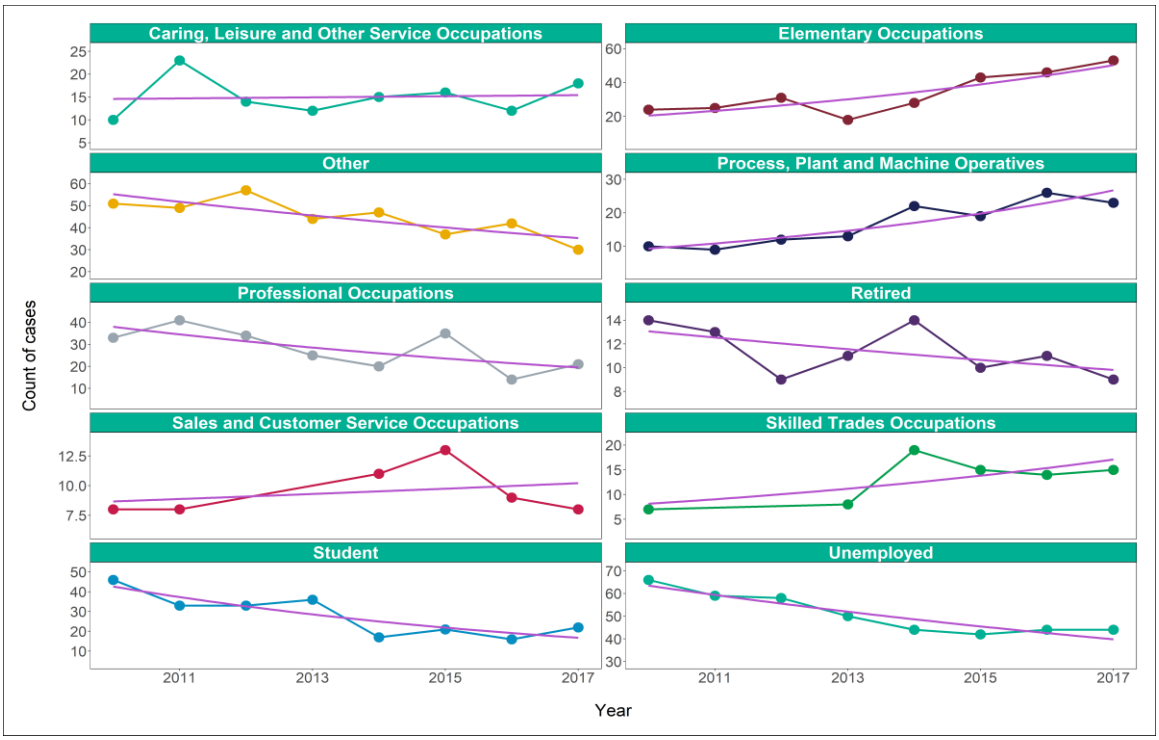


To investigate the occupational association with TB further – particularly those classified as 'other' or 'none' in the broad classification used in figure 10a above – an experimental analysis was carried out by mapping the occupation of patients with TB (free text data field in ETS) against the Office for National Statistics, Version 7 of the Standard Occupational Classification 2010 Index (ONSSoc2010) (June 2018 edition) [6]. This classification uses a hierarchical structure which groups occupations by major, sub-major, minor and unit groupings. For example, the major classification includes group 1 for managers, directors and senior officials and is further subdivided into more discrete categories such as production managers and directors. (Note – the occupation data in ETS is based on free-text entries and in some instances, doesn't provide

sufficient descriptive evidence to accurately classify to the ONSSOC2010 Index, so the analysis below is based on approximations). Prisoners, the unemployed, retired, agency/temporary and other groups are also not represented by the ONSCOC2010 Index, but for the purpose of this analysis were nonetheless categorised as separate groupings. The data on trends in prisoners are presented separately in section 7: Tackling TB in underserved populations[4].

The data shows some quite striking patterns since the year 2000 in certain occupational major (Figure 10b) and minor groupings. Notably, the incidence in elementary occupations, such as factory and warehouse operatives, has risen from 19 patients in 2000 to 53 in 2017 while the number of new patients in the professional occupation grouping has fluctuated around 20 to 30 new patients a year in most years. Improvements in occupation recording may be the explanation for the changes observed, however these could also be a genuine increase. Nonetheless, it should be noted that this analysis was experimental and so these findings should be interpreted in that light.

Figure 10b: Trends in occupational category of TB patients aged 16 to 65 years, East Midlands, 2010 to 2017 by ONS Standard Occupational Classification



Clinical characteristics

Site of disease

As in previous years, in 2017, pulmonary disease remained the most common site for tuberculous disease (194 patients, 55.3% of all new infections). Tuberculous lymph nodes (intra/extrathoracic) and pleural sites were the next most common sites with the intrathoracic lymph nodes being the second most common site of disease (60 patients, 17.1% of all new infections). All other sites for TB were uncommon in 2017 (Table 2).

Table 2: Site of disease of TB patients, East Midlands, 2017

Disease site	Count of patients	%
Pulmonary	194	55.3
Miliary	8	2.3
Bone/joint (spine)	23	6.6
Bone/joint (other - not spine)	6	1.7
CNS (meningitis)	11	3.1
CNS (other - not meningitis)	6	1.7
Gastrointestinal/peritoneal	17	4.8
Extrathoracic lymph nodes	58	16.5
Intrathoracic lymph nodes	60	17.1
Pleural	25	7.1
Extrapulmonary-other	20	5.7
Other	11	3.1

*patients may have disease at more than 1 site, so the total % will not equal 100%
†CNS: Central nervous system

Previous history of tuberculosis

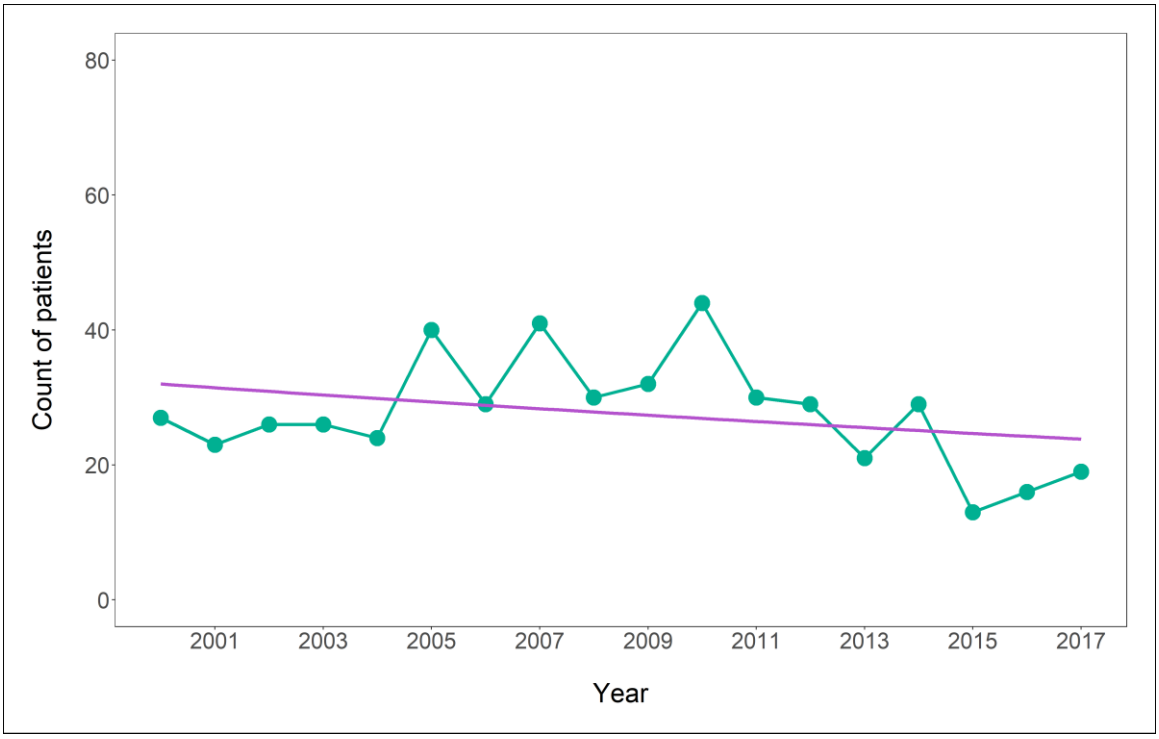
In 2017, information on previous diagnosis (active TB more than 12 months before, either in the UK or abroad) was recorded for 92.9% (326) of patients. Of these, 5.8% of patients were previously diagnosed with TB more than 12 months before their current notification (19 patients). Although the number of patients presenting as new diagnoses each year, who have previously had TB has declined since the year 2000, the proportion of the total new diagnoses has remained broadly flat at around 6% over that period.

In 2017, of those who were newly diagnosed with TB that had previously been diagnosed with TB (where their ethnicity was known) 55.6% were of white ethnicity, however the proportion varies from year-to-year with fewer cases in recent years.

Of those with white ethnicity that previously had TB, in 2017 only a minority of these had any risk factors for TB, such as homelessness. Since the year 2000, of those with white ethnicity and who had previously had TB, 60.2% of these patients were aged 65 years or older.

Where known, the number of years since the previous diagnosis for all patients in 2017 ranged from 1 to 68 years with a median of 7.5 years.

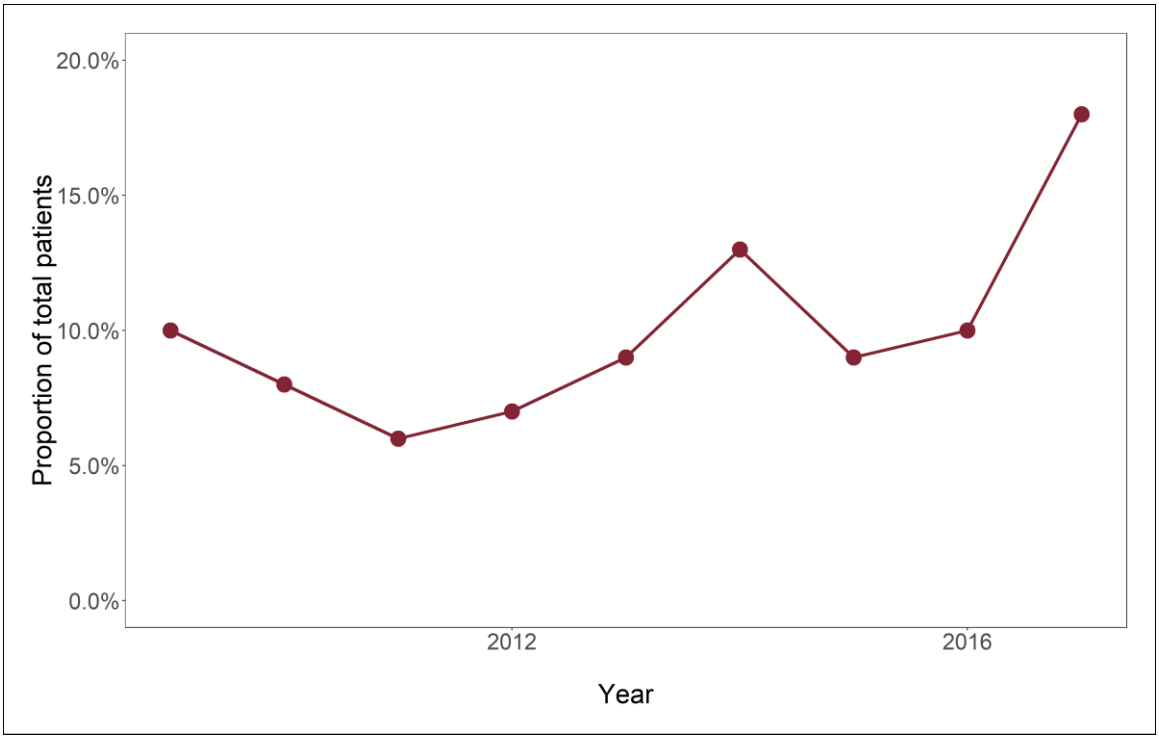
Figure 11: Trends in the count of total TB patients who have previously had TB, 2000 to 2017, East Midlands



Supervised treatments

Since around 2009 there has been a steady increase in all patients with TB, and particularly those with a previous diagnosis of TB, being enrolled into DOT programmes – where the patient is monitored and observed taking their anti-TB treatment to improve compliance with treatment (Figure 12). In 2009, 10% of all patients with TB were on DOT, whereas by 2017 this had increased to 18%. The increase is more marked in those with a previous history of TB. In 2009, only 17% of patients with a previous history of TB were on DOT, whereas in 2017 this had increased to 44%.

Figure 12: Trends in proportion of TB patients that are receiving directly observed treatment, 2009 to 2017, East Midlands



Laboratory confirmation of TB

Laboratory tests data collection

Laboratory data on culture confirmed TB isolates from the National Mycobacterium Reference Service were matched to TB case notifications, and the results were used to report culture confirmation. Results for microscopy, PCR and histology are also collected in ETS.

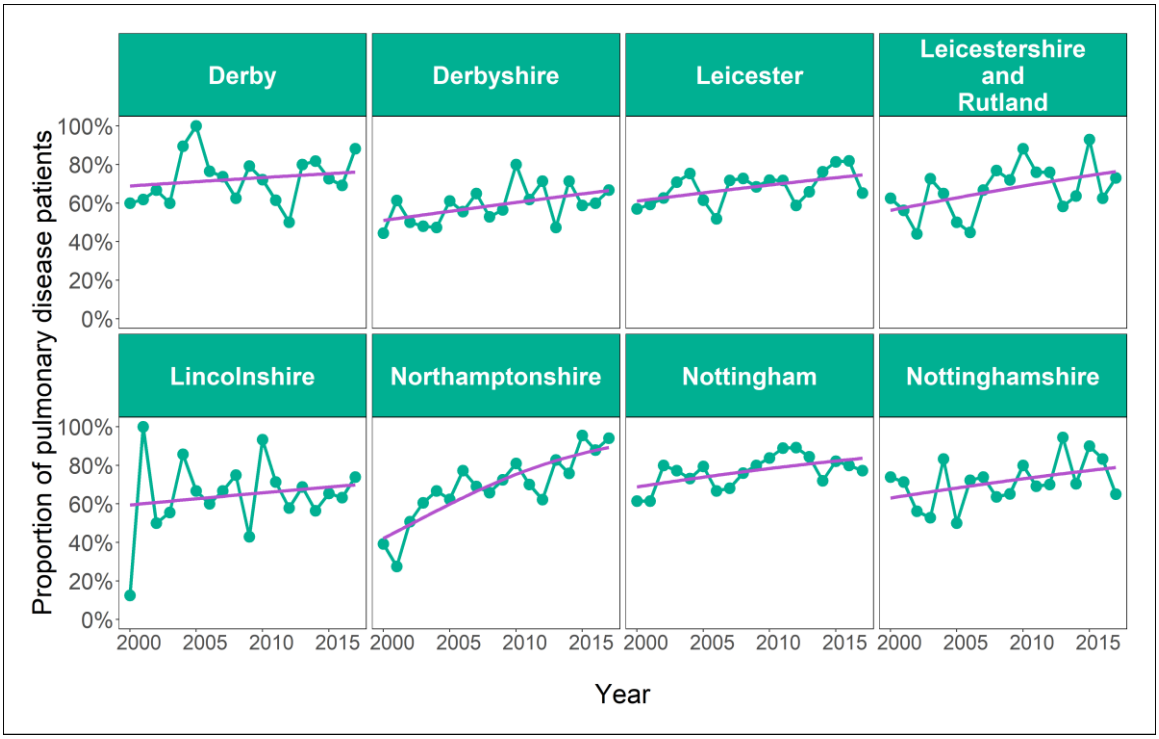
Culture confirmation and speciation

In 2017, 61.0% (214) of all patients were culture confirmed, this was a similar proportion to that in 2016. This proportion was higher among those with pulmonary TB (73.1%, 144 patients) compared to patients with extra-pulmonary TB (45.1%, 69 patients).

Although most pulmonary TB patients in the East Midlands were confirmed by culture in 2017 there was quite marked variation in culture confirmation by UTLA area – for example ranging from 65% culture confirmed in Leicester and Nottinghamshire to 94% in Northamptonshire (figure 13). However, small numbers of new diagnoses in areas such as Northamptonshire may be skewing these results. Of more interest is the longer-term trend in the proportion of patients whose diagnosis was confirmed by culture. Figure 13 demonstrates that in all local authority areas, confirmation by culture has improved (upward trend) but there is still scope for some areas to reach the proportion diagnosed by culture of the best performers.

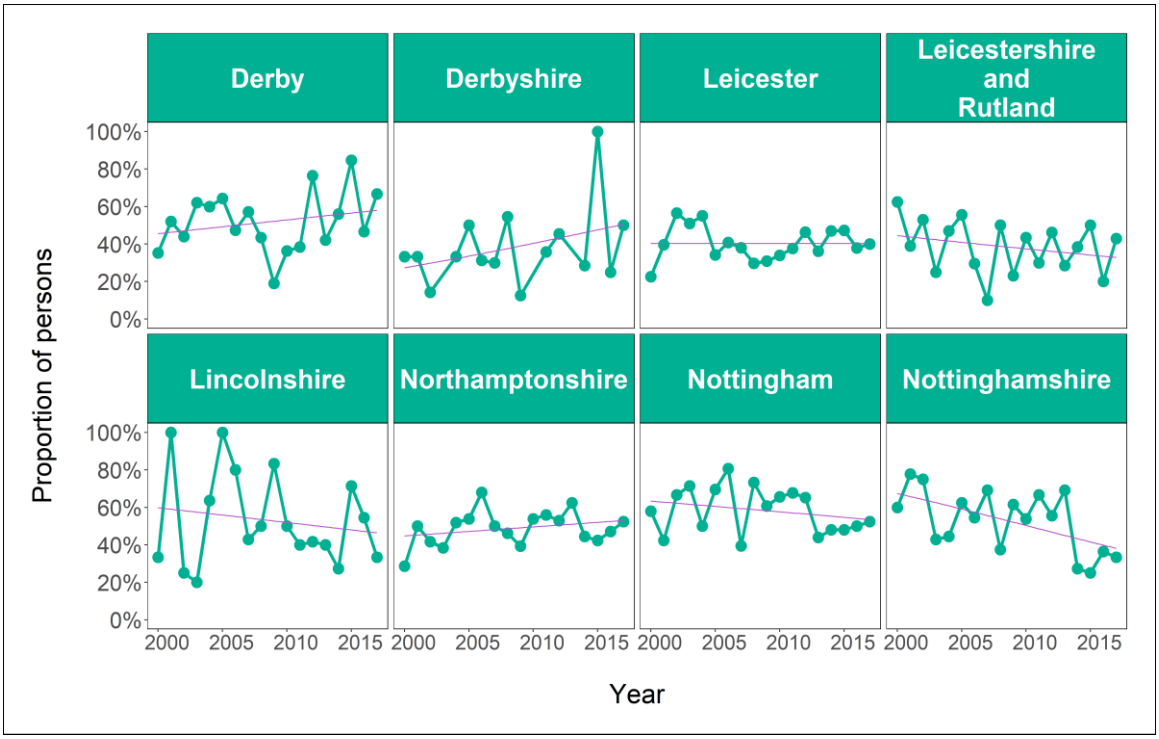
In 2017, 98% of cultured isolates were Mycobacterium tuberculosis, the remaining 2% being of other rarer species within the Mycobacterium tuberculosis complex (Mycobacterium africanum and Mycobacterium microti).

Figure 13: Proportion of culture confirmed pulmonary TB isolates by UTLA, 2000 to 2017



Unsurprisingly, the proportion of extra-pulmonary TB confirmed with culture is much lower than for pulmonary TB, reflecting the difficulty in obtaining clinical samples from non-pulmonary sites. However, again there is marked variation with Derbyshire achieving 66.7% culture confirmation for this group, whereas for Nottinghamshire and Lincolnshire only 33.3% of extra-pulmonary TB patients had their diagnosis confirmed with culture. However, small numbers may skew the results (figure 14). Once again, the trend data (figure 14) is more informative, showing an improved performance for several areas (Derby and Northamptonshire), but a worsening trend for others, particularly Lincolnshire and Nottinghamshire.

Figure 14: Proportion of culture confirmed extra pulmonary TB isolates, 2000 to 2017



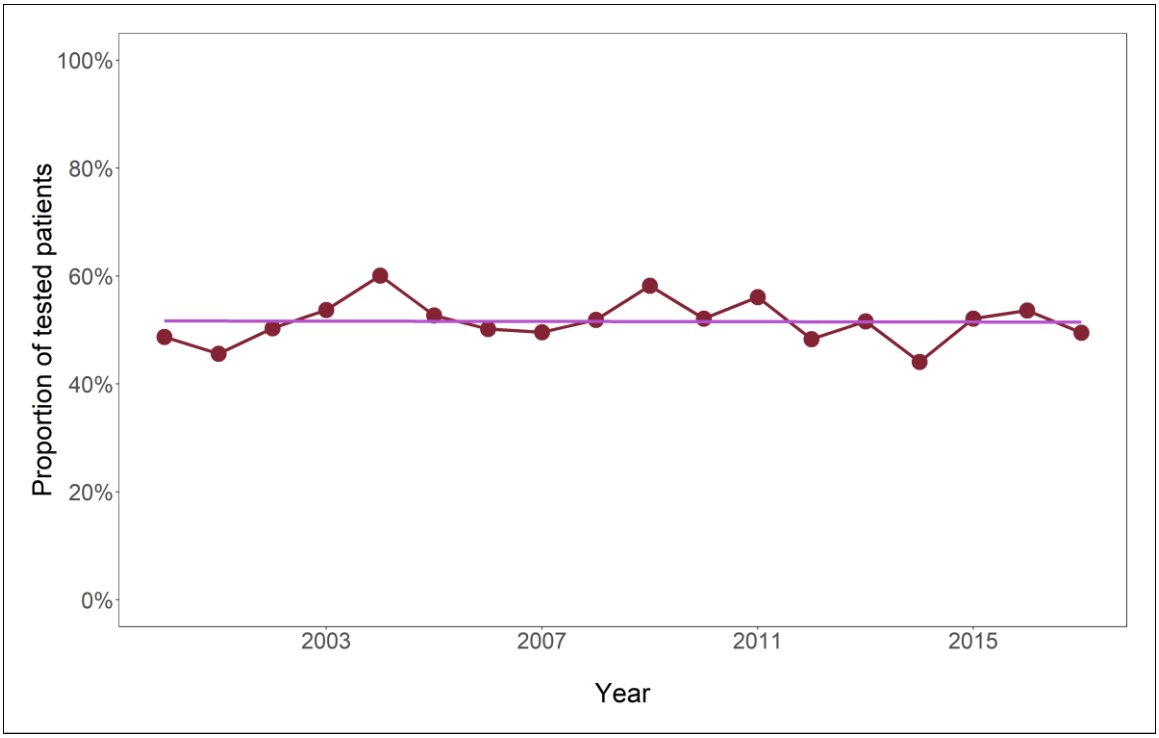
TB Monitoring Indicator 8: Proportion of pulmonary TB patients that were culture confirmed

Sputum smear

Sputum smear results are used to assess the infectiousness of pulmonary TB cases with smear-positive cases deemed more infectious than smear-negative results. In 2017, 50.3% (99) of the 197 patients with pulmonary TB had a sputum smear (microscopy) result reported. Of these, 49.5% were sputum smear positive (49). No age group stood out as being more likely to be smear positive, although smear positivity was not reported in children.

Overall for the East Midlands, the proportion of patients with pulmonary TB who have a sputum smear result reported in ETS has decreased. In 2005, 74.5% of patients had a sputum smear result (positive or negative). This has dropped to 50.3% in 2017. Of pulmonary TB cases that had a smear test reported, the proportion with a smear positive result have broadly remained the same between 44% and 60% [figure 15].

Figure 15: Proportion of pulmonary TB patients with a sputum smear positive result, 2000 to 2017



Other laboratory test results

Very few patients had other PCR or histology tests according to the data entered onto ETS. These data may not reflect the true situation and so this may be an area to work on in improving the data quality.

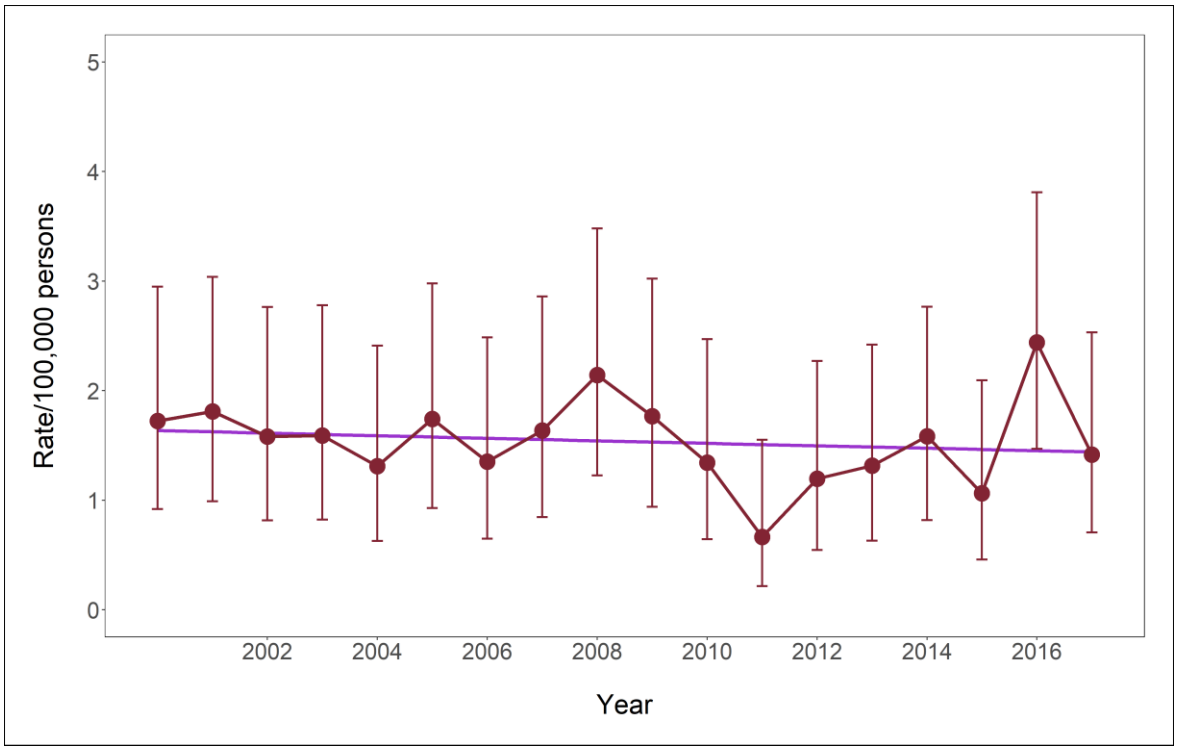
TB transmission

Rate of TB in UK-born children

The incidence of tuberculosis in UK-born children is considered a marker of transmission within the locality. On a year-on-year basis the number of children in the East Midlands diagnosed with TB is small relative to the overall total; the trend has slowly declined since the year 2002, although the trend is not statistically significant. Fortunately, the increase in incidence in children in 2016 has returned to the longer-term trend, although the number of new notifications in future years will need monitoring (figure 16).

In 2017, there were 11 new notifications of TB in UK-born children aged 14 years and under within the East Midlands, a rate of 1.4 per 100,000 population. In 2017, there were 8 UK-born new notifications of TB in children aged less than 5 years, down from 11 patients in 2016.

Figure 16: TB case rates of UK born children aged 0 to 14 years, for the East Midlands, 2000 to 2017



TB Monitoring Indicator 5: Incidence of TB in UK born children aged less than 15 years

Strain typing and clustering

The National TB Strain Typing Service (NTSTS) in England, established in 2010, prospectively typed TB isolates using 24 loci MIRU-VNTR. Clustered patients (with indistinguishable MIRU-VNTR strain types) may reflect people with TB that are part of the same chain of transmission but could also reflect common endemic strains circulating either within England or abroad. MIRU-VNTR strain typing can be used to refute transmission between individuals who have distinguishable strain types, but an indistinguishable strain type does not confirm transmission. Additional epidemiological information is required to assess whether patients with indistinguishable strain types reflect recent transmission.

In December 2016, MIRU-VNTR strain typing for East Midlands TB isolates was replaced by WGS-based single nucleotide polymorphism (SNP) typing. Clusters identified using WGS are defined based on people with TB isolates who are within 12 SNPs of each other. The smaller the number of SNPs difference between isolates, the more closely related the isolates are, increasing the potential that they are linked. The higher level of resolution provided by WGS when combined with additional clinical and epidemiological information should improve our understanding of whether patients are likely to be part of the same transmission chain and may also help determine the timing and direction of transmission. Within the Field Service, there is a designated TB cluster investigator whose role is to review and identify clusters within and across PHE Centres. Cluster information is regularly provided to the East Midlands, which are routinely reviewed for epidemiological links and where appropriate prioritised for targeted public health investigation and action.

In 2017, of the people notified with culture-confirmed TB in the East Midlands, 90.2% (193/214) had a WGS result that could be used to report relatedness (based on sequencing coverage and quality). In 2017, the proportion of people that clustered with at least 1 other person at a cut-off of 12 SNPs was 26.4% (51/193) – a similar figure to that shown nationally (23.3%) (Table 3). The proportion identified at 5 and 2 SNP cut offs are also shown in Table 3. Of those clustering at 12 SNPs, 31 (60.7%) patients were UK-born and 19 (37.3%) were born outside of the UK and for one the country was unknown.

Of the 21 clusters identified at a 12 SNP cut off in 2017 for patients with TB in the East Midlands, the majority (85.7%; 18) were small (<5 people) and 42.8% (9) were clusters that only had 2 people in them. 7 patients were clustered to other patients with TB outside of the East Midlands. Only 3 clusters had 5 or more people.

Table 3: WGS cluster data 2017

SNP cluster threshold	Cluster status	Count	%
12 SNPs	Clustered	51	26.4
	Not clustered	142	73.6
5 SNPs	Clustered	43	22.3
	Not clustered	150	77.7
2 SNPs	Clustered	40	20.7
	Not clustered	153	79.3

Delay from onset of symptoms to start of treatment

Time from symptom onset to treatment start for all patients and those with pulmonary TB

Information on the time from symptom onset to starting treatment was recorded for 94% (330 patients) – all types of TB and for 92.4% (182 patients) for those with pulmonary TB in 2017 (Tables 4). The median time between symptom onsets to starting treatment for all TB patients was 97 days with an interquartile range (IQR) of 53 to 172 days. The median time between symptom onsets to starting treatment for pulmonary TB patients was 83 days with an interquartile range (IQR) of 46 to 139 days. The median time for starting treatment for pulmonary TB in patients from the East Midlands was longer than the median delay to treatment commencement for England for patients (79 days IQR: 39-143); as the interquartile ranges overlap, the difference is not significant [2].

In the East Midlands in 2017, 30.6% of all patients with TB started treatment within 2 months of symptom onset and 60% within 4 months. There has been an increase in the proportion of TB patients starting treatment more than 4 months after symptom onset from 34.7% in 2016 to 40% in 2017 although this difference was not statistically significant.

In the East Midlands, 34.1% of pulmonary TB patients started treatment within 2 months of symptom onset and 67.1% within 4 months. There has been an increase in the proportion of pulmonary TB patients starting treatment more than 4 months after symptom onset from 28.9% in 2016 to 33.0% in 2017 although this difference was not statistically significant.

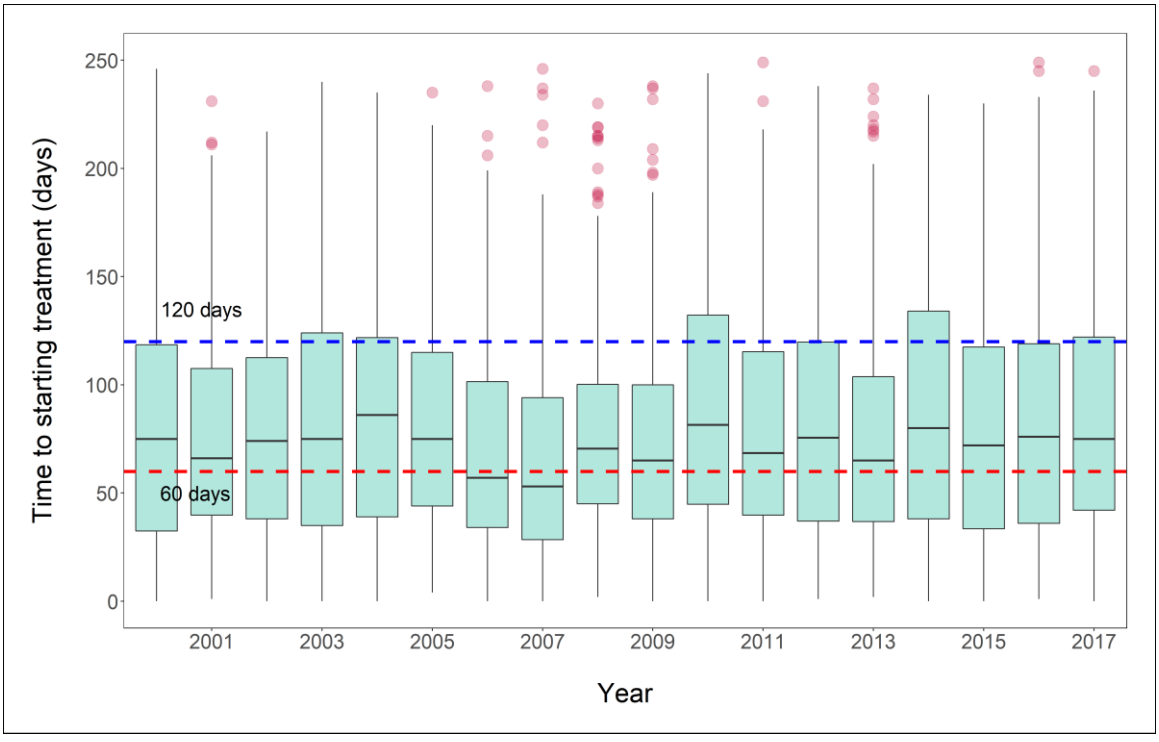
The median time from onset of symptoms (all TB patients) to starting treatment varies from year-to-year in the East Midlands, however since 2008 has remained at approximately 80 to 100 days (figures 17a and 17b). This suggests there is scope to reduce the time from development of symptoms to presenting for diagnosis and commencement of treatment as the earlier TB is diagnosed, the less likely it is that transmission to others will occur.

Table 4: Time between symptom onset and starting treatment for pulmonary TB patients, East Midlands, 2011 to 2017

Year	0-2 months		2-4 months		4+ months		Total
	Count	%	Count	%	Count	%	
2011	75	40.8	57	31	52	28.3	184
2012	69	35	63	32	65	33	197
2013	75	41.7	61	33.9	44	24.4	180
2014	74	36.1	57	27.8	74	36.1	205
2015	79	39.9	65	32.8	54	27.3	198
2016	71	39.4	57	31.7	52	28.9	180
2017	62	34.1	60	33	60	33	182

*excluding asymptomatic patients, and those with missing onset dates

Figure 17a: Box plot of time between symptom onset for pulmonary disease and treatment start, East Midlands, 2000 to 2017

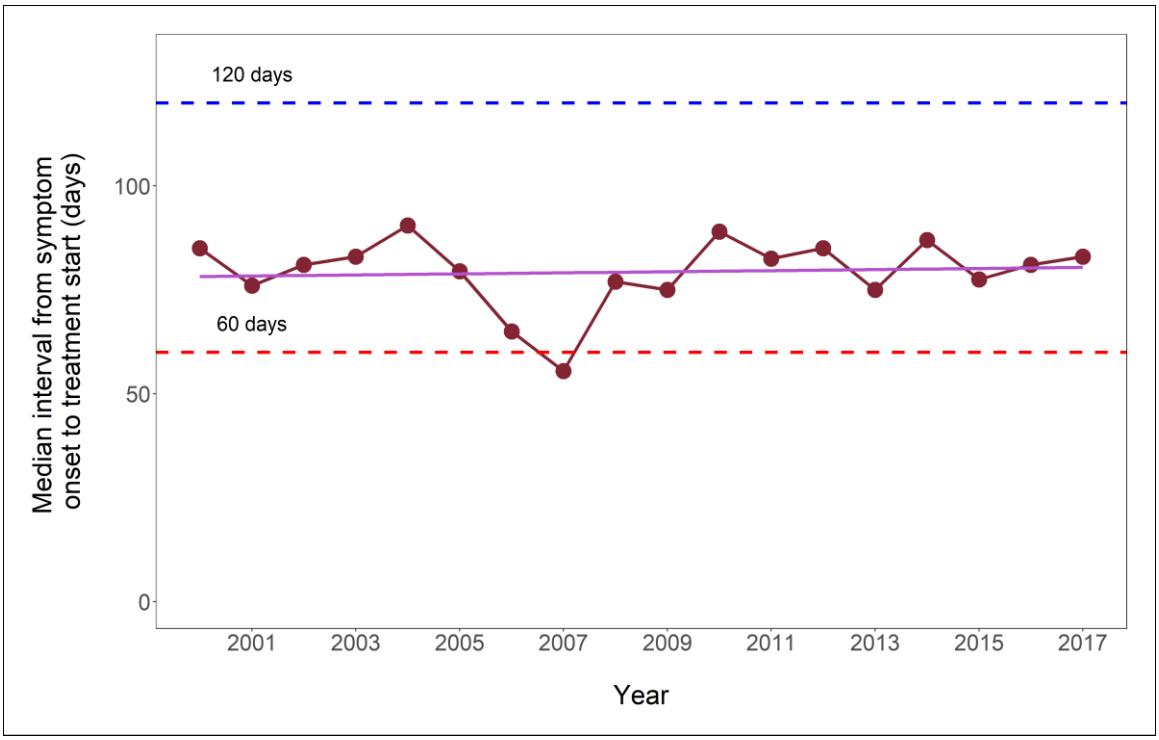


*excluding asymptomatic patients, those with missing onset dates and those with a symptom to onset delay of more than 250 days (outliers). The red dotted line corresponds to 60 days, and the blue dotted line to 120 days interval.

For an explanation of how to interpret box plots, please see Appendix B: Description of data sources and definitions and other explanations

TB Monitoring Indicator 6: Proportion of pulmonary TB patients starting treatment within 2 months of symptom onset

Figure 17b: Median time between symptom onset for pulmonary disease and treatment start, East Midlands, 2000 to 2017

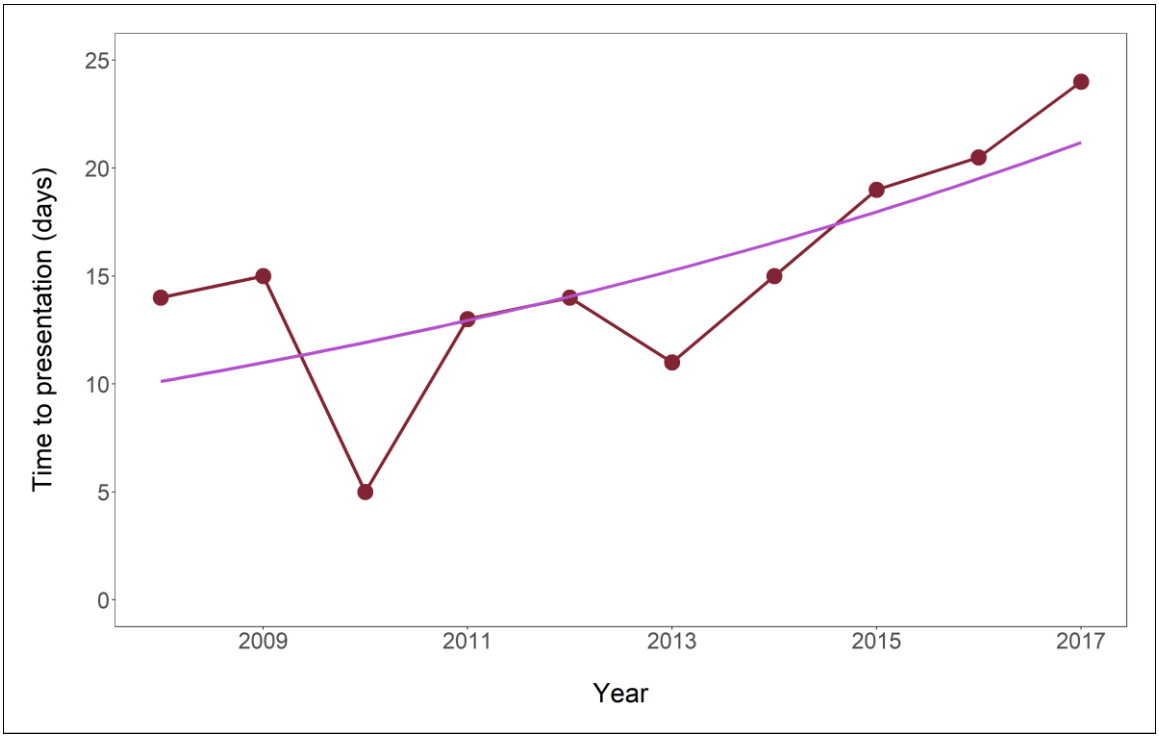


*excluding asymptomatic patients, those with missing onset dates and those with a symptom to onset delay of more than 250 days (outliers). The red dotted line corresponds to 60 days, and the blue dotted line to 120 days interval.

TB Monitoring Indicator 7: Proportion of pulmonary TB patients starting treatment within 4 months of symptom onset

Delays between the onset of symptoms and commencement of treatment can occur due to patient factors, for example a patient not seeking medical advice in a timely manner and service delays, such as healthcare professionals not recognising the symptoms are due to TB, through to delays in starting treatment even though the diagnosis has been made. Since 2008, the median delay from symptom onset to presentation, such as seeking medical help from any source including general practice, hospital, has varied from a low of 5 days to 24 days – although there is considerable variation around the median. The trend is upwards (figure 17c) indicating a continuing need to educate the public about the symptoms of TB and when to seek medical help.

Figure 17c: Median time between symptom onset and presenting for medical advice, pulmonary TB only, East Midlands, 2008 to 2017



Delays can also occur between initial presentation and diagnosis/onset of treatment, such as clinicians not recognising that the symptoms and signs were consistent with TB. The median interval from presentation to diagnosis for patients with pulmonary TB in 2017 was 33 days; although there is year-to-year variation, the delay has been in most years around 30-35 days since 2009. Although mostly below 60 days, by time the period from onset of symptoms to presentation is also added, most patients are not starting treatment within 60 days of onset of symptoms. This suggests there is also work to do with healthcare professionals as well as the public to improve the recognition of TB at an earlier stage.

Once patients are diagnosed, there is little delay in commencement of treatment – most patients start treatment within a day of diagnosis.

Characteristics of TB patients with a delay from onset of symptoms to diagnosis/treatment of more than 4 months

Patients (all TB sites) that have a long-time interval from onset of symptoms to diagnosis (>60 days) and then commencement of treatment are typically around 40 years of age (median 41 years), whereas the median age for pulmonary TB patients was 47 years of age.

For males, the proportion of TB patients with a delay in starting treatment of more than 2 months (where the delay is known) was 61.9%, 130/210. This was a similar proportion for females which was 60.3%, 85/141.

The proportion of pulmonary TB male patients with a delay in starting treatment of more than 2 months (where the delay is known) was 62.0%, 75/121. This is a higher proportion than for females (55.3%, 42/76).

The proportion of patients with TB (all types) with a delay was highest in those aged 65+, where 42 of the 56 (75.0%) patients in that age group in 2017 experienced a delay in starting treatment of 60 days or more since their symptoms started. The proportion experiencing the same delay in patients who had pulmonary TB was also highest in those aged 65+ where 30 of the 39 (76.9%) patients diagnosed in 2017 experienced a delay of more than 60 days. Clearly it is important to reduce the time for symptom onset to treatment start (particularly with pulmonary TB), as this is key to reducing transmission. It is therefore concerning that in all age groups (except those aged less than 25 years), for pulmonary TB, that the majority were starting treatment more than 60 days after their symptoms started.

The proportion with a symptom onset to commencement of treatment >60 days within each ethnic group shows that there is not particular difference between the common ethnic groups with TB and delay in commencement of treatment. In 2017, for those identifying of white ethnicity, 62.8% experienced a delay in commencing treatment of >60 days. For those identifying as Black-African this was 65.4%, for Indian ethnicity, 59.6%, while Pakistani ethnicity was 54.5%. For other ethnic groups the number of patients is small so not particular pattern can be discerned.

TB outcomes in drug-sensitive cohort

Drug-sensitive cohort

For the purposes of TB outcome reporting, the drug-sensitive cohort excludes all patients with rifampicin-resistant TB isolates (initial or amplified) including multidrug-resistant TB (MDR-TB, initial or amplified), and non-culture-confirmed patients treated for MDR-TB [7]. Under this definition, all patients whose TB has resistance to isoniazid, ethambutol and/or pyrazinamide but without resistance to rifampicin are included in the drug sensitive cohort. TB outcomes among patients with drug-resistant disease are considered in chapter 6.

Treatment outcomes for the drug sensitive cohort are reported separately for the following groups:

- For patients with an expected duration of treatment less than 12 months, outcomes at 12 months are reported. This group excludes individuals with central nervous system (CNS) disease, who would be treated for 12 months. In addition, those with spinal, cryptic disseminated or miliary disease are excluded from this group, as CNS involvement cannot be reliably ruled out for the purposes of reporting.
- For patients with CNS, spinal, cryptic disseminated or miliary disease, the overall outcome recorded for treatment outcome is reported. However, for patients notified in 2016, information on the final outcome was collected in 2017 and may only be 1 year after start of treatment for many patients, and treatment may still be ongoing.

Due to the length of time of treatment, the most current treatment outcome data is reported for patients whose TB was notified in 2016. In line with national reporting, outcomes are reported for those that started treatment and those who did not, such as diagnosed post-mortem; died without starting treatment; lost to follow up without starting treatment. In 2016, 341 patients with TB were notified, of these 200 (96.2%) were sensitive to rifampicin and are included in the drug sensitive cohort.

Outcomes for TB patients with expected treatment of less than 12 months

For patients notified in 2016 in the drug sensitive TB cohort – defined as those with no initial or acquired resistance to rifampicin or multidrug resistance at any time, and no initial or acquired resistance and not treated empirically as multidrug resistant without culture – 92.2% (305) had non-CNS, spinal, miliary or cryptic disseminated disease. Of these, 74.8% (228) completed treatment within 12 months (Table 5). This is a reduction from previous years and represents a further decline from a high of 88.1% in 2013; this adverse trend will therefore need to be monitored (figure 18). This is also lower than the proportion of patients in England completing treatment at 12 months (84.4%) [2].

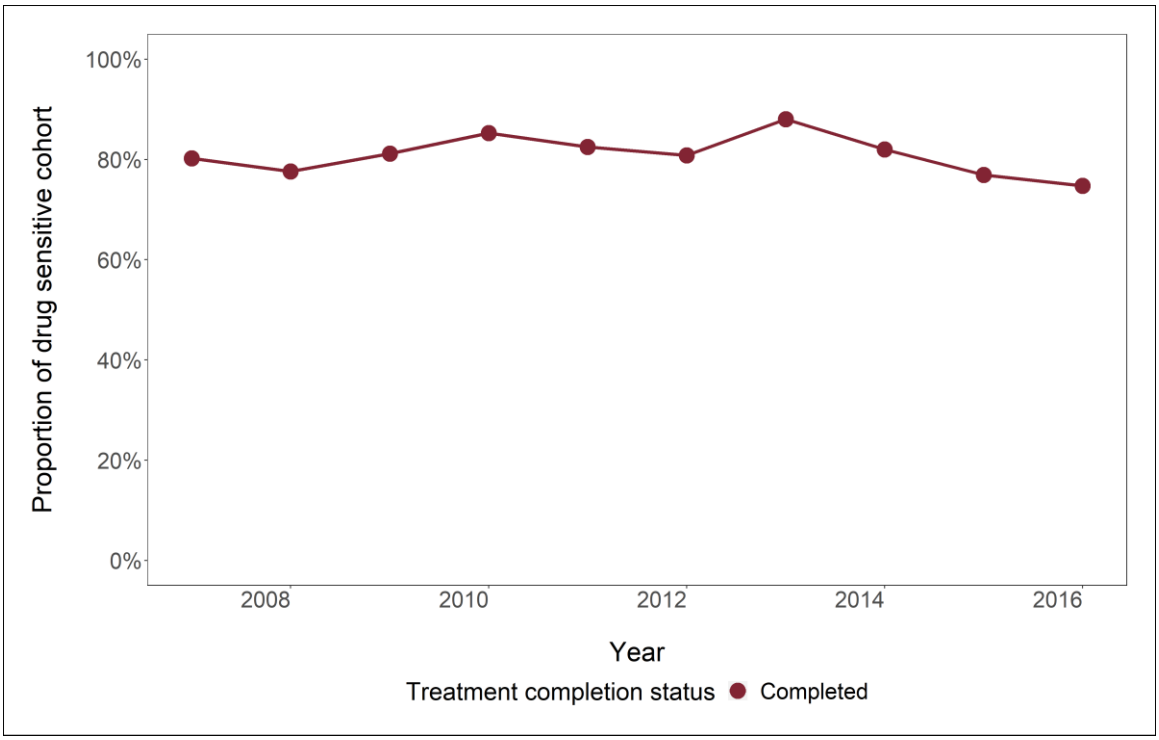
Table 5: Number and proportion completing treatment at 12 months, East Midlands, 2007 to 2016

Year	Count	%	Total
2007	382	80.3	476
2008	333	77.6	429
2009	392	81.2	483
2010	371	85.3	435
2011	363	82.5	440
2012	354	80.8	438
2013	317	88.1	360
2014	278	82.0	339
2015	233	76.9	303
2016	228	74.8	305

*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

TB Monitoring Indicator 10: Proportion of drug sensitive TB patients who had completed a full course of treatment by 12 months

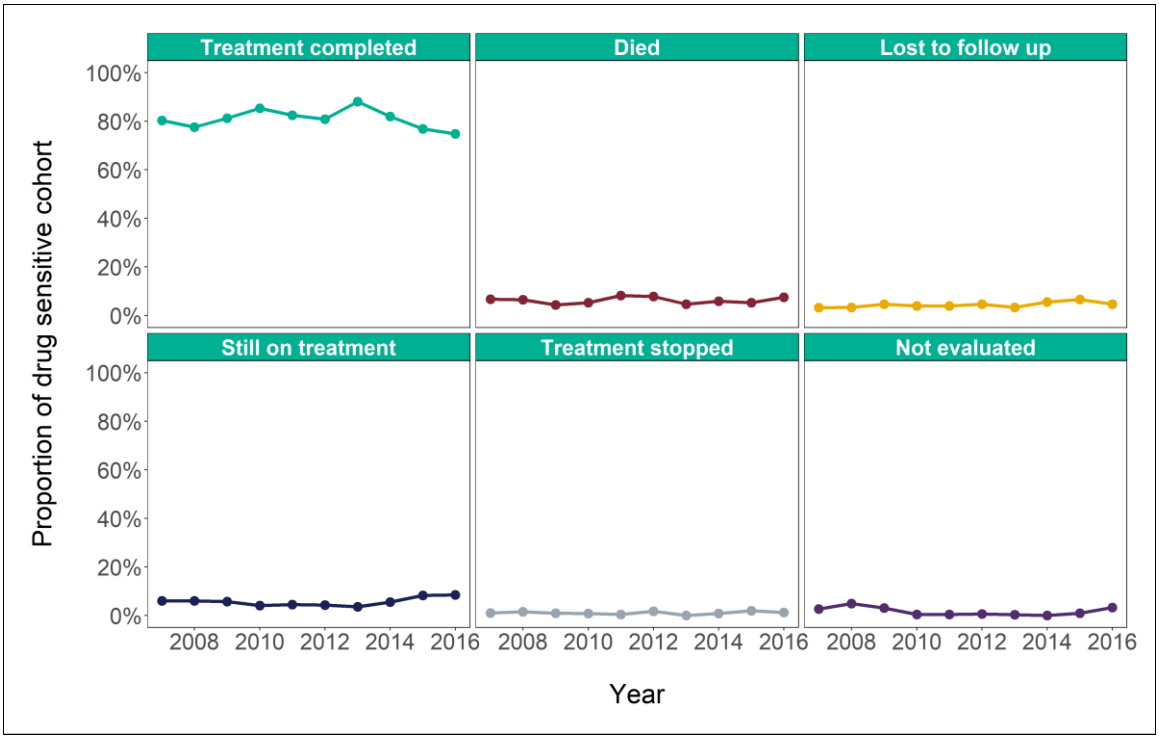
Figure 18: Proportion of drug sensitive cohort patients completing treatment at 12 months, East Midlands, 2007 to 2016



*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

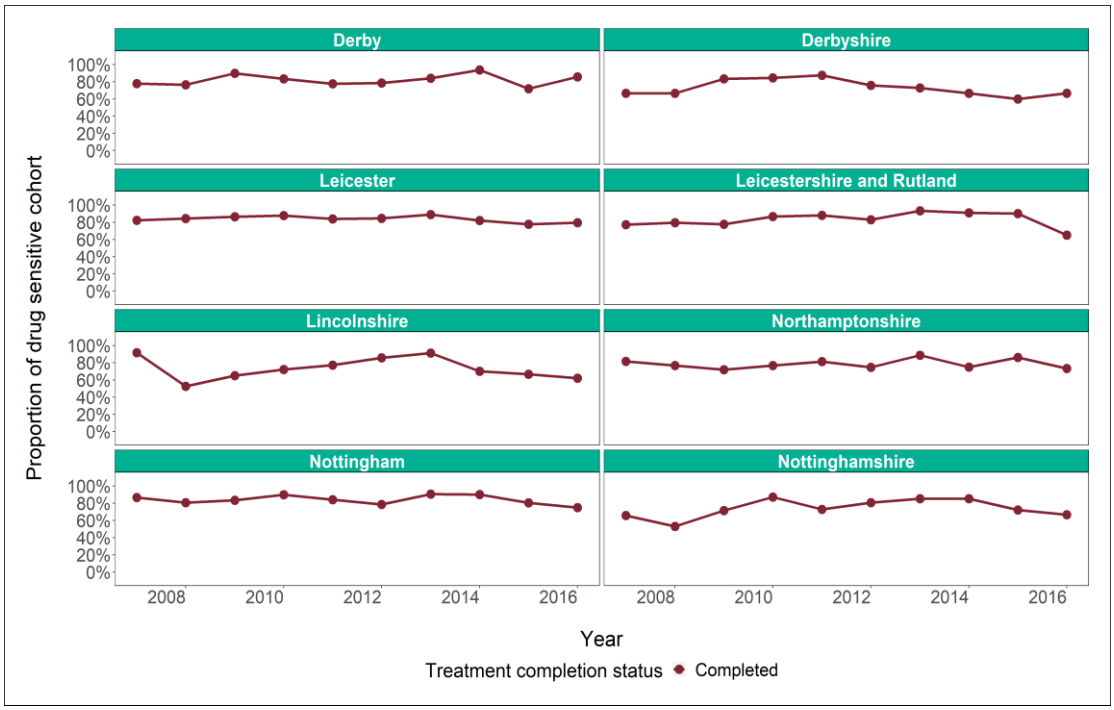
In this cohort 7.5% died, 4.6% were lost to follow up, 8.5% were still on treatment at the end of 12 months, a small proportion (1.3%) had their treatment stopped and 3.3% had not had their treatment outcome evaluated – figure 19* and table 7 below. These figures have been fairly stable from year-to-year for some time.

Figure 19: Outcomes of treatment for the drug sensitive cohort at 12 months after treatment commencement, East Midlands, 2007 to 2016



*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

Figure 20: Outcomes of treatment for the drug sensitive cohort at 12 months after treatment commencement by UTLA, 2007 to 2016



*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

Treatment completion proportions in 2016 varied by UTLA area, ranging from 62.1% (Lincolnshire) to 85.7% (Derby). The trends in treatment completion by UTLA are displayed in figure 20 and tabulated in table 6 below.

Table 6: Proportions completing treatment for the drug sensitive cohort at 12 months after treatment commencement by UTLA, 2007 to 2016

UTLA	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	%									
Derby	77.8	76.5	89.7	83.3	77.6	78.6	84.0	93.8	71.9	85.7
Derbyshire	66.7	66.7	83.3	84.6	87.5	75.9	72.7	66.7	60.0	66.7
Leicester	82.3	84.3	86.4	87.8	83.8	84.6	89.0	82.1	77.7	79.5
Leicestershire and Rutland	77.1	79.4	77.6	86.5	87.9	82.9	93.3	90.9	90.0	65.0
Lincolnshire	91.7	52.6	65.0	72.2	77.3	85.7	91.3	70.0	66.7	62.1
Northamptonshire	81.7	76.8	71.8	76.7	81.4	74.7	88.6	75.0	86.1	73.3
Nottingham	86.7	80.6	83.3	89.8	84.1	78.6	90.6	90.0	80.4	75.0
Nottinghamshire	65.6	52.9	71.4	87.1	72.7	80.6	85.2	85.3	72.2	66.7

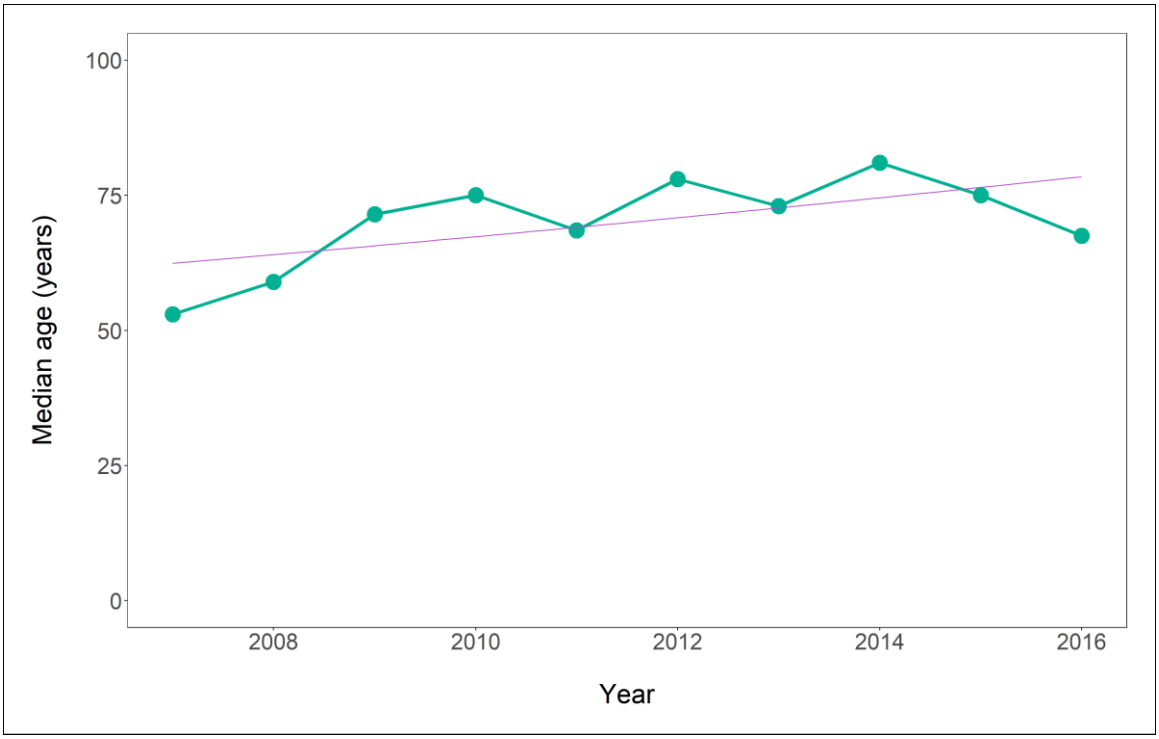
*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

The most common reason for not completing treatment at 12 months (those notified in 2016) was still being on treatment (26 patients, 8.5%) [Table 9] – a similar proportion to those notified in 2015. The next most common reason was death. Of the patients that were originally notified in 2016, 23 (7.5%) died. For most of these it was unknown if TB contributed to the death or not (56.5% of those that died). However, in 5 (21.7% of those that died) patients, TB either caused or contributed to the patient's death. Deaths from or contributed to by TB, should be avoidable, so it is particularly important to know if TB caused or contributed to death, therefore the cause of death data quality needs improving, in order to provide a clearer picture of the situation in future.

Since 2007, the trend in the median age of patients (drug sensitive cohort) that have died is towards older age, with the median age in 2016 being 67.5 years, although there is fluctuation from year-to-year (figure 21). Understanding why patients die as a result of their TB or where it contributed to their death tend to be older, may provide insights into how to prevent this outcome.

A more in-depth analysis of TB cases that died between 2014-2016 (n=77) was carried out recently in the East Midlands using both ETS data and cohort review forms. This found that cases that died were statistically more likely to be 70+ years old; of white ethnicity; UK-born; have pulmonary disease; and have 1 or more comorbidity when compared to TB cases that had not died. However, this was an experimental analysis based on only 77 cases and should be interpreted with care, as for 45 of these cases (58.4%) the relationship of TB to death was unknown.

Figure 21: Age trend of patients who have died where TB caused or contributed to the death for the drug sensitive cohort, 2007 to 2016



*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

Fourteen patients were lost to follow up (4.6%). Where the reason for loss of follow up was known 9 of these patients had left the UK. There were 4 (1.3%) patients whose treatment had been stopped and 10 (3.3%) whose treatment outcome had not be evaluated at 12 months.

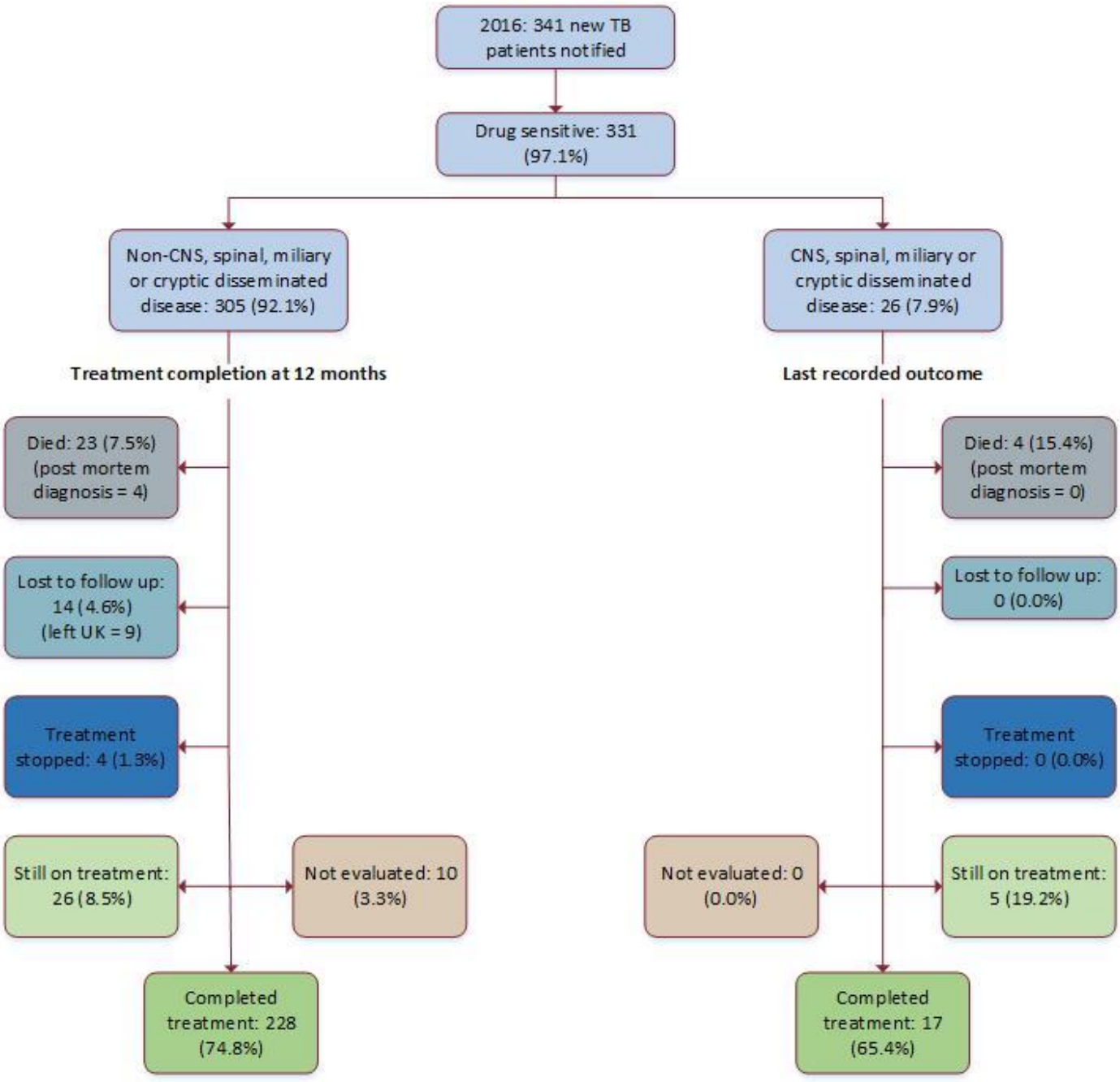
Where ethnicity was known in those lost to follow up, in those identifying as Indian ethnicity in those diagnosed in 2016 was 3.4%, whereas for those of White ethnicity the lost to follow up was 5.7%.

Table 7: TB outcome at 12 months, East Midlands, patients diagnosed in 2016

Treatment outcome	Count	%
Treatment completed	228	74.8
Still on treatment	26	8.5
Treatment stopped	4	1.3
Died	23	7.5
Lost to follow up	14	4.6
Not evaluated	10	3.3
Total	305	100.0

*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

Figure 22: Flow chart showing TB outcome for drug sensitive cohort, East Midlands, patients diagnosed in 2016



*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

The majority of patients notified in 2016 (47.9%, 146) completed treatment between 6 and 8months (Table 8). There were 17 patients (5.6%) for whom treatment took longer than 12 months to complete and for 20% there was another outcome (including death, loss to follow up, treatment having been stopped and treatment outcome not having been evaluated).

Table 8: Time to treatment completion for drug sensitive patients with expected treatment duration of less than 12months, East Midlands, 2016

Time to complete treatment	Count	%
<6 months (168 days)	26	8.5
6-8 months	146	47.9
8-10 months	34	11.1
10-12 months	21	6.9
>12 months	17	5.6
Other outcome (death, lost to follow up, treatment stopped, not evaluated	61	20.0
Total	305	100.0

* Excludes patients in the DR cohort and those with CNS, spinal, miliary or cryptic disseminated TB. Treatment completed at last recorded outcome

Outcomes for drug sensitive cohort of patients with CNS, spinal, miliary or cryptic disseminated TB

Of the 26 patients with CNS, spinal, miliary or cryptic disease notified in 2016, 17, (65.4%) had completed their treatment, 5, (19.2%) were still on treatment and 4 (15.4%) had died at the last recorded outcome (Table 9). The median treatment time for those that completed treatment was 239 days (IQR 177 – 365) (approximately 8 months).

Table 9: Overall outcome for patients with rifampicin sensitive, CNS, spinal, miliary or cryptic disseminated disease, East Midlands, patients notified in 2016

Treatment outcome	Count	%
Treatment completed	17	65.4
Still on treatment	5	19.2
Treatment stopped	0	0.0
Died	4	15.4
Lost to follow up	0	0.0
Not evaluated	0	0.0
Total	26	100.0

*Excludes rifampicin resistant, multidrug resistant TB, and patients with CNS, spinal, miliary or cryptic disseminated disease

Deaths and lost to follow up in the drug sensitive cohort (all patients including those with CNS, miliary and cryptic disseminated disease)

Overall, 8.5% (28) of drug-sensitive patients notified in 2016 had died at the last recorded outcome with 75% recorded as having pulmonary TB (21 patients).

The proportion of all drug-sensitive patients notified in 2016 and lost to follow up at the last recorded outcome was 4.2% (14 patients), of these 9 (64.3%) had left the UK and the remainder were recorded as ‘other or unknown reason’.

Drug resistant TB (including outcomes in the drug resistant cohort)

Drug resistance

TB Monitoring Indicator 9: Proportion of culture confirmed TB patients with drug susceptibility testing reported for the 4 first-line agents

TB Monitoring Indicator 18: Proportion of culture confirmed TB patients with any first-line drug resistance

TB Monitoring Indicator 19: Proportion of culture confirmed TB patients with multi-drug resistant TB

Overall initial drug resistance

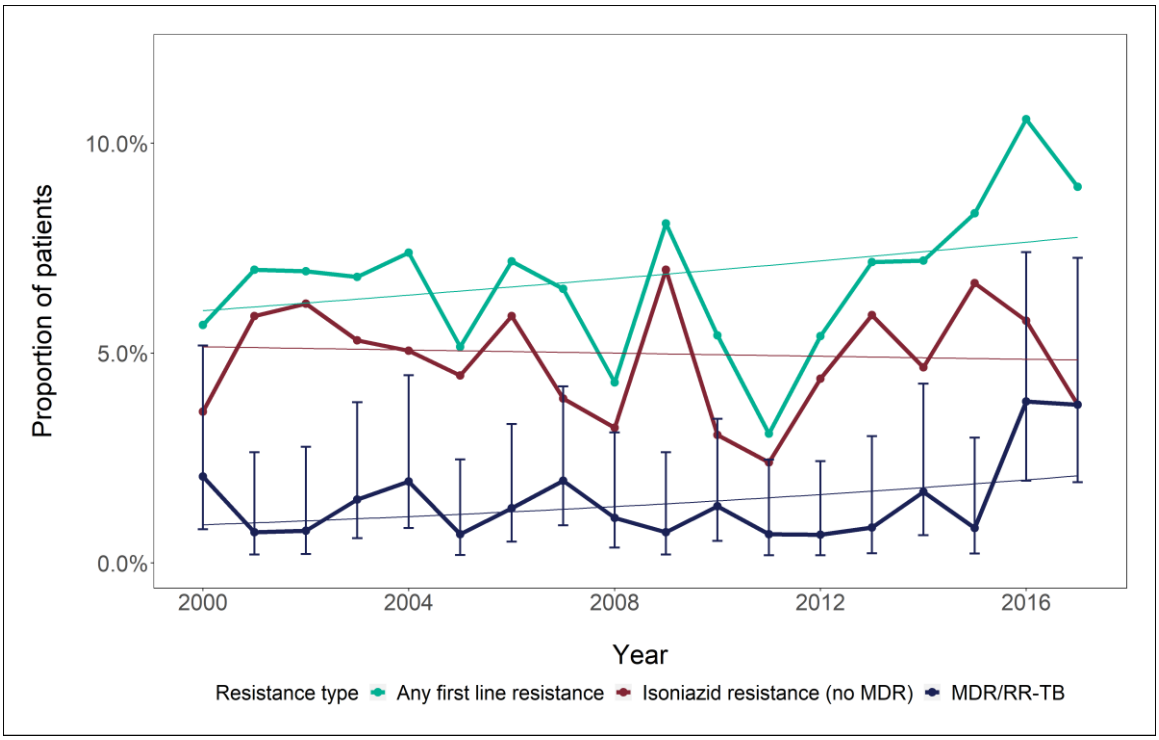
There are a wide range of anti-TB antibiotic drugs; resistance may occur to 1 or more of these antibiotics and may occur in complex combinations. A distinction is made between first, second and third line TB antibiotic drugs depending upon their clinical effectiveness. First-line drugs include isoniazid, rifampicin, pyrazinamide and ethambutol. Second-line drugs at the time of the data being generated were injectable agents, such as amikacin, capreomycin and kanamycin; fluoroquinolones, for example, moxifloxacin, ofloxacin, ciprofloxacin, and other oral bacteriostatic agents. MDR-TB patients have initial resistance to at least isoniazid and rifampicin. Extensively, drug-resistant TB patients (XDR-TB) have initial MDR and resistance to at least 1 injectable agent and at least 1 fluoroquinolone[7].

In 2017, 98.6% (211) of culture-confirmed patients had drug susceptibility test (DST) results for all 4 first-line drugs (isoniazid, rifampicin, ethambutol and pyrazinamide) and 99.1% (212) had results recorded for at least isoniazid and rifampicin. Of those with DST results for at least isoniazid and rifampicin, the proportion of patients with TB resistant to 1 or more first-line drugs was 9.0% (19 patients), which was a non-significant decrease from 2016 (10.6 %, 22 patients). The proportion of patients with isoniazid-resistant TB without MDR decreased (non-significant) from 5.8% (12 patients) in 2016 to 3.8% (8 patients) (Figure 23).

In 2017, out of the culture-confirmed patients with DST results for at least isoniazid and rifampicin, there was a higher proportion of TB resistance to 1 or more first-line drugs in females (13.8%, 11/80) compared to males (6.1%, 8/132), however this difference was not significant. There was also a higher proportion of resistant TB among those born

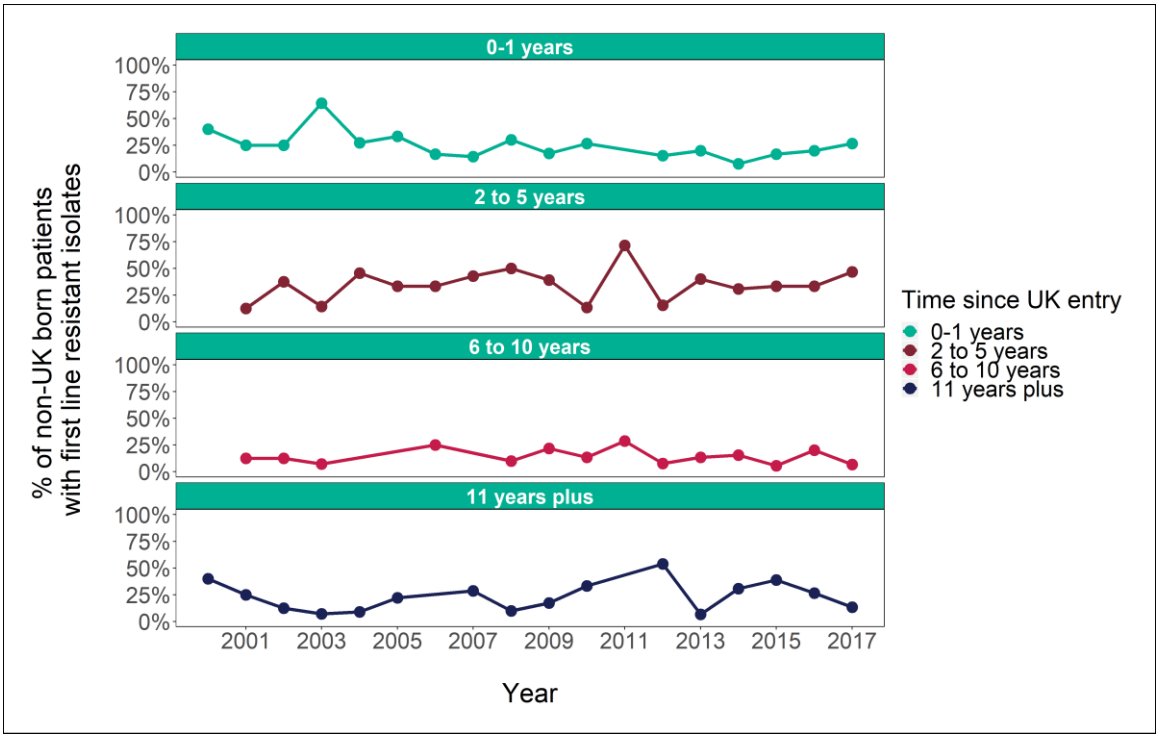
outside of the UK (10.8%, 15/139) than UK born (6.5%, 4/62). Again, although the overall numbers are small, it is perhaps interesting that they are not dropping at the same pace as the overall count of patients with TB is falling. The vast majority of the patients with first-line resistant isolates are non-UK born, so considering the reductions in overall incidence of TB in non-UK born patients that increase is surprising (data not shown).

Figure 23: Trend in the proportion of patients with TB isolates which have resistance to first-line drugs, 2000 to 2017



Of the non-UK born patients with TB isolates that are first-line resistant, most have been in the UK for 2 years or more, so these patients with isolates displaying resistance are not recent arrivals in the UK; this therefore suggests either reactivation of latent disease or exposure through links to other higher risk countries/communities (figure 24).

Figure 24: Trend in the proportion of patients who are not UK born with TB isolates which have resistance to first-line drugs, 2000 to 2017



Drug-resistant cohort

The drug resistant (DR) cohort includes culture confirmed patients with initial and acquired MDR/ Rifampicin resistant (RR)-TB, as well as those treated with a second-line regimen for MDR/RR-TB without resistant phenotypic DST results. TB patients may be treated with a second-line regimen in the absence of phenotypic DSTs if they were diagnosed abroad, were diagnosed with genotypic methods, were a contact of an MDR/RR-TB case or for other clinical reasons.

The numbers in the DR cohort (including those without a culture result) have increased from 2 patients in 2015 to 10 patients in 2016 and 11 in 2017, however there is a lot of year-to-year variability and the numbers are small in any one year, so no particular trend can be established. The 2017 MDR/RR-TB and XDR patients and are explained below in more detail.

Multi-drug resistant/rifampicin resistant TB (MDR/RR) patients

The proportion of MDR/RR TB patients (culture confirmed with DST results for at least isoniazid and rifampicin) was 3.9% (8 patients) in 2016 and 3.8% (8 patients) in 2017; although this is higher than the proportion of MDR TB patients in England (1.7%), the number of patients in any one year varies widely from year to year, so no particular

inference should be derived from this difference. In addition, there were also 3 patients in 2017 treated for MDR TB without DST results.

Extensively Drug Resistant (XDR) patients

XDR patients are reported as a subset of MDR patients and have resistance to isoniazid and rifampicin, plus any fluoroquinolone and to at least 1 of the 3 injectable second-line drugs. These patients are rare in the East Midlands. However, there were a small number (<5) patients treated as part of an outbreak cluster in 2017 for XDR-TB.

TB outcome at 24 months for patients with rifampicin resistant disease

Due to the length of time of treatment for patients with drug resistant TB, the most current treatment outcome data is reported for patients notified in 2015. In 2015, there were only 2 patients with DR TB, 1 had completed treatment at 24 months and 1 case was lost to follow up having left the UK.

TB Monitoring Indicator 13: Proportion of drug resistant TB patients who had completed treatment at 24 months

TB in under-served populations

Social risk factors

Patients with TB in the East Midlands with recognised, reported risk factors form a relatively small part of the overall number of people with TB for the region. Nonetheless although the numbers are small the trends are increasing, for example in homelessness and drug or alcohol misuse. In 2017, information on social risk factors was completed for 256 (76.7%) patients aged 15 years and above; 19.1% of patients had 1 or more social risk factors (Table 10). This was an increase from 11.3% in 2016 and the highest proportion recorded since the start of social risk factor data collect. A social risk factor for the acquisition of TB is defined as current/history of homelessness, current/history of drug use, current/history of imprisonment or current alcohol misuse. Homelessness was the most common social risk factor (7.8%) followed by drug misuse (5.9%), alcohol misuse (5.0%) and imprisonment (4.2%) (Table 11). These risk factors are not mutually exclusive as 5.5% of patients (14) had multiple risk factors recorded. Very few patients with TB over the years have a recorded history of being an immigration centre detainee, with none having been recorded as such in 2017 (however the data quality for this risk factor is poor). Overall the data quality for risk factor recording could be improved – with in recent years, around 20% to 22% of patients with TB having no risk factor data recorded.

Table 10: Number and proportion of patients with TB who had any risk factor social risk factor recorded, East Midlands, 2017

Year	Count	%	Total
2010	25	6.5	384
2011	29	8.0	363
2012	24	6.6	362
2013	29	9.5	305
2014	34	12.4	275
2015	30	11.0	273
2016	30	11.3	265
2017	49	19.1	256

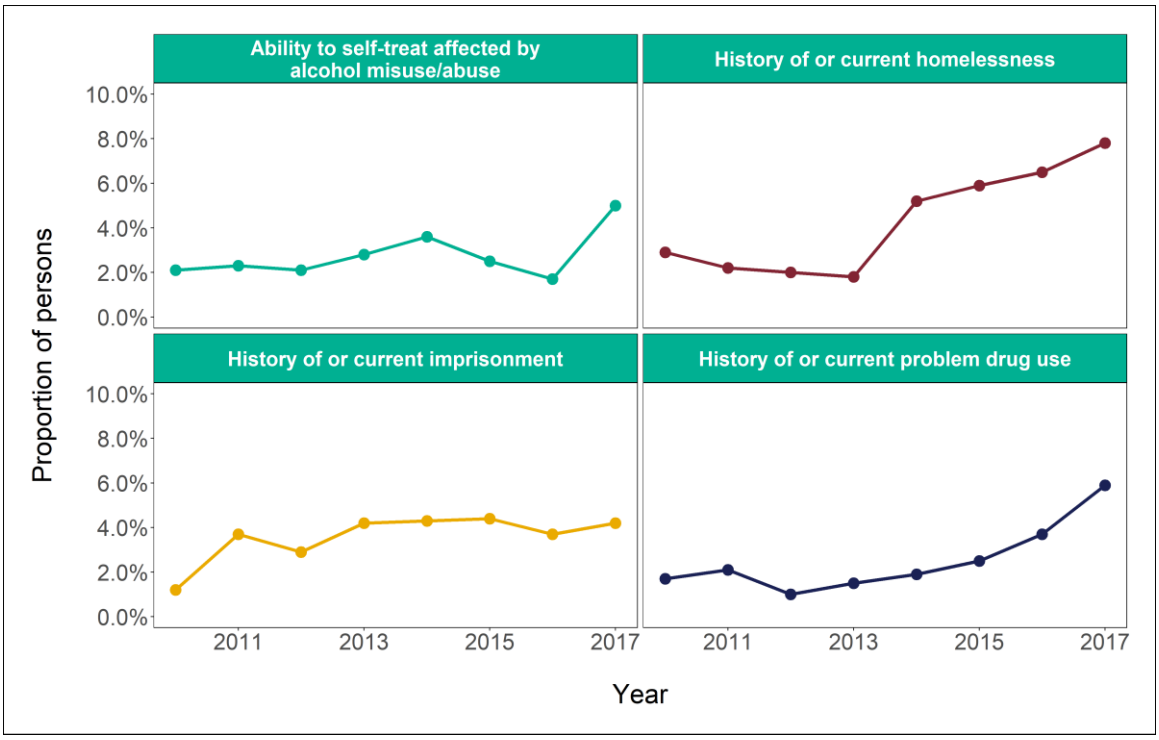
* For patients 15 years and over. Total number of patients for the year with risk factor data recorded

There was a statistically significantly higher proportion of TB patients with recorded social risk factors in men (over the age of 15 years), of 24.0%, 37/154 as compared to females, 11.8%, 12/102) p=0.015 and in UK born patients (27.0%, 24/89) compared to non-UK born patients (14.0%, 23/164) p=0.011.

Individuals with social risk factors were statistically significantly more likely to be a pulmonary TB case than those without social risk factors. Of the 49 patients with risk factors, 77.6%, (38/49) had pulmonary disease, compared to those without risk factors where 54.1% (112/207) had pulmonary disease, p=0.003.

There was a statistically significantly higher proportion of patients receiving DOT within those that reported having 1 or more social risk factors (61.4%, 27/44) compared to those without any social risk factors recorded (9.7%, 19/196) p<0.0001.

Figure 25: Trend in key social risk factors among TB patients, East Midlands, 2009 to 2017



Treatment completion at 12 months for drug-sensitive TB patients notified in 2016 with at least 1 social risk factor was significantly lower than for patients with no social risk factors (53.6% vs 80.0%), p = 0.014. Treatment completion in those patients with at least 1 social risk factor in the East Midlands was lower than for England as a whole (80.0%)[2]. There were too few patients with risk factors to meaningfully compare the other outcomes (death, lost to follow up, still on treatment or treatment stopped) with those with no risk factors.

Table 11: TB outcome at 12 months, East Midlands, drug-sensitive patients diagnosed in 2016 with at least 1 social risk factor

Outcome at 12 months	No known risk factors		At least 1 risk factor		Total
	Count	%	Count	%	
Treatment completed	184	80.0	15	53.6	199
Died	12	5.2	3	10.7	15
Lost to follow up	7	3.0	2	7.1	9
Still on treatment	18	7.8	4	14.3	22
Treatment stopped	4	1.7	0	0.0	4
Not evaluated	5	2.2	4	14.3	9
Total	230	99.9	28	100.0	258

* For patients 15 years and older. Excludes rifampicin resistant TB and patients with CNS, spinal, miliary or cryptic disseminated disease

TB Monitoring Indicator 17: Proportion of patients with drug sensitive TB with at least 1 social risk factor who completed treatment within 12 months

Deprivation

TB has always been a disease associated with social deprivation and continues to be so. In any one year, approximately 40% of patients with TB are from the most deprived quintile and 70% from the bottom 2 quintiles for deprivation; 2017 was no exception with 41.6% of patients being from the most deprived quintile and 27.9% from the second most deprived quintile (Figure 26). For 2017, the rate of TB in the most deprived quintile was approximately 6-times higher than that in the least deprived quintile (15.3/100,000 vs 2.5/100,000) (Figure 27). Further strategies to address the ‘health-need’ gap for this group of patients are needed as the gap would appear to be static rather than improving.

Figure 26: TB case proportion by deprivation, East Midlands, 2010 to 2017

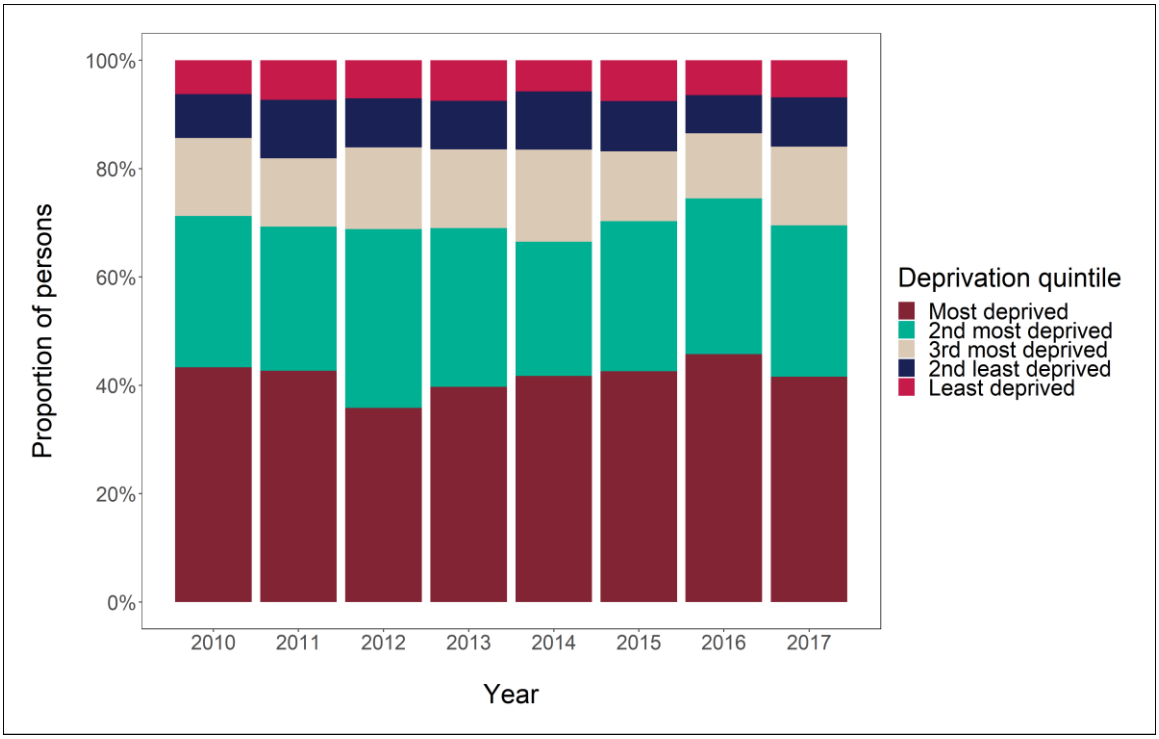
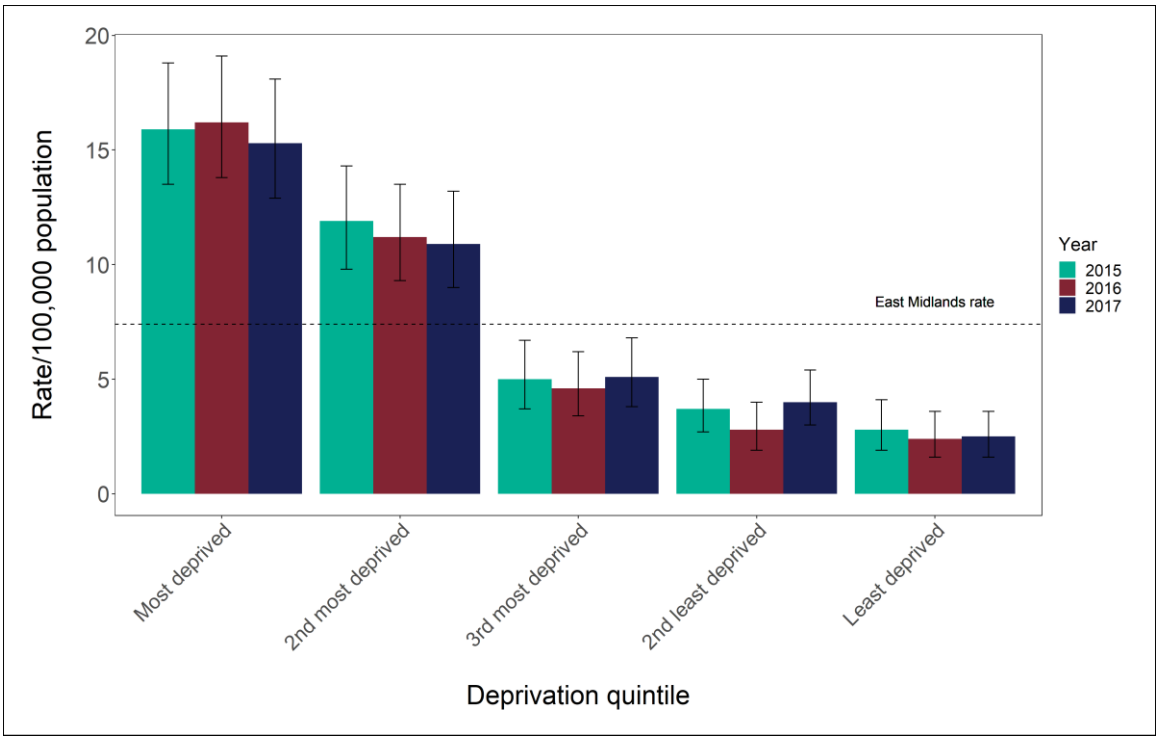


Figure 27: TB rate per 100,000 population by deprivation quintile with East Midlands overall rate, East Midlands, 2015 to 2017



Prisoners

One of the recognised social risk factors for having TB is a history of imprisonment. In the East Midlands since 2011, the number of people with TB who are or have a history of imprisonment is low ranging from 10 to 14 per year, or 2.9 – 4.4% of the total number of people with risk factors recorded. This compares with a population prevalence of imprisonment of 0.13% for the UK, therefore although small compared to the total numbers, prisoners are over-represented in the East Midlands population with TB [8].

TB-HIV co-infection and HIV testing of TB patients

HIV testing

TB complicating HIV infection is a well-recognised and particularly lethal clinical state, but can be successfully treated with a combination of highly active antiretroviral therapy (HAART) and appropriate TB antibiotic treatment[7]. For this reason, it is essential that all patients with TB should undergo HIV testing so that if they are diagnosed as having TB-HIV co-infection they can start curative TB treatment and HAART as soon as possible, and in so doing extend their life expectancy and reduce the risk of TB and HIV transmission to others.

Although the enhanced TB surveillance system does not collate data on HIV positivity in TB patients, it does collate data on whether patients were offered HIV testing as part of their care.

In 2017, data on HIV testing was recorded for 323 patients with previously unknown HIV status (excluding those diagnosed with TB at post-mortem). Of these 91.6% (296) were offered and received an HIV test – a similar figure to those offered and receiving testing in England overall (93.3%)[2]. There was, however, variation by UTLA of residence with the proportion being offered and receiving testing ranging from 74.1% in Lincolnshire to 100% in Derby and Derbyshire (Figure 28). Data on test results are not collected in ETS. HIV testing was not offered for 22 patients (6.8%) in 2017.

Only 30% of children were offered and received HIV testing (where their HIV status was not already known and they hadn't died), as compared to 93.6% of adults. While there may be good clinical reasons why children are not being offered HIV testing, this difference may represent an inequality which needs addressing, particularly as children in previous years are also less likely to be offered a test than adults. Patients were more likely to be offered and receive HIV testing if they were not born in the UK – 94.4% (203) were tested in 2017 as compared to 85.7% (90) of those that were UK-born. HIV testing is not therefore universal for patients presenting with TB (where their status is not already known).

Figures 28 and 29 below show the proportion of patients with TB who have been offered HIV testing in 2017 by UTLA and the trend since 2000, respectively. Although the overall coverage of HIV testing is good, there are some UTLA areas within the East Midlands where 20+% of patients were not offered HIV testing in 2017 and over a number of years. This is an important area to understand why such variation exists and implement improvements where appropriate.

Figure 28: HIV test status by UTLA area, East Midlands, 2017

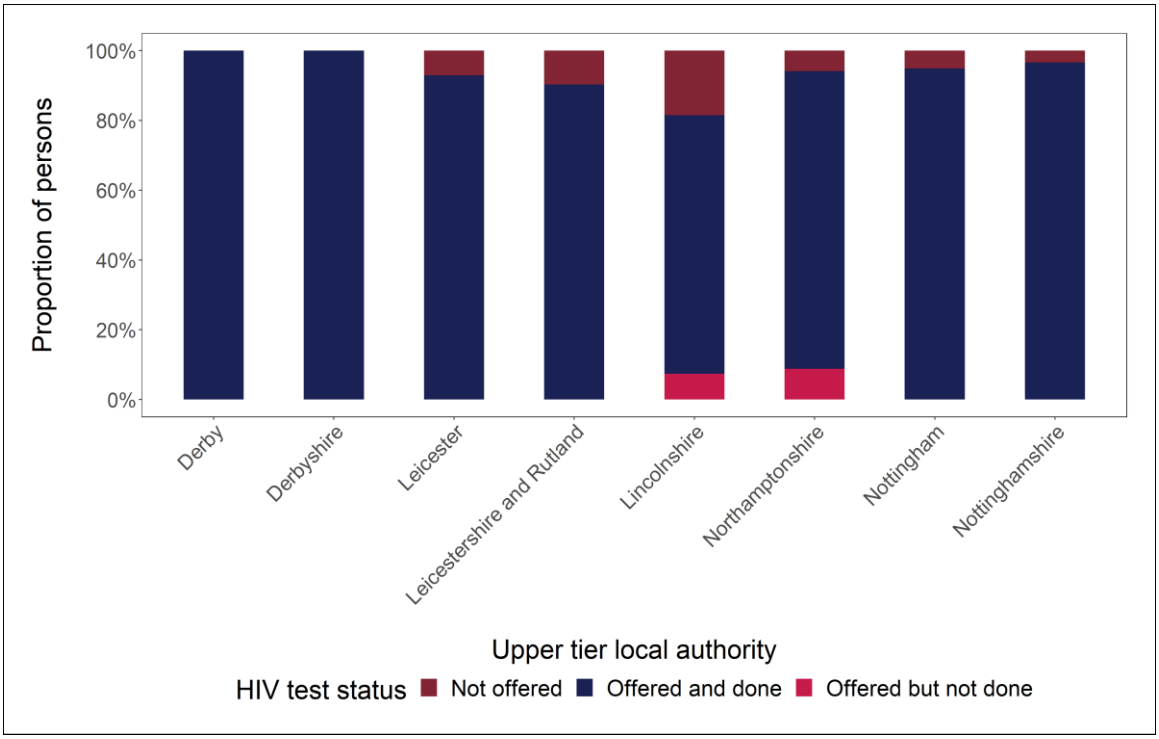
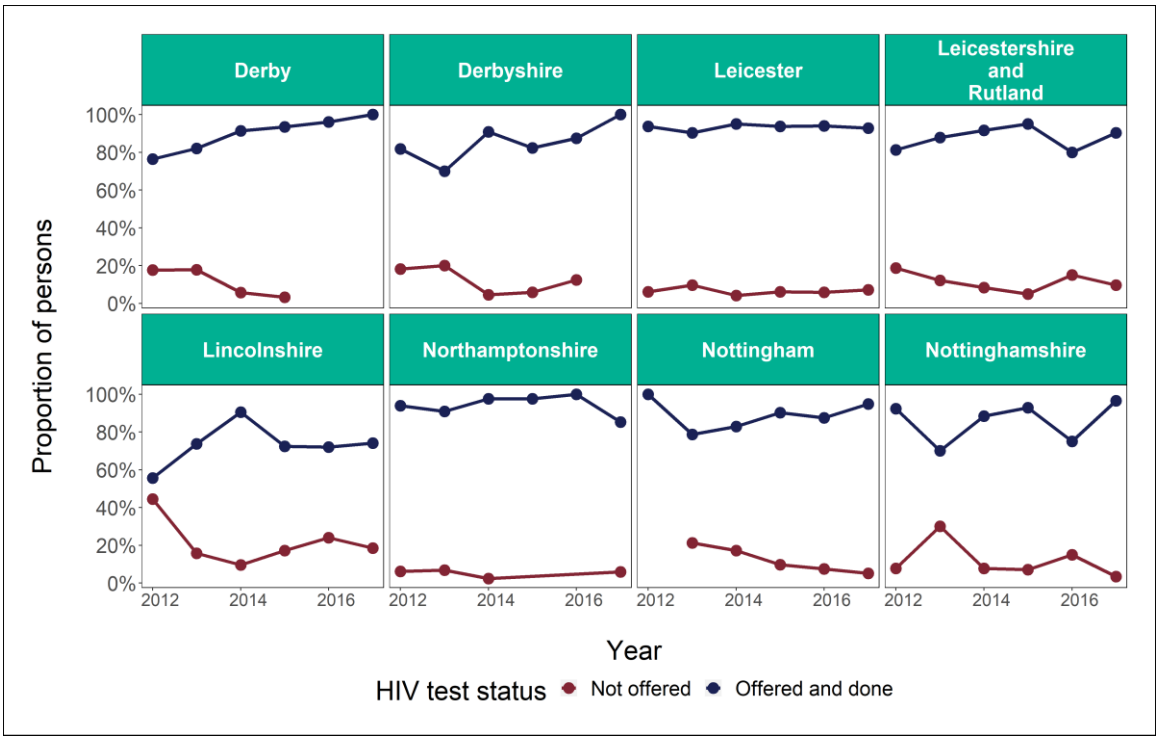


Figure 29: HIV test status by UTLA area, East Midlands, 2012 to 2017



Note: excludes patients where TB was diagnosed post-mortem and also those where their HIV status is already known.

TB Monitoring Indicator 16: Proportion of TB patients offered an HIV test

TB-HIV co-infection rates

To estimate co-infection nationally, TB notifications are matched annually by anonymously linking reports in ETS with the SOPHID and HANDD HIV datasets[i] for patients aged 15 years and older (see Tuberculosis in England: 2017 for methods[2]. The most recent year for which TB-HIV co-infection data are available for England is 2017. TB and HIV co-infection in the East Midlands is uncommon. In 2017, 3% of TB patients aged 15 years and above in the East Midlands were co-infected with HIV, a similar proportion to those identified nationally (2.8%). This is down from a peak of 8.5% in 2004[2].

[i] SOPHID: Survey of Prevalent HIV Infections Diagnosed. HANDD: HIV and AIDS New Diagnoses Database

BCG vaccination

BCG vaccine coverage

The BCG immunisation programme is a risk-based programme. The vaccine is recommended for individuals at higher risk of exposure to TB, particularly to protect against serious forms of the disease in infants. Detailed information on the BCG programme can be found in the 'Green Book'[9].

In the East Midlands none of the UTLA areas meet the criteria (TB incidence ≥40 per 100,000 population) for a universal neonatal BCG vaccination programme and therefore the BCG programme is selective. However, it is important to note that some localised areas (middle super output areas) in the region do have rates greater than 40/100,000. It may be appropriate to consider whether BCG vaccine is indicated in these limited areas.

From April 2015, neonatal BCG has been included as part of the Cover of Vaccination Evaluated Rapidly (COVER) programme and so data from the universal programme are publicly available[10]. For the selective programme it is difficult to gain denominator figures and provide meaningful coverage figures.

BCG vaccination status of TB patients

Historically, BCG vaccination was widely provided in adolescence in the UK and variably internationally to protect against the development of TB infections. BCG vaccination however is not 100% protective against TB. Where BCG vaccination has been recorded, between 70% and 80% of patients with TB since 2010 had previously been vaccinated with BCG [figure 30]. However, for a lot of patients, the data on BCG vaccination status is not recorded. Where prior BCG vaccination has been recorded, the median interval between vaccination and diagnosis of TB is around 30 to 40 years [figure 31]. People diagnosed with TB are more likely to have been vaccinated with BCG if they are not born in the UK compared with those who were [figure 32].

Figure 30: Trend in prior BCG vaccination in TB patients, 2010 to 2017

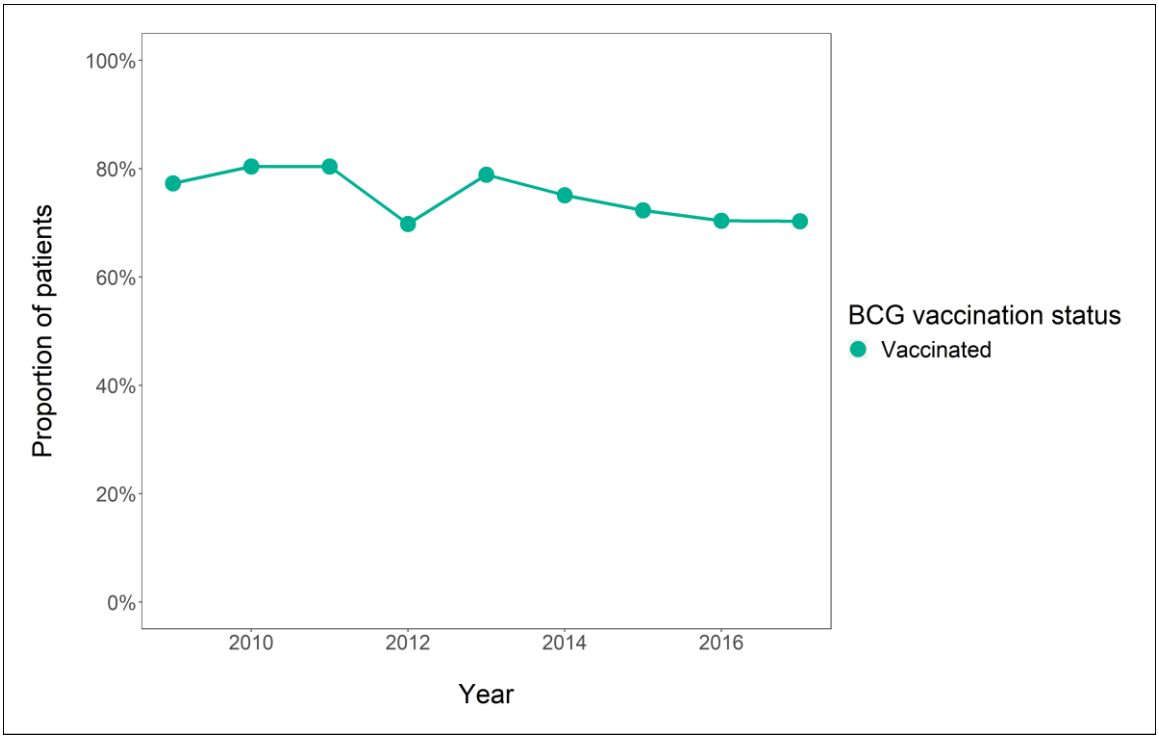


Figure 31: Trend in interval between BCG vaccination and diagnosis of TB, where BCG vaccination is recorded, 2008 to 2017

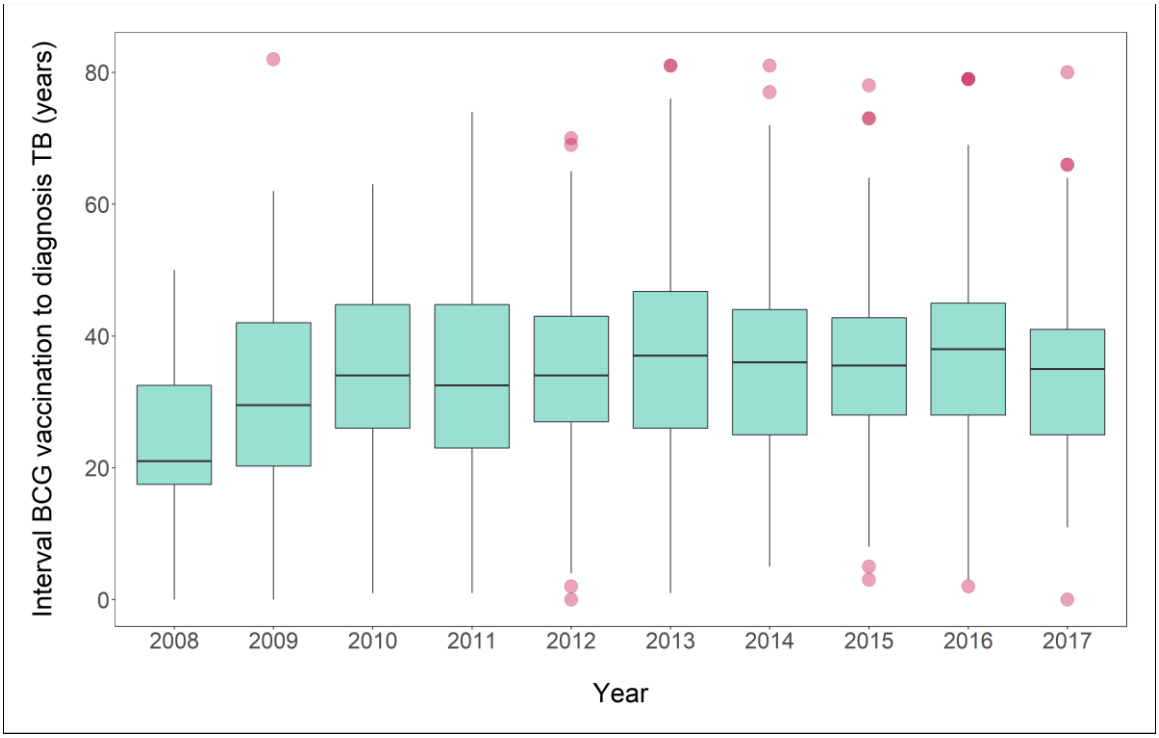
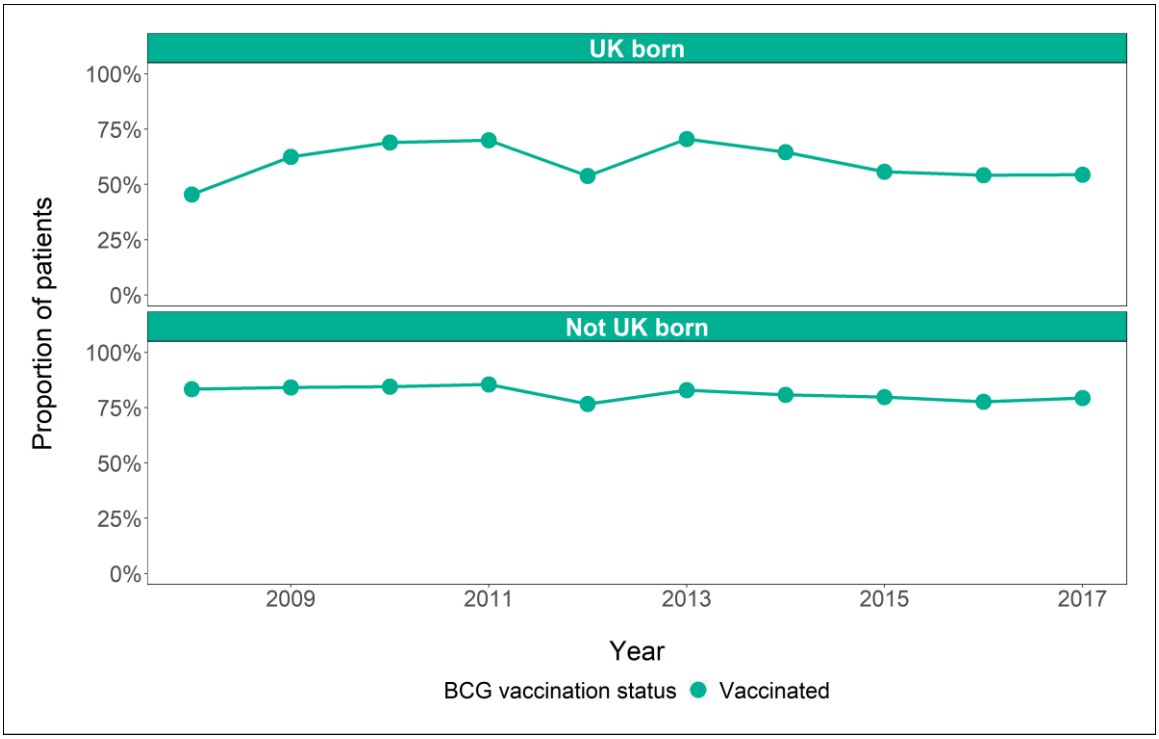


Figure 32: Trend in BCG vaccination status and whether UK born or not, 2008 to 2017



Latent TB infection testing and treatment

This report, derived from the ETS surveillance system, which is a national case register and management system for patients of active TB, does not record latent TB infection (LTBI). A new development has been the establishment of a national programme for the screening and treatment of LTBI for new migrants introduced by the Department of Health and PHE, which began in April 2015. Information for this programme is currently collected separately to the ETS[3].

Individuals are eligible for the national LTBI testing programme if they are aged 16-35 years and entered the UK from a high incidence country (≥150 patients per 100,000 or sub-Saharan Africa) within the last 5 years, and had been living in that high incidence country for 6months or longer. Eligible individuals are primarily identified prospectively by GP practices during the new patient registration process; however, some CCGs also search retrospectively through GP clinical systems or use community or secondary care services for identification.

Laboratory testing providers were selected for high TB incidence and burden CCGs[ii] following a national NHS procurement process and establishing a laboratory provider framework[11]. As per national programme clinical guidelines, individuals who receive a positive diagnostic result (IGRA) are referred to secondary care to rule out active TB and initiate LTBI treatment[12].

4 CCGs in the East Midlands have latent TB testing and treatment programmes that commenced in 2016: NHS Leicester City, NHS Nottingham City, NHS Southern Derbyshire CCGs and NHS Nene CCG, however data for the latter are not available. Details of the numbers of patients eligible for inclusion, their positivity and treatment outcomes are tabulated below.

[ii] High incidence is here defined as >20.0 cases per 100,000; high burden is defined as ≥0.5% of the TB case burden in England.

Table 12: Number of patients eligible for testing in the LTBI programme

Clinical Commissioning Group	2016	2017	Total
	Eligible for testing		
NHS Leicester City CCG	426	1,566	1992
NHS Nottingham City CCG	218	40	258
NHS Southern Derbyshire CCG	33	13	46

Table 13: Proportion of eligible patients found to be positive in the LTBI programme

Clinical Commissioning Group	Number positive	Total Number*	Proportion positive
NHS Leicester City CCG	324	1,992	16.3
NHS Nottingham City CCG	29	258	11.2
NHS Southern Derbyshire CCG	6	46	13.0
National Total	**4088**	**23572**	**17.3**

Treatment outcomes are only available for NHS Nottingham City CCG and are tabulated below.

Table 14: Treatment outcomes from the latent TB infection programme *

Clinical commissioning group (CCG)	Positives who should be referred for treatment (n)	(n)	Treatment start/referred (n)	(n)	(%)	(%)	Cohort who should have completed treatment (n)	(n)	Completed treatment (n)	(n)	(%)	(%)
	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017	2016	2017
NHS Nottingham CCG	25	34	12	26	48.0	76.5	12	26	12	16	100.0	61.5
National Total	**926**	**1364**	**597**	**823**	**64.5**	**60.3**	**568**	**741**	**480**	**526**	**84.5**	**71.0**

* Note: a borderline positive result is treated as positive in terms of referrals; borderline negative is treated as negative.

Outbreaks and incidents

The PHE East Midlands Health Protection Team was involved in investigating 40 TB incidents or outbreaks during 2017 (Table 15) – an increase from 31 in 2016. The most common incidents reported involved patients of TB in hospital/healthcare settings (30%, 12/40). Lincolnshire reported the highest number of TB incidents in the East Midlands in 2017.

Table 15: Number of TB incidents reported to East Midlands HPT by setting and UTLA, East Midlands, 2017*

UTLA	Incident setting									
	Care Home	College/ University	Community	Custodial Institution	Homeless	Hospital/ Healthcare setting	Household	School/ Nursery	Workplace	Total
Derby City			1	1	1	2		1		**6**
Derbyshire										**0**
Leicester City		2				3	1	3		**9**
Leicestershire County and Rutland	1						1	1	3	**6**
Lincolnshire						6	1		3	**10**
Northamptonshire	1		1			1			1	**4**
Nottingham City	1			1						**2**
Nottinghamshire	1		1				1			**3**
Total	**4**	**2**	**3**	**2**	**1**	**12**	**4**	**5**	**7**	**40**

* Data source: HPzone

Discussion

This report of TB in the East Midlands includes data up until end of 2017 provides the latest epidemiological picture of TB in the area.

The incidence of TB in the East Midlands has increased in 2017 for the first time since 2012. Although this increase was not significant, it is of concern as we are over halfway through the implementation period of the Collaborative TB strategy 2015-2020, which aims for a year-on-year reduction in TB incidence and health inequalities[3.] This trend will require monitoring and renewed efforts are required to ensure targets of TB control and elimination are met.

The reasons for this increase are currently unclear and likely to be multifactorial. Although the East Midlands figures remain below the TB rate for England as a whole[2] there remains variation in TB across the East Midlands. The highest rates of TB continue to be concentrated in the large urban areas of Leicester City, Nottingham City, Derby City and Northampton town where the latent TB screening programme has now been targeted. The UTLAs Leicester City, Derby City, Derbyshire, Leicestershire and Rutland and Nottinghamshire all experienced increases in TB incidence from 2016 to 2017.

Decreases were noted in the non-UK born population in the East Midlands for 2017 however the TB rate in the non-UK born population is 13-times higher than the UK-born population; with India being the most common country of birth. Over half of the non-UK-born patients in the East Midlands were within those that had been in the UK for more than 6 years (60%). The decreases in rates of TB in the non-UK born population are in part due to the pre-UK entry screening policies [13]. In 2005, the UK piloted the pre-entry screening of long-term migrants to the UK for active pulmonary TB in 15 high TB incidence countries. In 2012, this pre-entry screening was extended to all countries with a high incidence of TB (>40 patients per 100,000 population). However other influences such as changes in migration patterns may have also contributed[14].

In contrast, the number and incidence rate of TB in the UK-born population remains low but has increased from 2016 to 2017. Although the rate in UK-born persons is substantially lower than those non-UK born, numerically they still contribute substantial numbers of new notifications each year (113 in 2017). Therefore, a focus on addressing TB rates in this group is important and will also be required if the East Midlands is to achieve the elimination of TB.

The time between symptom onset and starting treatment for pulmonary TB patients is of concern and has broadly remained unchanged over the last 5 years. The proportion of pulmonary TB patients starting treatment more than 4 months after onset has increased in 2017, accounting for approximately a third of patients which is similar to national

figures. This delay in treatment increases the opportunity for TB transmission to others and the risk of adverse outcomes for the patient. Based on the median delays of 83 days from symptom onset to commencing treatment for pulmonary patients, the longest delay was found to be between presentation to healthcare and diagnosis (over 4 weeks for those with pulmonary disease) highlighting the need for further education and awareness surrounding TB amongst healthcare professionals. Patients typically presented to a healthcare setting, 3.5 weeks (median) after onset of symptoms.

TB outcomes for drug sensitive patients within the East Midlands has further declined with those completing treatment decreasing from a peak of 88.1% in 2013 to 74.8% in 2016 and is well below the England overall figure 84.4%. Geographical variation was seen across the East Midlands and ranged from 62.1% to 85.7%.

The number of MDR/RR TB patients in the East Midlands remained similar to 2016. The associated workload of DR patients should not be underestimated, with DR patients in the East Midlands from 2015 taking up to 24 months to complete treatment. Culture confirmation, particularly for pulmonary patients, is important to ensure DR patients can be identified and effective treatment regimens put in place.

In 2017, there was an increase in the proportion of TB patients with 1 or more social risk factors with this being the highest proportion reported since the start of the data collection in 2010. In the East Midlands there is a clear trend between the acquisition and development of TB and deprivation. Reducing TB in underserved populations is 1 of the priority areas outlined in the TB strategy. Those with social risk factors were statistically more likely to have pulmonary disease and require DOTs. In addition, treatment completion rates at 12 months were lower in those with at least 1 social risk factor compared to those without, with a higher proportion of patients having died, being lost to follow up or still on treatment. This probably reflects the complex clinical and social needs of these patients and underlines the need for good management of such patients, as described in the NICE guidance for vulnerable patients[15] and a need to tackle ongoing social and economic factors outlined in the resource ‘Tackling tuberculosis in under-served populations’[4].

Although the offer and uptake of HIV testing was high, the offering and uptake of tests was not universal across all groups and geographies. UK guidance states all TB patients should be offered a test, regardless of age or ethnicity[16].

This is the first year we have been able to present data for the LTBI screening programme. For the East Midlands overall, there was an increase in the number of tests between 2016 and 2017 with Leicester City CCG reporting the second highest number of tests nationally for 2017[(2)]. Where data were available it showed positivity to be between 11.2% and 16.3% of those tested in East Midlands CCGs.

Conclusion and recommendations

Although there was a substantial decline in TB incidence in the East Midlands between 2012 and 2016, there was a slight increase in the number of TB patients in 2017. This trend will require monitoring as we are over halfway through the implementation period of the Collaborative TB strategy 2015-2020 which aims for a year-on-year reduction in TB incidence[3]. Certain risk groups continue to be more likely to be affected than others within the East Midlands. This underlines the need for services to work collaboratively, across the range of health and social care issues, to strive towards effective and sustained TB control to achieve a marked reduction in TB and in health inequalities associated with the disease.

Recommendations for NHS and PHE East Midlands derived from the data presented in this report are included below in line with the strategy areas for action (AfA):

Improve access to services and ensure early diagnosis (AfA1)

TB Networks to explore reasons behind the delay in diagnosis in order to identify areas for improvement and intervention.

TB Networks to reduce the delay in TB diagnosis through raising awareness of TB among local communities affected by TB, other service providers and primary care. This includes utilising the resources available from TB Alert. http://www.thetruthabouttb.org/professionals/professional-education/

East Midlands TB Control Board and TB Networks to encourage the use of the RCGP TB e-learning module. http://elearning.rcgp.org.uk/course/info.php?id=107

Provide universal access to high quality diagnostics (AfA2)

TB Networks to increase the proportion of patients that have a diagnostic laboratory result, particularly culture results to ensure prompt identification of drug resistance and allow WGS to identify clusters.

Improve treatment and care services (AfA3)

TB Networks to continue their supportive case management of complex TB patients, offer DOT where indicated and consider the use of innovative approaches such as VOT to improve case management.

TB Networks to implement or continue cohort review as a tool to improve local TB control and as a measure of treatment outcomes and contact tracing activity working towards the KPIs agreed by the East Midlands TB Control Board.

TB Networks to encourage universal HIV testing for all those diagnosed with tuberculosis and ensure where possible, tests are carried out[16].

TB Networks to ensure information is completed accurately on the PHE ETS system, particularly with respect to dates of onset of symptoms, evaluation of treatment completion and TB relationship with death.

To reduce drug-resistant TB (AfA6)

TB Networks to continue supporting patients to complete treatment, using DOT or VOT where indicated, and to have plans in place to minimise patients being lost to follow-up.

TB Networks to use the British Thoracic Society (BTS) MDR-TB Clinical Advice Service to support MDR-TB case management.

To tackle TB in under-served populations (AfA7)

East Midlands TB Control Board and TB Networks to encourage the use of the resource 'Tackling TB in Under-Served Populations'[(4)] to take appropriate local action and better meet the needs of USPs.

TB Networks, to ensure appropriate access to services, treatment and support to enable patients to complete treatment.

TB Networks are encouraged to use 'Tackling TB - local government's public health role'[5], a joint publication from PHE and the Local Government Association to help support USPs with TB

To implement new entrant latent TB screening (AfA8)

CCGs to sustain the roll out of the new migrant LTBI screening programme within the 4 high-burden CCGs identified within East Midlands.

Appendix A: Notes on the report

About the Field Service

The Field Service (FS) supports Public Health England (PHE) centres and partner organisations through the application of epidemiological methods and public health microbiology to inform public health action. It does this in 2 main ways, firstly by providing a flexible expert resource, available, as and when needed, to undertake epidemiological investigations for key health protection work and secondly through the expert analysis, interpretation and dissemination of surveillance information to PHE Centres, local health partners, service providers and commissioners of services. Within the FS network, excellence and innovation is encouraged, we foster academic collaborations and take active part and lead in research, development and training.

Intended audience

This report is for use by healthcare professionals who diagnose and/or care for people with TB, commissioners involved in planning and financing TB services, public health professionals working to improve TB control and the health of at-risk populations, researchers with an interest in TB, and government and non-governmental organisations working in the field of TB. In particular this report is for the use of the East Midlands TB Control Board.

Aim of report

This report describes the recent epidemiology of TB in East Midlands. It includes local trends, which areas and population groups have a high burden of disease, and detail on the care of patients.

Further TB information

The national report of TB in England is available at https://www.gov.uk/government/publications/tuberculosis-in-england-annual-report. Additional data on TB notifications in the UK to the end of 2017, and breakdowns by country, can be found in the Official Statistic for TB, ‘Reports of patients of tuberculosis to ETS systems: United Kingdom, 2000 to 2017’. This is available at https://www.gov.uk/government/collections/tuberculosis-and-other-mycobacterial-diseases-diagnosis-screening-management-and-data.

As part of the Collaborative TB Strategy for England 2015-2020, TB Strategy Monitoring Indicators are available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020_.pdf). Where data for these indicators are presented in this report, the indicator name is shown.

A number of TB indicators at UTLA and Clinical Commissioning Group level can be found at http://fingertips.phe.org.uk/profile/tb-monitoring.

[Note: data presented for TB monitoring indicators at East Midlands level DO NOT need to suppress small numbers due to the large size of the underlying population and the fact that these are not accompanied by any identifiable information].

Appendix B: Description of data sources and definitions and other explanations

Data sources

This report is based on TB case notifications made to the PHE ETS system in England to the end of 2017. The information is updated annually to take into account denotifications (where the patient was found not to have TB), late notifications and other updates. The data presented in this report supersedes data in previous reports.

Diagnostic laboratories serving acute hospitals are the first place in which TB infection-related samples are received and processed within the pathway of clinical diagnosis and management of suspected TB patients. Results for microscopy, polymerase chain reaction (PCR), histology and culture are collected in ETS. Appropriate referral of positive cultures to the PHE National Mycobacterial Reference Service is an important part of the routine work of the diagnostic laboratories in the investigation and management of TB patients.

The National Mycobacterial Reference Service (NMRS) culture positive samples and undertakes molecular diagnostic methods to define species of *Mycobacterium*, TB antibiotic (drug) susceptibility and organism relatedness. Historically, organism relatedness has been determined by Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats (MIRU-VNTR) typing, however this has been superseded in recent years by WGS.

Screening of people exposed to a patient with active TB is a key strategy to find and treat active and latent TB, and prevent further transmission. The outcomes of contact tracing activities are discussed by cohort reviews undertaken in most areas of East Midlands (for more information on the purpose of cohort reviews, please see the Collaborative Tuberculosis Strategy for England, 2015 to 2020: (https://www.gov.uk/government/publications/collaborative-tuberculosis-strategy-for-england) [(3)].

Definitions

BCG	Bacillus Calmette-Guérin vaccination
CI	Confidence interval
CCG	Clinical Commissioning Group
Cluster	2 or more patients notified within the time period of analysis with TB cause by strains with ≤12 SNP differences
CNS	Central nervous system
Cohort review	The systematic review of all TB patients notified by a TB service in a 3-4 month period, looking at standard outcomes in terms of patient care and number of contacts screened
Cryptic disseminated TB	Systemic illness without localising features
DOT	Directly observed treatment
Drug	In the context of TB control, a drug is an anti-TB antibiotic
Drug resistant cohort	The drug resistant cohort includes any patients with rifampicin resistant TB (initial or acquired), including MDR-TB (initial or acquired), as well as those without culture confirmation treated with an MDR-TB regimen
Drug-sensitive cohort	The drug sensitive cohort excludes all TB patients with rifampicin resistant TB (initial or acquired) including MDR-TB (initial or acquired), and non-culture confirmed patients treated with an MDR-TB regimen
DST	Drug sensitivity testing, based on phenotypic analysis of cultured TB isolates
ETS	Enhanced TB surveillance system
First-line drug resistance	First-line anti-TB antibiotic drug resistance is defined as resistance to at least 1 of the first-line antibiotics – such as isoniazid, rifampicin, ethambutol, pyrazinamide
HAART	Highly active antiretroviral therapy
IGRA	Interferon-gamma release assay – blood test for TB infection which does not differentiate between active disease and LTBI
IMD 2015	The Index of Multiple Deprivation 2010 rank for each LSOA, based on deprivation score assigned, relative to other LSOAs in the PHE East of England area
IQR	Interquartile range
LSOA	Lower super output area (geographic definition)
LTBI	Latent TB infection
MDR	Multidrug resistance: patients initially resistant to at least isoniazid and rifampicin

Miliary TB	TB infection spread via the bloodstream to all parts of the body
MIRU-VNTR	Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats
PCR	Polymerase chain reaction
Post-mortem diagnosis	A patient diagnosed at post-mortem is defined as where TB was not suspected before death, but a TB diagnosis was made at post-mortem, with pathological and/or microbiological findings consistent with active TB that would have warranted anti-TB treatment if discovered before death
Pulmonary tuberculosis	A pulmonary case is defined as a patient with TB involving the lungs and/or tracheobronchial tree, with or without extra-pulmonary TB diagnosis. In this report, in line with the WHO's recommendation and international reporting definitions, miliary TB is classified as pulmonary TB due to the presence of lesions in the lungs
Second-line drugs	Second-line drugs include injectable agents, including amikacin, capreomycin and kanamycin; fluoroquinolones, such as moxifloxacin, ofloxacin, ciprofloxacin) and other oral bacteriostatic agents
SNP	Single nucleotide polymorphism – mutation of 1 base pair in the genome of an *M. tuberculosis complex* isolate
TB	Tuberculosis
UTLA	Upper tier local authority (geographic definition)
VOT	Video observed therapy
WGS	Whole genome sequencing
XDR	Extensive drug resistance: patients initially MDR and resistant to at least 1 injectable agent (amikacin, capreomycin or kanamycin) and at least 1 fluoroquinolone (moxifloxacin, ofloxacin or ciprofloxacin)

Treatment outcome

Information on outcomes were reported for all patients reported in the previous year, excluding those with known rifampicin resistant disease: outcomes for these were reported at 24 months. Definitions for outcome are based on World Health Organization (WHO) and European definitions but adapted to the UK context. In this report, all data was obtained from the ETS matched dataset provided in August 2017.

Proportions

All proportions in this report are calculated among patients with known information or a known result, except where otherwise stated.

Confidence intervals

A 95% confidence interval for incidence was obtained using the relevant procedure in R.

Population denominator

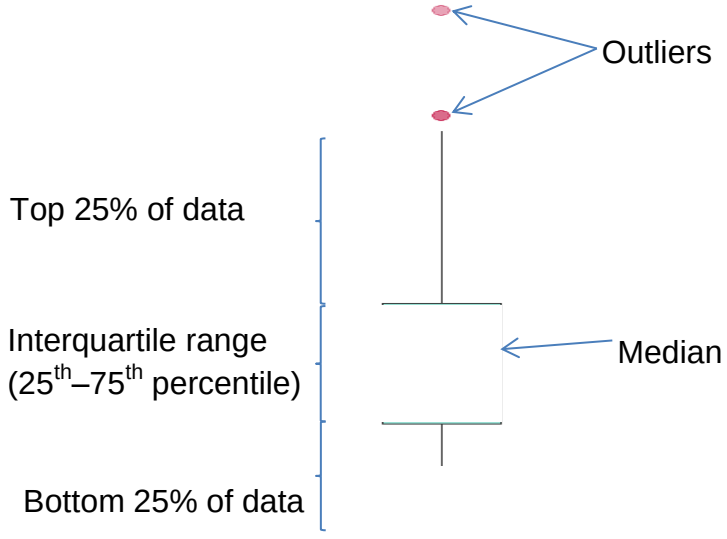
Tuberculosis rates by geographical area (Centre, local authority, MSOA and LSOA), age, sex and place of birth were calculated using ONS mid-year population estimates. Tuberculosis rates by ethnic group were calculated using population estimates from the Labour Force Survey (LFS) [http://www.esds.ac.uk/findingData/qlfs.asp]. The LFS is based on a population sample, so estimates are liable to sampling errors, particularly for small population subgroups, and should be interpreted with caution.

Cluster definitions

Analysis of clustering in the East Midlands was carried out on patients that clustered in the East Midlands and notified between 2010 and 2017.

Strain typing was performed by the National Mycobacterial Reference Service using WGS. Analysis was undertaken on strain type clusters as defined above. Analysis of clustering in East Midlands was carried out on patients that clustered in East Midlands and notified between 2010 and 2017.

Interpretation of box plots



Appendix C: TB among East Midlands residents

Table C1a: TB new notifications numbers East Midlands Public Health England Centre, 2000 to 2017

Patients with TB	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Persons	414	544	471	458	418	533	566	534	483	524	494	492	497	413	400	357	341	351

Table C1b: TB new notifications incidence rate East Midlands Public Health England Centre, 2000 to 2017

Patients with TB	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Rate	9.9	13	11.2	10.8	9.7	12.3	13	12.1	10.9	11.7	11	10.8	10.9	9	8.6	7.6	7.2	7.4
Lower confidence limit	9	11.9	10.2	9.8	8.8	11.3	11.9	11.1	9.9	10.7	10	9.9	9.9	8.1	7.8	6.9	6.5	6.6
Upper confidence limit	10.9	14.1	12.2	11.8	10.7	13.4	14.1	13.2	11.9	12.8	12	11.8	11.9	9.9	9.5	8.5	8	8.2

Table C2a: TB patient numbers by UTLA of residence, East Midlands, 2000 to 2017

UTLA	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Derby	46	46	59	39	28	36	40	55	45	40	53	34	34	37	35	28	29
Derbyshire	37	29	30	25	28	43	30	28	32	15	36	32	22	28	18	9	10
Leicester	262	196	199	155	263	226	216	177	206	207	188	184	158	142	125	130	137
Leicestershire and Rutland	51	43	33	37	43	56	50	40	51	41	35	38	38	24	24	23	33
Lincolnshire	6	14	14	18	13	25	16	20	20	21	23	31	26	34	36	30	29
Northamptonshire	67	83	56	75	79	69	66	64	79	68	65	80	46	47	48	50	38
Nottingham	52	40	36	48	57	82	80	80	55	69	67	60	58	50	53	48	43
Nottinghamshire	23	20	31	21	22	29	36	19	36	33	25	38	31	38	18	23	32

Table C2b: TB rate per 100,000 by local authority of residence, East Midlands, 2000 to 2017

UTLA	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Derby	19.9	19.8	25.3	16.6	11.8	15.1	16.7	22.7	18.4	16.2	21.3	13.6	13.5	14.7	13.8	10.9	11.3
Derbyshire	5	3.9	4	3.4	3.7	5.7	4	3.7	4.2	2	4.7	4.1	2.8	3.6	2.3	1.1	1.3
Leicester	92.7	68.7	68.9	52.7	87.2	73.7	69.4	56.1	64.4	63.7	57	55.4	47.2	42	36.3	37.2	38.8
Leicestershire and Rutland	7.9	6.6	5	5.6	6.5	8.4	7.4	5.9	7.5	6	5.1	5.5	5.4	3.4	3.4	3.2	4.5
Lincolnshire	0.9	2.1	2.1	2.7	1.9	3.6	2.3	2.9	2.8	3	3.2	4.3	3.6	4.6	4.9	4	3.9
Northamptonshire	10.6	13	8.7	11.6	12.1	10.4	9.8	9.4	11.6	9.9	9.4	11.4	6.5	6.6	6.6	6.8	5.1
Nottingham	19.3	14.7	13.1	17.2	20	28.6	27.8	27.5	18.7	23	22	19.5	18.7	15.9	16.6	14.8	13.1
Nottinghamshire	3.1	2.7	4.1	2.8	2.9	3.8	4.7	2.4	4.6	4.2	3.2	4.8	3.9	4.7	2.2	2.8	3.9

Rates calculated using ONS mid-year population estimates
Note: Data for Rutland suppressed, because annual counts are below 5.

Table C3: Average TB number and rate per 100,000 population by Clinical Commissioning Group of residence, East Midlands, 2015 to 2017

CCG	Average count per year 2015-2017	Average rate / 100,000 population per year 2015-2017
NHS Bassetlaw CCG	1	1.2
NHS Corby CCG	3	4.4
NHS East Leicestershire and Rutland CCG	13	4.1
NHS Erewash CCG	3	3.1
NHS Hardwick CCG	1	0.9
NHS Leicester City CCG	131	37.7
NHS Lincolnshire East CCG	16	6.7
NHS Lincolnshire West CCG	7	2.8
NHS Mansfield and Ashfield CCG	6	2.9
NHS Nene CCG	42	6.5
NHS Newark and Sherwood CCG	3	2.2
NHS North Derbyshire CCG	5	1.8
NHS Nottingham City CCG	48	14.9
NHS Nottingham North and East CCG	7	4.7
NHS Nottingham West CCG	4	3.6
NHS Rushcliffe CCG	4	3.2
NHS South Lincolnshire CCG	6	3.8
NHS South West Lincolnshire CCG	4	2.9
NHS Southern Derbyshire CCG	34	6.5
NHS West Leicestershire CCG	13	3.4

*rates calculated using ONS mid-year population estimates

Table C4: TB patient numbers, East Midlands, 2000 to 2017

Age group	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0-9 years	13	17	13	8	9	11	14	12	11	14	11	5	8	13	11	9	16	8
10-19 years	21	102	35	42	27	46	37	32	25	41	28	25	27	26	17	23	11	27
20-29 years	63	92	109	94	98	123	139	138	105	116	115	112	109	81	76	61	65	57
30-39 years	69	87	84	82	109	118	114	107	122	118	114	111	106	86	88	89	77	78
40-49 years	67	74	72	68	52	75	81	65	61	65	92	67	77	59	60	56	61	61
50-59 years	56	49	44	60	33	64	60	81	63	66	53	67	60	66	56	42	52	41
60-69 years	52	39	39	37	37	31	56	46	41	44	26	39	43	34	29	35	25	37
70 years plus	73	83	74	67	52	65	65	53	54	60	55	66	67	48	63	42	34	42

Table C5: TB patient rate by age, East Midlands, 2000 to 2017

Age group	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
0-9 years	2.5	3.4	2.6	1.6	1.8	2.2	2.8	2.4	2.2	2.8	2.1	1	1.5	2.4	2	1.6	2.8	1.4
10-19 years	3.9	18.8	6.4	7.6	4.8	8.2	6.6	5.7	4.4	7.3	5	4.5	4.9	4.8	3.2	4.3	2	5
20-29 years	12.3	18.3	21.9	18.7	19.1	23.2	25.5	24.7	18.4	20.2	19.8	19.1	18.4	13.5	12.5	9.9	10.5	9.1
30-39 years	10.8	13.5	13.1	12.8	17.3	19.1	18.8	18.1	21.1	20.7	20.2	19.9	19.3	15.7	16	16	13.6	13.5
40-49 years	12	13.1	12.4	11.5	8.6	12	12.7	10	9.2	9.7	13.6	9.9	11.4	8.8	9.1	8.7	9.6	9.8
50-59 years	10.4	8.9	7.8	10.6	5.8	11.3	10.6	14.5	11.4	11.9	9.4	11.7	10.3	11.1	9.2	6.7	8.1	6.3
60-69 years	13.2	9.9	9.8	9	8.8	7.1	12.6	9.8	8.4	8.8	5	7.4	8	6.3	5.3	6.4	4.6	6.9
70 years plus	15.2	17.1	15.1	13.5	10.4	12.9	12.8	10.3	10.4	11.3	10.2	12.2	12.1	8.5	10.8	7	5.5	6.5

*rates calculated using ONS mid-year population estimates

Table C6: Number of TB patients by place of birth, UK and non UK born, East Midlands, 2000 to 2017

Where born	var	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
UK born	n	120	120	127	116	111	95	114	118	119	146	122	142	127	116	132	99	94	113
	Rate	3.1	3.1	3.2	2.9	2.8	2.4	2.9	3	3	3.6	3	3.5	3.1	2.8	3.2	2.4	2.3	2.8
	LCL	2.6	2.5	2.7	2.4	2.3	1.9	2.4	2.5	2.5	3.1	2.5	3	2.6	2.4	2.7	2	1.8	2.3
	UCL	3.7	3.7	3.9	3.5	3.4	2.9	3.5	3.6	3.6	4.3	3.6	4.1	3.7	3.4	3.8	2.9	2.8	3.3
Not UK born	n	101	100	119	182	225	291	233	278	296	340	351	331	354	292	258	251	242	226
	Rate	46.4	44.7	47.2	72.9	90.4	99.4	68.3	75.7	76.5	89.8	85.3	76.1	80.3	63.3	55.8	50.9	48.2	37.6
	LCL	37.8	36.4	39.1	62.7	78.9	88.3	59.8	67.1	68.0	80.5	76.6	68.1	72.1	56.2	49.2	44.8	42.3	32.9
	UCL	56.4	54.4	56.5	84.3	103.0	111.5	77.6	85.2	85.7	99.8	94.8	84.8	89.1	71.0	63.0	57.6	54.7	42.9

Table C7: First-line drug resistance among TB patients with culture confirmed disease, East Midlands, 2000 to 2017

First-line resistance	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
No. of isolates	11	19	18	18	19	15	22	20	12	22	16	9	16	17	17	20	22	19
Proportion of isolates %	5.7	7	6.9	6.8	7.4	5.2	7.2	6.5	4.3	8.1	5.4	3.1	5.4	7.2	7.2	8.3	10.6	9

*culture confirmed patients with drug susceptibility testing results for at least isoniazid and rifampicin

Table C8: Time between symptom onset and starting treatment for all TB patients, East Midlands, 2011 to 2017

Year	0-2 months		2-4 months		4+ months		Total
	Count	%	Count	%	Count	%	
2011	131	39.5	95	28.6	106	31.9	332
2012	109	30	105	28.9	149	41	363
2013	116	38	93	30.5	96	31.5	305
2014	124	32.9	103	27.3	150	39.8	377
2015	120	35.2	104	30.5	117	34.3	341
2016	111	34.4	100	31	112	34.7	323
2017	101	30.6	97	29.4	132	40	330

*excluding asymptomatic patients, and those with missing onset dates

Table C9: Social risk factors among TB patients, East Midlands, 2017

Risk factor	Count of patients	Proportion of patients
Ability to self-treat affected by alcohol misuse/abuse	15	5.0
History of or current problem drug use	18	5.9
History of or current homelessness	23	7.8
History of or current imprisonment	11	4.2

* For patients 15 years and over. Total number of patients for the year with risk factor data recorded

Appendix D: Surveillance data quality

Table E1: Percentage completeness of key data fields in ETS for 2017 with percentage change from 2016, East Midlands

East Midlands	Demographic				Clinical				Social risk factor							
	NHS Number*		Ethnic group	UK/non-UK born	HIV Testing#	Previous TB diagnosis		Previous TB treatment^	Drug misuse		Alcohol misuse		Homelessness		Prison	
	ETS	Lab	Known	Known	Known	Known	Reported$	Reported	Known	Reported	Known	Reported	Known	Reported	Known	Reported
Percentage complete 2017	97	80	98	97	94	93	97	68	91	98	90	97	89	98	79	97
Percentage change from 2016	+1	0	-2	-2	+1	+3	+3	-7	-2	-2	-3	-2	-3	0	-5	-1

Table E2: Percentage completeness of diagnosis, death and treatment data fields in ETS for 2017 with percentage change from 2016, East Midlands

East Midlands	Diagnosis					Death		Treatment					
	Sputum smear status**	Site of disease	Symptom onset date^	Date first presented	Date diagnosed^	Date of death†	Relationship between TB and death§	Start of Treatment date^	Date treatment completed@	Treatment Outcome reported at 12 months§		Treatment Outcome reported at 24 months¥	
	Known#	Known	Known	Known	Known	Known	Known	Known	Known	Known	Reported‡	Known	Reported
Percentage complete 2017	50	100	97	89	94	97	48	97	99	97	99	100	100
Percentage change 2016 to 2017	-8	-	-1	+1	+1	-3	-17	-1	-1	-2	-1	-	-

**Pulmonary patients only. †Patients notified in 2015 that have treatment outcome died only. ‡Data are reported but may be reported as unknown. # Data are reported and has a known value. ^Excludes patients diagnosed post-mortem. ¥ For patients notified in 2015 and still on treatment at 12 months. @Patients notified in 2015 that have completed treatment only. §For patients notified in 2016

Key: 99- 100% complete | 95 - 98% complete | <95% complete | % increase | No change | % decrease | 100% reached

Appendix E: Local authority TB epidemiological summaries

Local authority TB epidemiological summaries will provide further information about TB patients among residents of East Midlands upper tier local authorities with an average of at least 50 TB patients per year over the previous 3 years. These will be available from your local FS team.

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