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Protecting and improving the nation's health

# Tuberculosis in North East Centre
## Annual review (2017 data)

Data from 2000 to 2017

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Public Health England
Wellington House
133-155 Waterloo Road
London SE1 8UG
Tel: 020 7654 8000
www.gov.uk/phe
Twitter: @PHE_uk
Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Field Service (North East)
For queries relating to this document, please contact: Angela Cox



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# Contents

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## Authors

This report was prepared by Angela Cox and Petra Manley of the Field Service (North East), National Infection Service, Public Health England, and Simon Howard of the North East Health Protection Team, Public Health England.

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# Foreword

A century ago, tuberculosis (TB) was one of England's most urgent public health priorities. Each year there were approximately 250 new cases per 100,000 population and the case fatality rate was almost 50%. Today, this rate has decreased significantly to 9.2 per 100,000, as has the case fatality rate to around 5%. Despite this reduction, TB is still a public health priority not least because of increasing international concern around multidrug resistant TB, which cannot be effectively treated using the normal courses of antibiotics. Also, for individuals, TB infection remains a very unpleasant disease, typically requiring many months of antibiotic treatment.

In 2017, as for the past 2 decades, the number of new cases in the North East remained very low, at just 4.2 per 100,000 population. This figure masks considerable in-region variation; for example, Middlesbrough had 13.5 cases per 100,000 population, and Newcastle upon Tyne has 10.5 cases per 100,000 population.

This report describes some of the North East's challenges. For example, 16% of people with TB have social risk factors, which can make treatment more difficult. The rate of TB in the most deprived communities (8.5 per 100,000 population) is almost 3 times higher than in the least deprived communities. We clearly need to do more to target these 'hard to reach' groups, and the North East TB Network has plans to pilot some screening work with a drug and alcohol service over the coming year.

Furthermore, 37% of our cases are in white UK-born people, more than twice the proportion seen nationally (14%). Time from onset of symptoms to diagnosis in white UK-born patients is typically higher than in other ethnic groups, partly because TB is often not initially considered as a possible diagnosis in this group. Almost a quarter (22%) of patients in the North East do not receive a diagnosis within 4 months of the onset of symptoms. The North East TB Network and Yorkshire, Humber & North East TB Control Board are continuing to work with GPs about the importance of considering TB in all patients presenting with persistent respiratory symptoms.

Finally, if we are to reach the international goal of eliminating TB as a public health threat, it is vital that we do more to tackle TB in low incidence regions such as the North East. This will require us to improve early identification of the disease, strengthen good clinical practice and develop more innovative ways of connecting with those who might be at risk of TB. Through concerted action between social, healthcare and public health teams, as well as third sector organisations, we can succeed in the reducing the burden of TB locally.

**Paul Davison, Deputy Director of Health Protection**
**PHE North East Centre**

# Lay summary

Tuberculosis is an infectious disease of public health concern. An estimated 10 million new cases occurred and caused 1.6 million deaths worldwide in 2017. In September 2018, the United Nations General Assembly held its first high-level meeting on TB to accelerate efforts to end the global TB epidemic. The intended outcome of this meeting is a Political Declaration on TB endorsed by Heads of State that will strengthen action and investments to end TB as we drive towards elimination by 2035.

This report focuses on TB in the North East of England and enables those involved in the management of TB to utilise the latest data to design public health strategies and clinical care to control TB and progress towards the goal of elimination by 2035.

In 2017, 110 people were notified with TB in the North East, the lowest number since 2000. The number of cases peaked in 2014 with 168 people diagnosed with TB. Since then, the number of people diagnosed with TB has fallen by 35% to 110 in 2017. The North East has lower notification rates of TB than England overall: 4.16 per 100,000 compared to 9.2 per 100,000 population.

Despite a decline in TB notifications of over 10% from 2016 to 2017, this was largely seen in people born outside the UK; however, there was very little change in TB notifications among those born in the UK.

Over 20% of people with pulmonary TB continue to experience a delay of more than 4 months between symptom onset and the start of treatment. The delays were highest in those born in the UK and aged over 65 years.

In 2017, 16% of people notified with TB had a social risk factor, such as drug and alcohol misuse, homelessness or a history of imprisonment. This was the highest proportion since 2010 when data collection on risk factors began. Outcomes in these individuals were worse than those without a social risk factor: 6.9% died compared to 4.9% of those without a risk factor.

There was a small increase in the proportion of people notified with drug sensitive TB (with an expected treatment duration of less than 12 months) who completed treatment by 12 months from 79% in 2015 to 81% in 2016. The proportion who died at the last recorded outcome was 6.5%, lower than in 2015 (11%).

# Executive summary

## National

A total of 5,102 cases of TB were reported in England in 2017[1], the lowest number since 2000. There was a decline in the TB incidence rate of 9.8% between 2016 (10.2 per 100,000 population) and 2017 (9.2 per 100,000 population).

## Regional

A total of 110 TB cases were reported in the North East of England in 2017 with a rate of 4.2 per 100,000 population. This represents a decrease compared to the previous year (121 cases, incidence of 4.6 per 100,000 in 2016).

## Local

Middlesbrough had the highest incidence of TB, at 13.5 per 100,000 population in 2017. This was an increase from the previous year (10.0 per 100,000 population in 2016). South Tyneside and Northumberland had the lowest rates in 2017 (0.7 and 1.3 per 100,000 population respectively).

## Age groups

In 2017 in the North East, the age specific TB rates were highest in the 20-24-year age group at 9.4 per 100,000 population. The rate in UK born children aged under 15 years was 0.9 per 100,000, this remained stable from the previous year.

## Ethnic groups

As in recent years, the most common ethnic group of TB cases in the North East was White, followed by Black African. Numbers of cases among the Bangladeshi group increased whilst other groups remained stable or saw a decrease in 2017 from the previous year.

In 2017, a greater number of TB cases were born outside the UK. TB rates in UK-born population remain very low at 2.0 per 100,000 while the rate in non-UK born population was 35.2 per 100,000. Although a decrease of 16.6 % in the rate was seen from the previous year.

## Clinical characteristics

In 2017, 54% (59/110) of TB cases reported in the North East had pulmonary disease, which is comparable with the figure for England (54.4%). Of those pulmonary cases, 39% (23/59) had a

sputum-smear result of which 74% were sputum-smear positive. In 2017, 69% of all TB cases were confirmed by culture, 73% among pulmonary cases, compared to 62% and 75% respectively among all cases in England.

## Treatment outcome

82% (98/119) of TB cases reported in the North East in 2016 in the entire drug sensitive cohort (excludes cases in the drug resistant cohort) had recorded as having completed treatment at the last recorded TB outcome. The most common reason for non-completion was due to death. 2% (2/119) of North East patients in the entire drug sensitive cohort were lost to follow up.

Among drug sensitive TB cases with non-CNS/spinal/miliary or cryptic disseminated disease, 81% of those notified in 2016 completed treatment within 12 months (compared with 79% in 2015). The most common reason for non-completion was due to death (7%) and lost to follow up (2%). Most of the cases where death was reported were seen in the 65+ years category and 43% of cases the relationship between TB and death was unknown.

Among drug sensitive TB cases with CNS, spinal, miliary or cryptic disseminated disease, 67% of those reported in 2016 completed treatment within 12 months; the reasons for non-completion were due to death (1 case), loss to follow up (1 case) and still on treatment (1 case).

## Drug resistance

Drug resistance increased among TB cases reported in the North East in 2017, with 5% of cases with isoniazid resistance and 3% of cases with multi-drug resistance. 57% of the resistant TB cases had pulmonary disease and 57% of resistance TB cases were born abroad.

Complete and accurate surveillance data provide the evidence to review case management standards and help identify opportunities for prevention.

Recommendations for local NHS and PHE staff include (i) ensuring that accurate and complete information is provided on the PHE enhanced TB surveillance system in a timely manner, and (ii) that best practice case management is followed for all patients, including universal HIV testing and obtaining sputum smear results. Reviewing of cases through cohort reviews ensures opportunities for prevention, early detection and successful treatment are not missed.

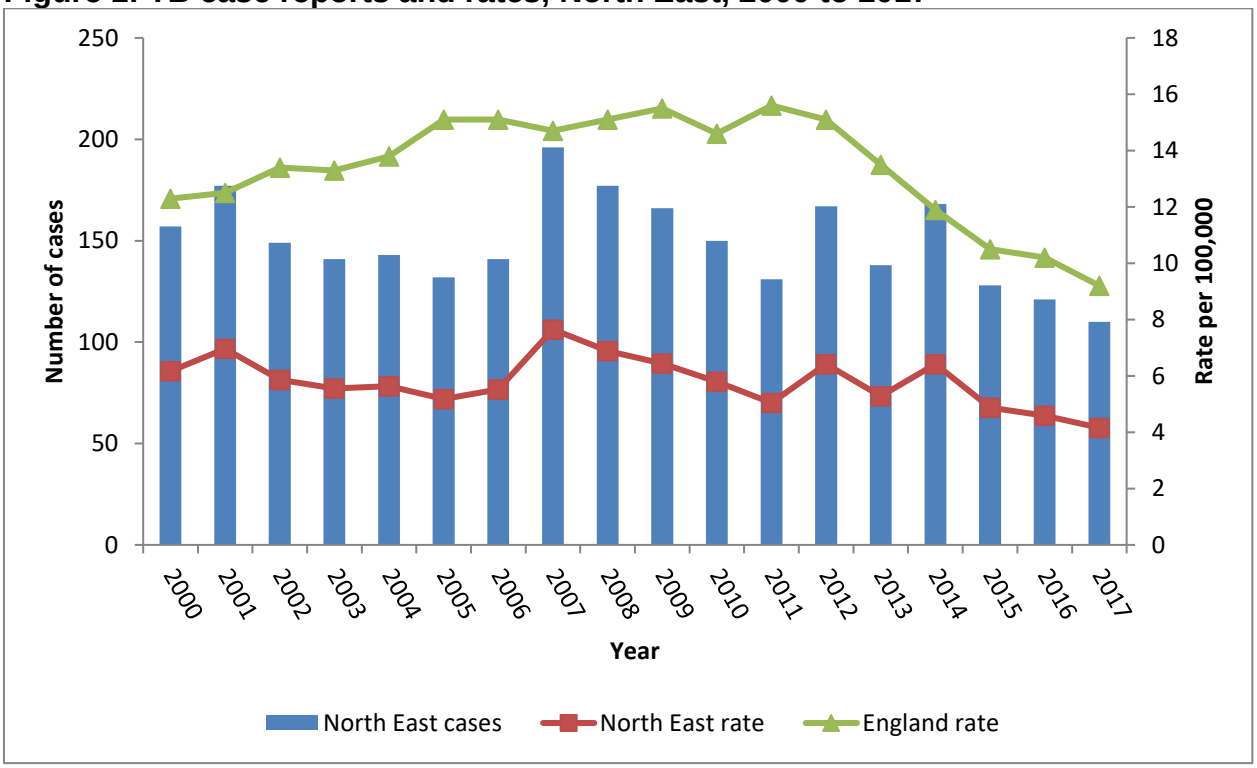
# TB notifications and incidence

## Overall numbers, rates and geographical distribution

In 2017, 110 TB cases were reported among North East residents, a rate of 4.2 per 100,000 population. This was a decrease of 9% compared to 2016 rate of 4.2 per 100,000 population (Figure1). The rate of TB in the North East remained well below the national figure of 9.2 per 100,000 population.

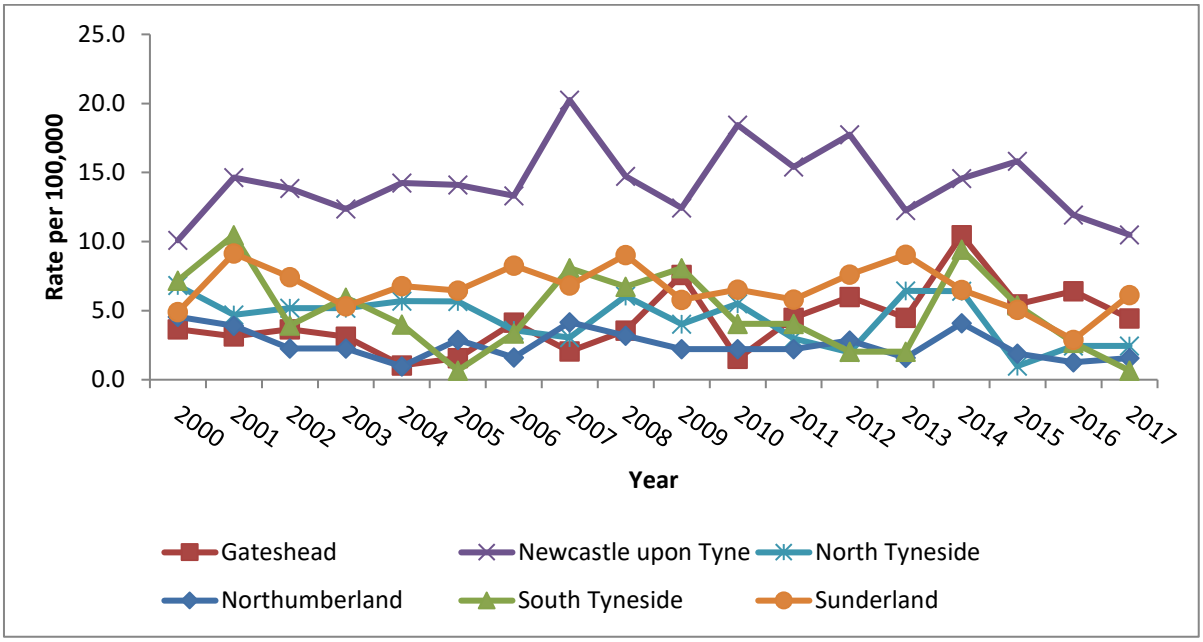
TB Monitoring Indicator 1: Overall TB incidence per 100,000 population

**Figure 1: TB case reports and rates, North East, 2000 to 2017**




Within the North East, the highest rates of TB were seen in Middlesbrough (13.5 per 100,000 population) and Newcastle upon Tyne (10.5 per 100,000 population), and the lowest in South Tyneside and Northumberland (Figure 2).

**Figure 2: TB case rates, by North East local authority of residence, North East, 2000 to 2017**



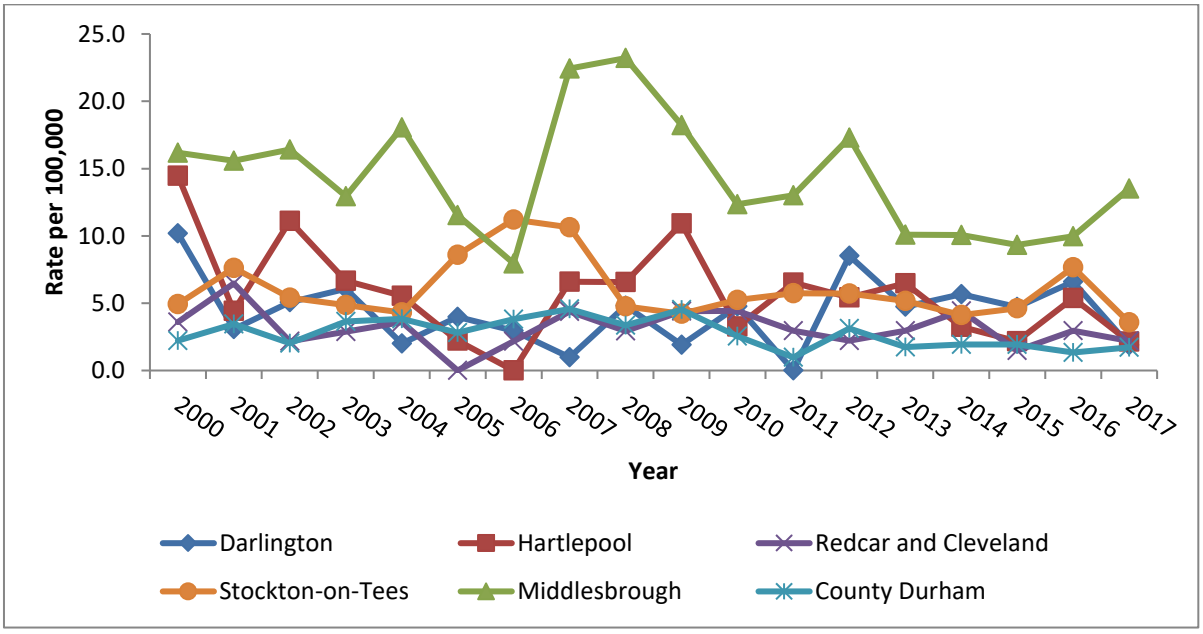
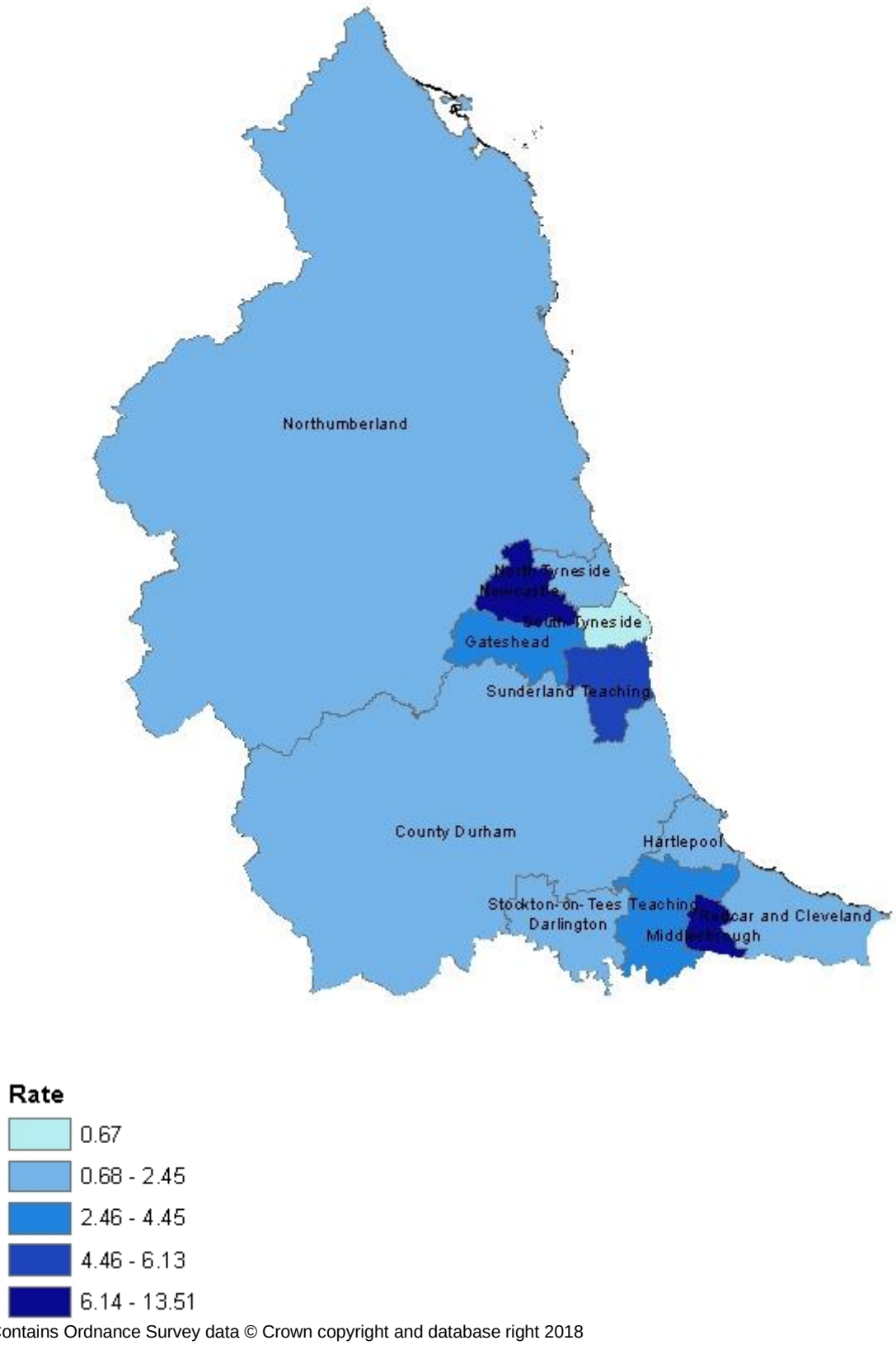



**Figure 3: TB case rate by upper tier local authority of residence, North East, 2017**



# Demographic characteristics

## Age and sex

Data on age and sex were available on all cases of TB reported in the North East in 2017. In 2017, 62% (68/110) of cases diagnosed with TB were male and 38% female (42/110). This equates to a rate of 5.2 per 100,000 population for males and 3.1 per 100,000 population for females.

The highest rates of TB were observed in those aged 20 to 29 years (8.1 per 100,000 population). When cases were stratified by age and sex, the highest rate was seen in males aged 30 to 39 (10.3 per 100,000 population). The highest rate for females was seen in those aged 20 to 29 (8.6 per 100,000 population). (Figure 4)

There were 7 cases reported in children aged under 15 years; a small increase on the previous year. This equates to a rate of 1.6 per 100,000 child population. Of those children, the majority were UK born with a rate of 0.9 per 100,000 UK born children, this figure remained stable from the previous year.

Of the children diagnosed with TB aged 5 and under, the majority were UK born.

**Figure 4: TB case reports and rate by age and sex, North East, 2017**

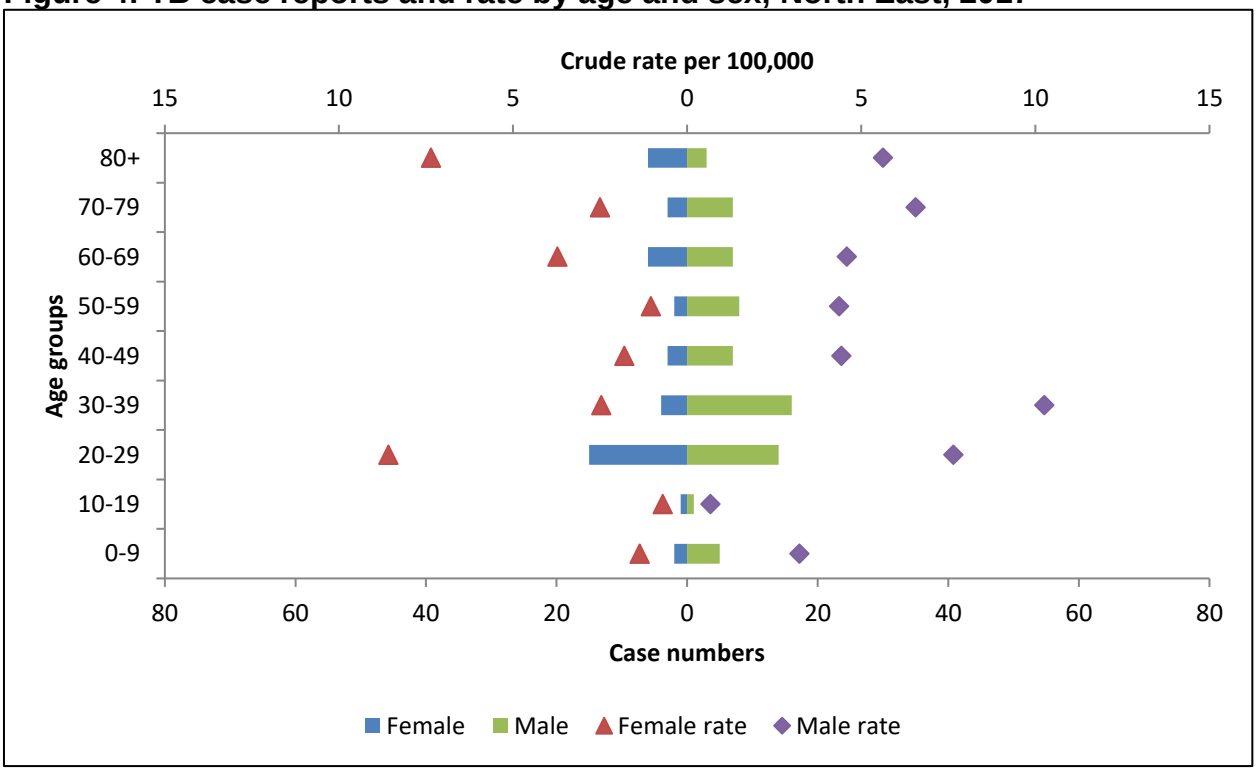
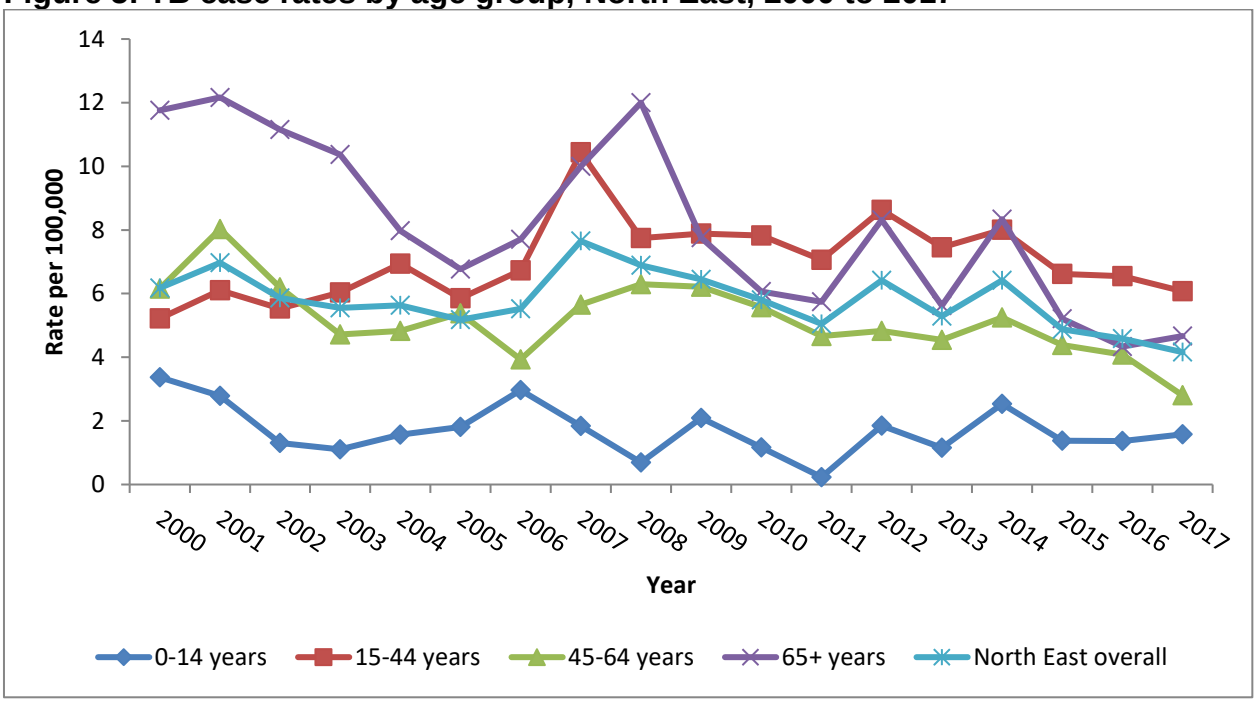


**Figure 5: TB case rates by age group, North East, 2000 to 2017**



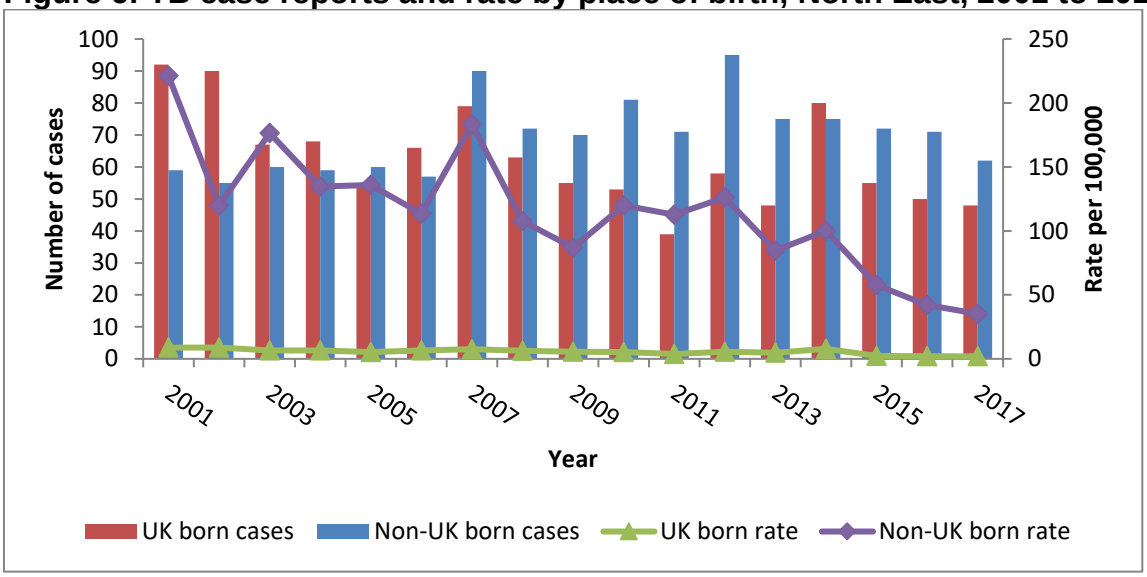

## Place of birth and time since entry

The rates of TB in the non-UK born population should be interpreted in the context of changes to the pre-UK entry screening policies. In 2005, the UK piloted the pre-entry screening of long-term migrants to the UK for active pulmonary TB from 15 high TB incidence countries. In 2012, this pre-entry screening was extended to all countries with a high incidence of TB (i.e. >40 cases per 100,000 population). [2]

In 2017, place of birth was known for all North East TB cases. Of these cases, 62 (56%) were born outside of the UK, with a non-UK born TB rate of 35.2 per 100,000 population. This is the lowest rate recorded for the non-UK born population since 2001 but is only slightly lower than 2016. The TB rate in non-UK born population remains very low at 1.9 per 100,000 population. Numbers of UK born cases decreased slightly from 50 in 2016 to 48 in 2017. (Figure 6)

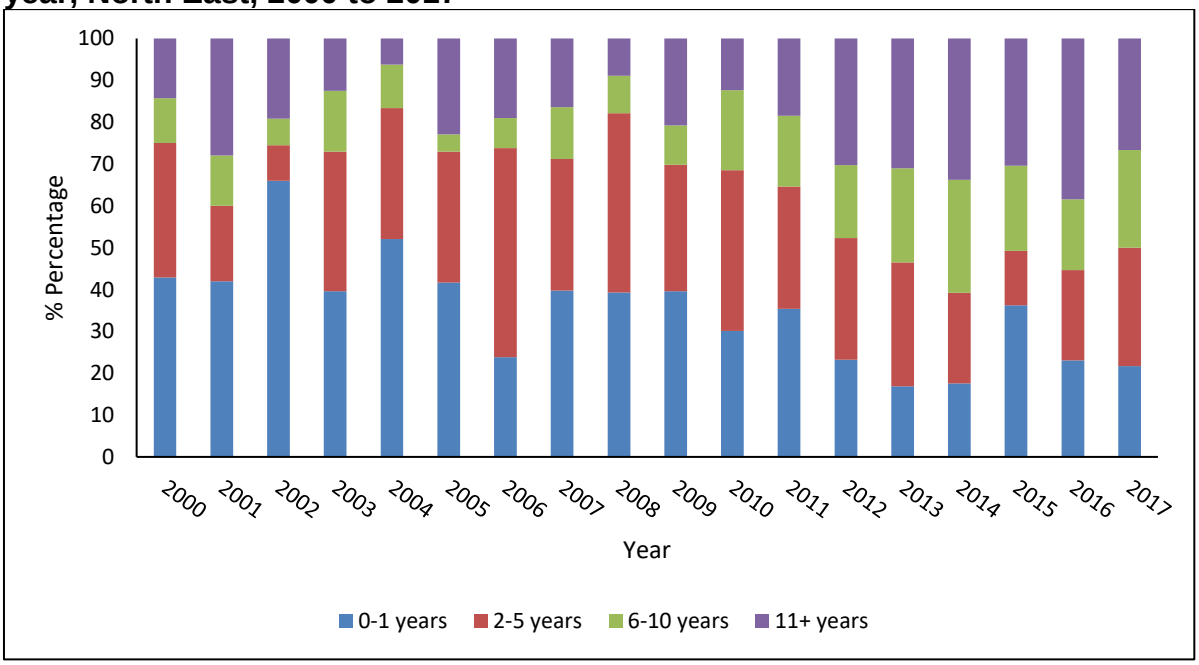
TB Monitoring Indicator 2: TB incidence in UK born and non-UK born populations

**Figure 6: TB case reports and rate by place of birth, North East, 2001 to 2017**




In 2017, data was available on time since entry to the UK for 60 (97%) non-UK born cases. A total of 16 cases (27%) had a time between entry to the UK and diagnosis of ≥11 years, 14 (23%) entered between 6 – 10 years, 17 (28%) entered between 2–5 years and 13 (22%) had a time between entry and diagnosis of less than 2 years. Among those born outside the UK, the proportion of cases who had been in the UK for less than 2 years has decreased slightly from the previous year.

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




Country of birth data was available for all the non-UK born cases. In 2017, the largest proportion of non-UK born TB patients were born in Pakistan (9, 15%) followed by India

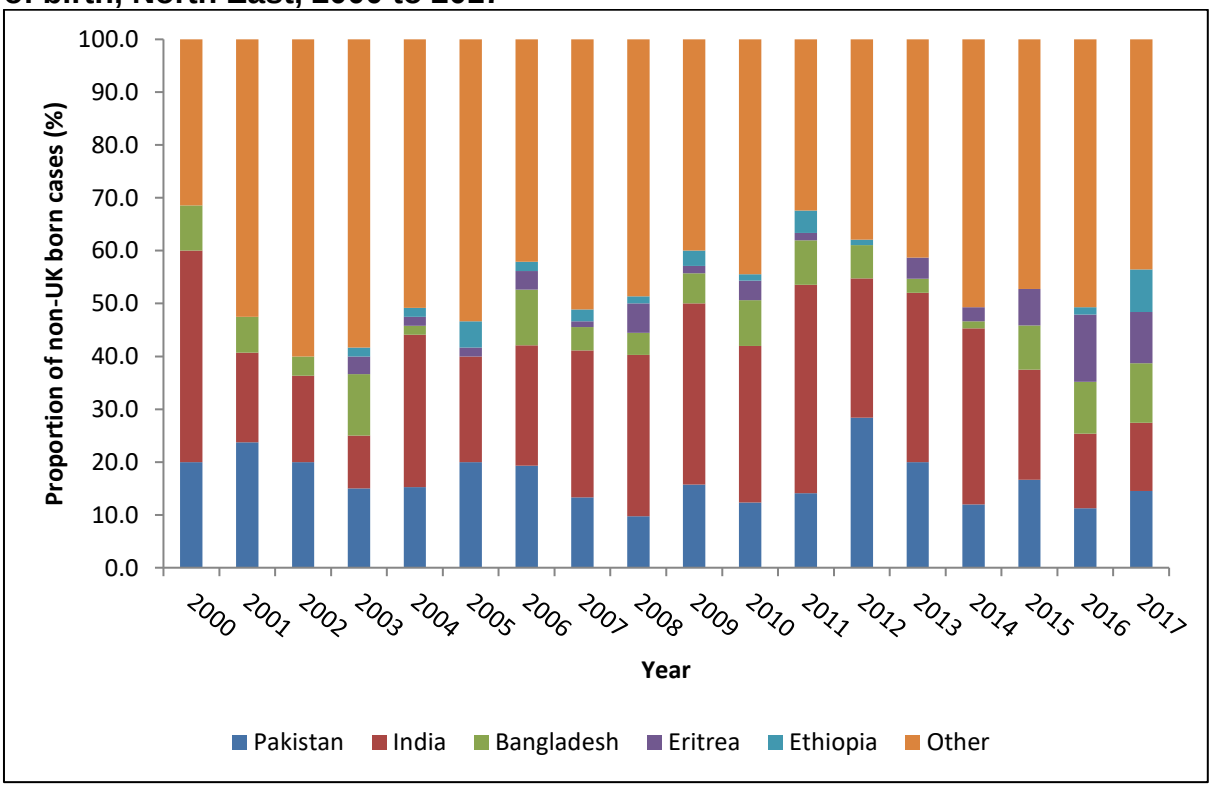
(8, 13%) and Bangladesh (7, 11%). The average time between entry to the UK and TB diagnosis varied by country of birth.

Over the past few years, people born in Pakistan and India have made up the highest proportion of cases born outside the UK.

**Table 1: Five most common countries of birth of non-UK born TB patients, North East, 2017**

| Country of origin | Number of cases | Proportion of non-UK born % |
|---|---|---|
| Pakistan | 9 | 15 |
| India | 8 | 13 |
| Bangladesh | 7 | 11 |
| Eritrea | 6 | 10 |
| Ethiopia | 5 | 8 |
| Others<5 | 27 | 44 |
| **Total non-UK born** | **62** | **100** |

**Figure 8: Trend in non-UK born TB case numbers in the 5 most common countries of birth, North East, 2000 to 2017**

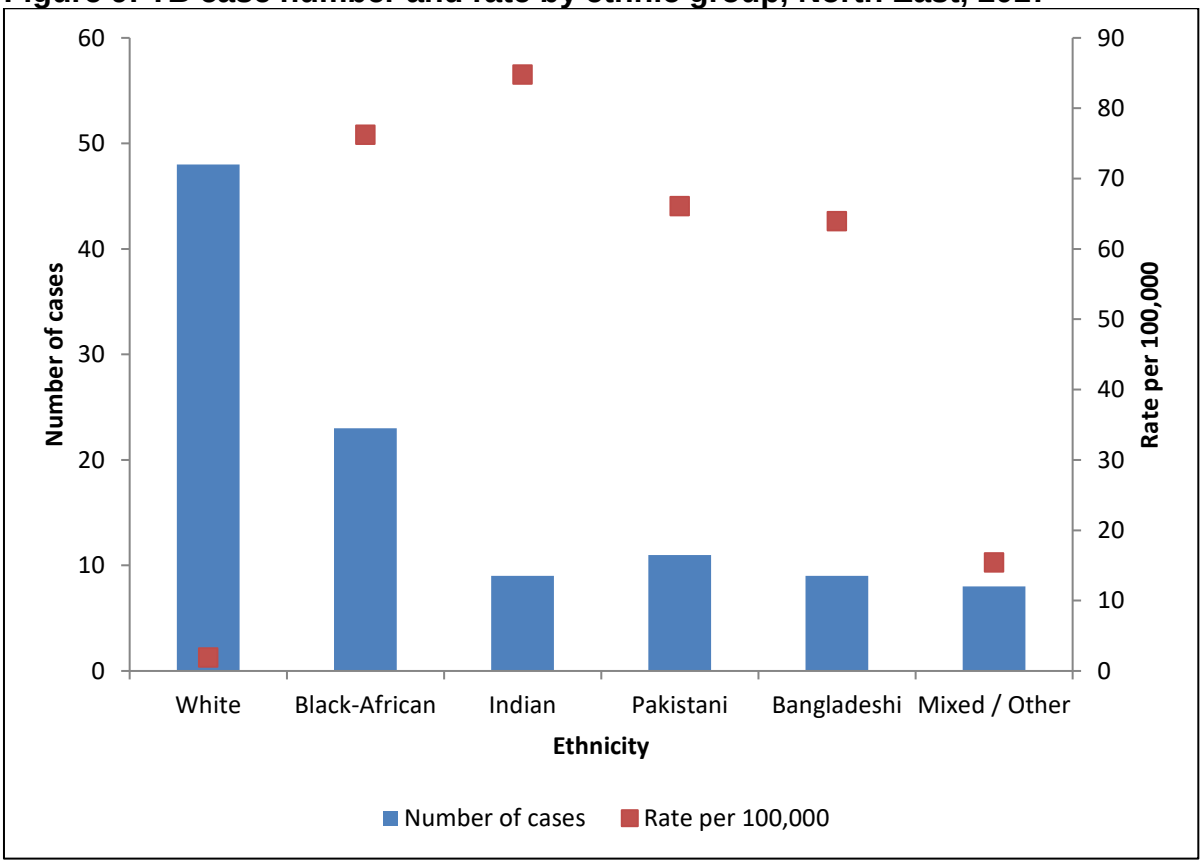


## Ethnicity

The rates in this section should be interpreted with caution, as population estimates, used as the denominators for the different ethnic groups were calculated using the Labour Force Survey, which is liable to sampling error for small population groups.[1]

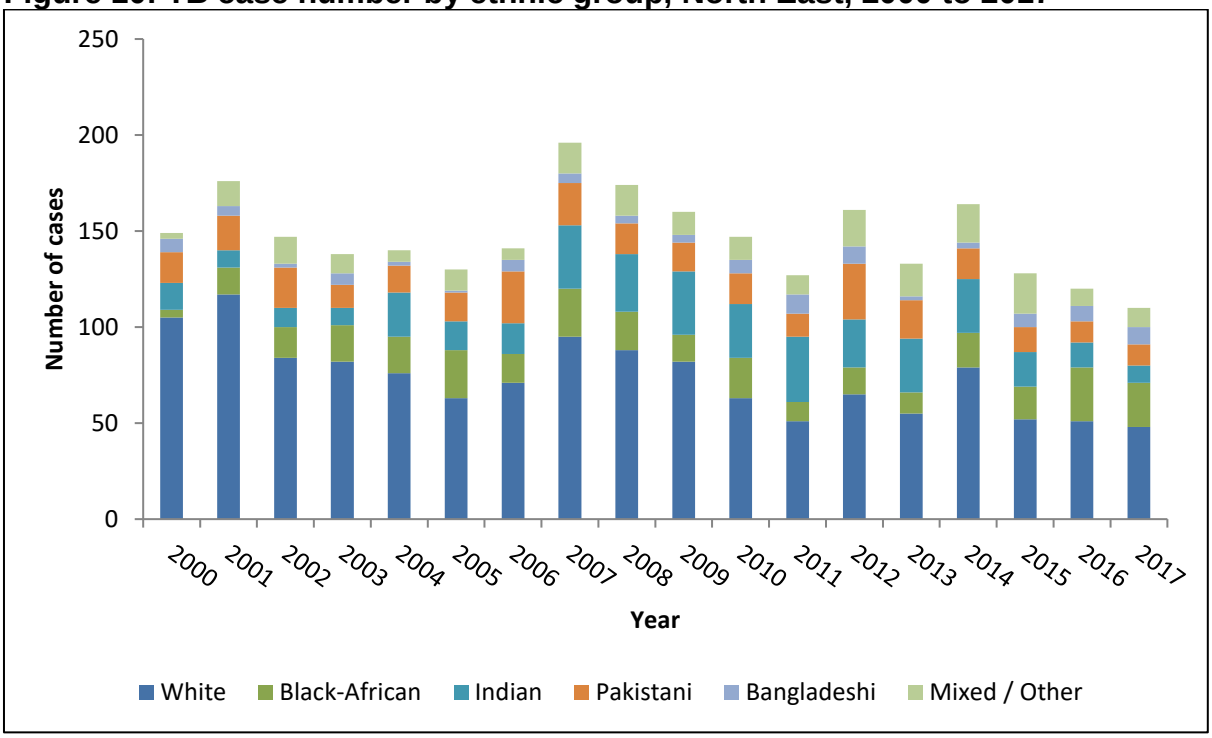
As in previous years the most common ethnic group was White, accounting for 44% (48/110) of TB cases, followed by Black-African and Pakistani. Due to the predominantly White population of the North East this equates to a rate of 1.9 per 100,000 white population. The rates in the other groups were much higher.

**Figure 9: TB case number and rate by ethnic group, North East, 2017**



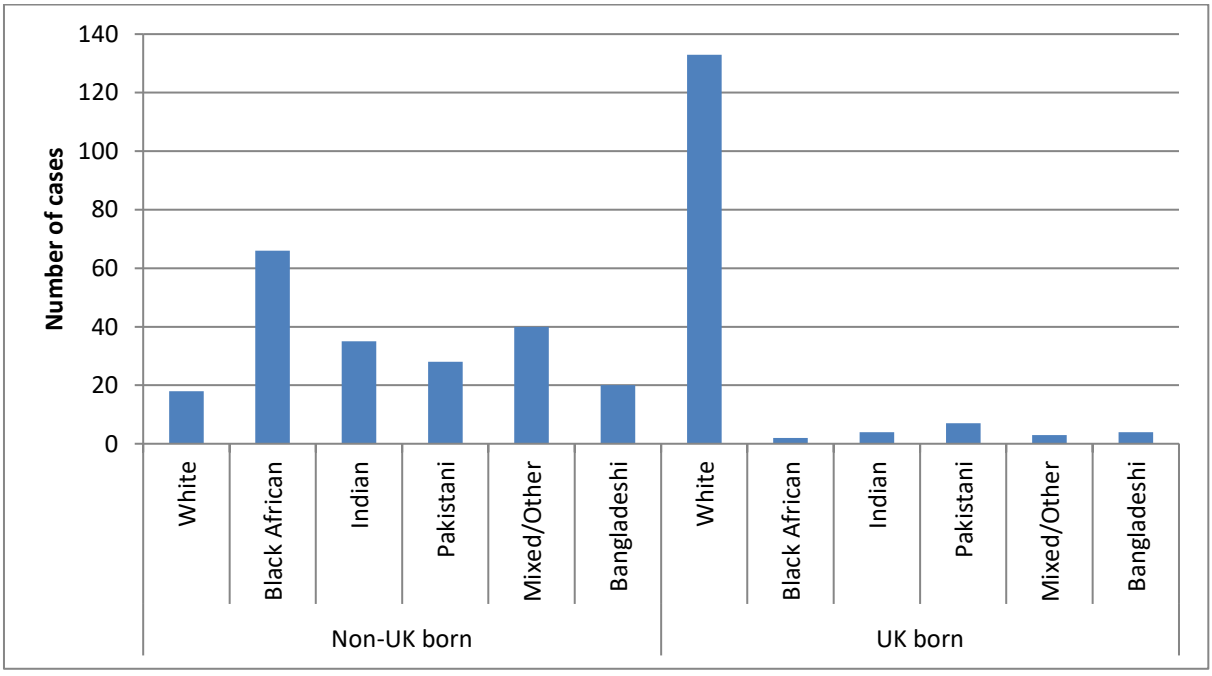

[1] The Labour Force Survey (LFS) was used to calculate population estimates based on a random sample of surveyed individuals, weighted to represent others in the region. Small populations are often underrepresented in the LFS sample, which may inflate TB rates for some ethnic groups

**Figure 10: TB case number by ethnic group, North East, 2000 to 2017**




Of the UK born TB cases reported in 2015-17 ([a]3-year data due to small numbers), the majority (87%, 133/153) were in the White ethnic group. Among the non-UK born reported in 2015-17, 32% (66/207) were in the Black African group; 19% (40/207) in the Mixed/Other group and 17% (35/207) were in the Indian group.

**Figure 11: TB case number by ethnic group and place of birth, North East, 2015 to 2017[a]**



## Occupation

In 2017, occupation was known for 97% (77/79) of North East TB cases aged between 18 and 65. The most common occupational category was ‘No occupation’ (38, 48%), followed by ‘Other’ (24, 30%) and ‘Healthcare worker’ (11, 14%). In the ‘No occupation’ category, the most frequently reported status was ‘Unemployed’ (23/38, 61%).

**Table 2: Occupational category of TB patients aged 18 to 65 years, North East, 2017**

| Occupation | Number of cases | % |
|---|---|---|
| Education | 4 | 5.1 |
| Health care worker | 11 | 13.9 |
| Other | 24 | 30.4 |
| No occupation | 38 | 48.1 |
| **Total** | **77** | |

# Clinical characteristics

## Site of disease

In 2017, most cases were diagnosed with pulmonary disease with or without extra pulmonary (+/- EP) sites (59, 53.6%). The most common extra pulmonary site was extra thoracic lymph nodes (15, 13.6%). Pulmonary disease was more common among those UK born than those born abroad (60%, 29/48 vs 48%, 30/62) and those with at least 1 social risk factor (87%, 13/15).

**Table 3: Site of disease of TB patients, North East, 2017[b]**

| Site of disease | Number of cases | Proportion (%) |
|---|---|---|
| Pulmonary +/-EP sites | 59 | 53.6 |
| Pulmonary ONLY | 54 | 49.1 |
| Lymph nodes (extra-thoracic) | 15 | 13.6 |
| IT lymph nodes | 13 | 11.8 |
| Pleural | 6 | 5.5 |
| Other (extra-pulmonary) | 6 | 5.5 |
| Pulmonary +EP sites | 5 | 4.5 |
| CNS (other) | 5 | 4.5 |
| Gastrointestinal | 4 | 3.6 |
| Bone/joint (spine) | 3 | 2.7 |
| Bone/joint (other) | 3 | 2.7 |
| Genitourinary | 1 | 0.9 |
| Miliary | 1 | 0.9 |

[b] patients may have disease at more than 1 site, so the total % will not equal 100%

## Previous history of tuberculosis

Data on whether a case had been previously diagnosed with TB was available for 107 (97.2%) cases in 2017. A previous diagnosis of TB was recorded for 8 (7.5%) of these patients; this figure was an increase in comparison to 2016 where 4% of cases had recorded a previous diagnosis of TB. Among those with a previous diagnosis of TB, 50% (4/8) were known to had previously been treated for TB, none of the cases were recorded as receiving DOT during this time. Time since previous diagnosis was known for 62.5% (5/8) of cases, with a median time since diagnosis of 61 years (IQR 23-65). A higher proportion of UK born cases had reported a previous diagnosis of TB compared to those born abroad (62.5% vs 37.5%).

## Hospital inpatient and directly observed therapy

24.3% (25/103) of cases were recorded as being an inpatient at time of diagnosis, this was more common among cases with at least 1 social risk factor (53%, 8/15). All cases with MDR TB were inpatients at the time of diagnosis.

# Laboratory confirmation of TB

## Laboratory tests data collection

Laboratory data on culture confirmed TB isolates from the National Mycobacterium Reference Service (NMRS) 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, 69% (76/110) of all TB cases reported in the North East were confirmed by culture, this figure remains static from the previous year. The figure increased to 73% (43/59) among pulmonary cases and was lower (66%, 33/50) for cases with extra pulmonary disease.

Of the culture confirmed TB cases reported in the North East in 2017, 97.3 % were identified as Mycobacterium tuberculosis (M.tuberculosis) infection, 1.3% were identified as M.bovis and 1.3% M.africanum.

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

## Sputum smear

Of the 59 pulmonary cases in 2017, 23 (39%) had a sputum smear result. Of these, 74% (17/23) were sputum smear positive. This is slightly lower than in 2016 (82%, 28/34).

## Other laboratory test results

Between 2015 and 2017, 13.4% (15/112) of TB cases that were not culture confirmed had an alternative positive laboratory result indicative of TB: either by microscopy, histology or PCR. Most of these alternative confirmations were provided by histology (6.3%, 7/112). A substantial proportion of cases which were not culture confirmed did not have any other known positive test result reported (86%, 97/112), and therefore we interpret that these cases were diagnosed based on clinical judgement. Nearly one third of all TB cases notified between 2015 and 2017 (27%, 97/359) were not confirmed by any laboratory method (culture, microscopy, histology and PCR).

# TB transmission

## Rate of TB in UK born children

TB in UK born children is used as an indirect indicator for recent TB transmission within the UK, since TB in children is likely to be caused by recent exposure (as opposed to reactivation of latent TB infection acquired some time previously).

In 2017 in the North East, the rate in UK born children was 0.9 per 100,000 population, this rate has remained static from 2016. This North East rate was lower than the England rate of 1.4 per 100,000 for 2017.

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

## Strain typing and clustering

In December 2016, Whole Genome Sequencing (WGS) was rolled out by NMRS-North and Central, covering the Midlands and North of England, at which time MIRU-VNTR typing (the previous method of strain typing) was discontinued. By 2017/18, the WGS typing for TB was extended to the whole of England and replaced any previous typing methods.

WGS of *Mycobacterium tuberculosis complex* isolates provides information on Single Nucleotide Polymorphism (SNP) differences between isolates and describes how isolates are related to each other. WGS provides good understanding of whether isolates are likely to be part of the same transmission chain and may also help determine the timing and direction of transmission. [3] [4] [5]

Epidemiologically linked patients involved in transmission are unlikely to be identified at SNP distances of more than 12 [6] therefore WGS clusters of TB are defined as patients with 1 or more “near neighbour” patients whose TB sequences differ by 12 SNPs or fewer. Additional epidemiological information is required to assess whether recent transmission may have occurred, and whether any additional public health action should be taken.

## Proportion of patients in clusters and geographical distribution

In 2017, there were 76 culture confirmed cases in the North East of which 93% (71/76) had an isolate that had WGS performed. Of those sequenced cases, 85% (60/71) had a cluster result; of those 17% (10/60) clustered within 12 SNP.[2]

## Size of clusters

40% of clusters comprised 3-4 cases and 60% comprised of 5-9 cases.

## Cluster Lineage

All cases were of Euro-American lineages.

## Characteristics of patients in clusters

Of the cases clustered within the North East, 90% (9/10) were pulmonary and mostly male and of Black African ethnicity.

[2] Clusters of TB are defined as patients with 1 or more ‘near neighbour’ patients whose whole genome sequences differ by 12 SNPs or fewer

# Delay from onset of symptoms to start of treatment

## Time from symptom onset to treatment start for patients with pulmonary TB

The time between onset of symptoms and starting treatment was available for 89% (98/110) of all cases and for 85% (50/59) of pulmonary TB cases notified in the North East in 2017 (Table 5). The remaining people were either asymptomatic at diagnosis, did not have a date of onset recorded or did not have a start of treatment recorded.

In 2017, 46% (23/50) of pulmonary cases started treatment within 2 months, and 32% (16/50) between 2 and 4 months from symptom onset. The remaining 22% (11/50) of pulmonary cases had a delay from symptom onset to treatment start of more than 4 months.

The median number of days between symptom onset and treatment start was 68 days. This was lower among those with pulmonary disease at 62 days.

**Table 4: Time between symptom onset and treatment start[c], North East, 2017**

| | Pulmonary | | Extra-pulmonary only | | Overall | |
|---|---|---|---|---|---|---|
| Time delay | n | % | n | % | n | % |
| <2 months | 23 | 46 | 14 | 30 | 38 | 39 |
| 2-4 months | 16 | 32 | 16 | 34 | 32 | 33 |
| Over 4 months | 11 | 22 | 17 | 36 | 28 | 29 |
| **Total** | **50** | | **47** | | **98** | |

[c] Excluding asymptomatic patients, and those with missing onset dates

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

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

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

Of the 11/50 pulmonary cases with a delay from symptom onset to treatment start of more than 4 months; the majority were male (9/11), UK born (8/11) and aged 45-64 (4/11).

# TB outcomes in drug sensitive cohort

## Drug sensitive cohort

For the purposes of TB outcome reporting, drug sensitive cases exclude all patients with rifampicin resistant TB (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, cases with 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 the next chapter (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 last recorded treatment outcome is reported.

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

In the North East, 81% (87/107) of TB cases notified in 2016 (excluding CNS, spinal, military or cryptic disseminated TB) completed treatment within 12 months, this is a slight increase on previous year. (Table 6)

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

**Table 5: Number and proportion completing treatment at 12 months, North East, 2001 to 2016**

| Year | Drug sensitive cases | Cases completed treatment at 12m | Proportion (%) |
|---|---|---|---|
| 2001 | 169 | 128 | 76 |
| 2002 | 145 | 103 | 71 |
| 2003 | 135 | 88 | 65 |
| 2004 | 128 | 96 | 75 |
| 2005 | 126 | 77 | 61 |
| 2006 | 138 | 98 | 71 |
| 2007 | 178 | 139 | 78 |
| 2008 | 166 | 122 | 73 |
| 2009 | 154 | 113 | 73 |
| 2010 | 140 | 114 | 81 |
| 2011 | 122 | 90 | 74 |
| 2012 | 152 | 119 | 78 |
| 2013 | 123 | 100 | 81 |
| 2014 | 136 | 112 | 82 |
| 2015 | 117 | 93 | 79 |
| 2016 | 107 | 87 | 81 |

**Table 6: TB outcome at 12 months, North East, patients diagnosed in 2016**

| Outcome | Number of cases | Proportion (%) |
|---|---|---|
| Treatment completed | 87 | 81 |
| Died | 7 | 7 |
| Lost to follow up | 2 | 2 |
| Still on treatment | 4 | 4 |
| Treatment stopped | 1 | 1 |
| Not Evaluated | 6 | 6 |
| **Total** | **107** | |

The most common reason for not completing treatment was death on or before starting treatment (7 of the 20 cases who did not complete treatment within 12 months).

Older patients were also less likely to complete treatment: just 48% (9/19) of TB cases aged 65 years and over diagnosed in 2016 completed treatment, with higher rates of death before or whilst on treatment 32% (6/19).

Treatment completion was slightly lower in females 79% (41/52) than males 84% (46/55). Treatment completion was also lower among the UK born that those born abroad (74% vs 86%). Those born abroad when compared to UK born were more often lost to follow up (3% vs 0%) and were less likely to die whilst on or before treatment (2% vs 14%)[3].

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

In the North East, nearly 70% of the 12 people notified in 2016 with rifampicin sensitive, CNS, spinal, miliary or cryptic disseminated disease, completed treatment within 12 months (Table 8); the remaining did not complete treatment due to death, still on treatment and stopped treatment.

**Table 7: TB outcome for patients with rifampicin sensitive, CNS, spinal, miliary or cryptic disseminated disease, North East, patients diagnosed in 2016 (excludes rifampicin resistant TB)**

| Outcome | Number of cases | Proportion (%) |
|---|---|---|
| Treatment completed | 8 | 67 |
| Died | 1 | 8 |
| Still on treatment | 1 | 8 |
| Treatment stopped | 1 | 8 |
| Not Evaluated | 1 | 8 |
| **Total** | **12** | |

## Deaths and 'lost to follow up' in the entire drug-sensitive cohort

Of the 119 cases notified in 2016, 8 cases (7%) had reported death as a reason for non-completion of treatment. Of these, the relationship between TB and death was unknown for 38% (3/8) of cases. TB caused, contributed to or was incidental to a total of 5 deaths.

The proportion of drug sensitive North East cases that were lost to follow up at the last recorded outcome has ranged from 1% to 9% overall since 2004. Of TB cases notified in 2016, 2% (2/119) were lost to follow up, all among non-UK born cases, equally represented by males and females.

[3] Causes of death reported to ETS were not necessarily based on review of death certificates completed in routine death registration

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

## Drug resistance

Anti-TB antibiotic drugs are a large family and resistance may occur to 1 or more of these antibiotics and may be 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 are injectable agents (e.g. amikacin, capreomycin, kanamycin), fluoroquinolones (e.g. moxifloxacin, ofloxacin, ciprofloxacin) and other oral bacteriostatic agents. MDR-TB cases are initially resistant to at least isoniazid and rifampicin. Extensively drug resistant TB cases (XDR-TB) are initially MDR and resistant to at least 1 injectable agent and at least 1 fluoroquinolone [8].

## Overall initial drug resistance and geographical distribution

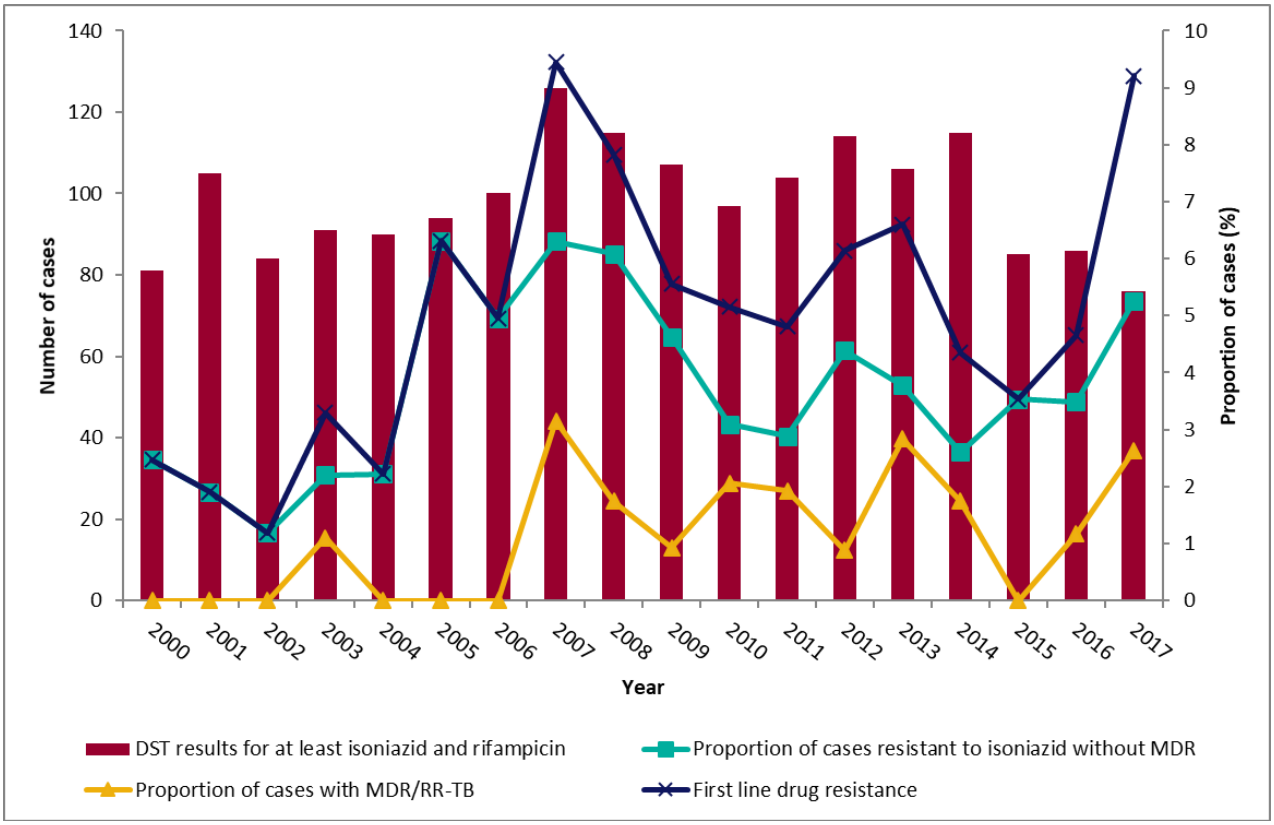
Denominator for this section is cases who had drug sensitivity testing for at least isoniazid and rifampicin (including both phenotypic testing and WGS prediction). Note: TB monitoring indicator 18 (first line drug resistance) excludes *M. bovis* cases with resistance to pyrazinamide.

In 2017, 9.6% (7/76) of the culture-confirmed TB cases in the North East were resistant to 1 or more first line drugs. This was the highest proportion of resistant isolates in recent years. In 2017, 4 (5.3%) isolates had isoniazid resistance without MDR, 2 (2.6%) cases were found to be multi-drug resistant (MDR), the remaining case had pyrazinamide resistance. (Figure 13).

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

**TB Monitoring Indicator 18: Proportion of culture confirmed TB cases with any first line drug resistance**

**Figure 13: Proportion of TB cases with initial first line drug resistance, North East, 2000 to 2017**




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

UK born cases that were culture confirmed had a higher proportion of isolates resistant to any first-line drug (3, 10.3%) when compared to those born abroad (4, 8.5%). The MDR cases were all non-UK born. The highest proportion of resistant isolates were identified in cases of Indian origin (2, 25%) followed by Bangladeshi (1, 20%).

## Acquired drug resistance

Acquired drug resistance is defined as a newly emerged resistance to 1 or more anti-TB antibiotics identified on repeat culture 3 or more months after the first specimen date. In addition, cases with a change from sensitive to resistant result following commencement of anti-TB antibiotic treatment are reclassified as acquired resistance (even if this is within the 3-month period). It should be noted that patients who acquire resistance are recorded in the year they were notified, not the year that they acquired resistance, therefore the numbers for recent years may still increase for those still on treatment.

The median time to development of drug resistance from date of start of treatment for cases from 2000 to 2017 was 147 days, increasing to 190 days from earliest specimen date.

## TB outcome at 24 months for patients with rifampicin resistant disease

There were no cases of rifampicin resistant disease reported in 2015.

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

# TB in under-served populations

## Social risk factors

Within the TB data collection system, data is collected on the presence or absence of 4 social risk factors (SRF) known to increase the risk of TB: current or history of homelessness, imprisonment, and drug misuse and current alcohol misuse. Data in this chapter, apart from area level deprivation, is presented for TB cases aged 15 and older.

In the North East in 2017, 16% (15/103) of TB cases aged 15 years and older had at least 1 SRF (Table 9), this has remained stable from previous year. Of the cases in 2017 with at least 1 SRF, 33% (5/15) had 2 or more SRFs.

**Table 9: Social risk factors among TB patients, North East, 2009 to 2017**

| Year | Total | Number with field completed | Number with any risk factor | % |
|---|---|---|---|---|
| 2009 | 157 | 98 | 14 | 14 |
| 2010 | 145 | 126 | 12 | 10 |
| 2011 | 130 | 112 | 15 | 13 |
| 2012 | 159 | 136 | 15 | 11 |
| 2013 | 133 | 119 | 12 | 10 |
| 2014 | 157 | 138 | 13 | 9 |
| 2015 | 122 | 108 | 14 | 13 |
| 2016 | 115 | 105 | 17 | 16 |
| 2017 | 103 | 95 | 15 | 16 |

During 2017 among people reporting social risk factors, the most prevalent risk factor was homelessness followed by drug use.

**Table 10: Social risk factors among TB patients, North East, 2017**

| Risk factor | n | % | Total |
|---|---|---|---|
| Prison | 5 | 5.3 | 95 |
| Homelessness | 9 | 8.9 | 101 |
| Alcohol misuse | 4 | 4.0 | 99 |
| Drug use | 6 | 6.0 | 100 |

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

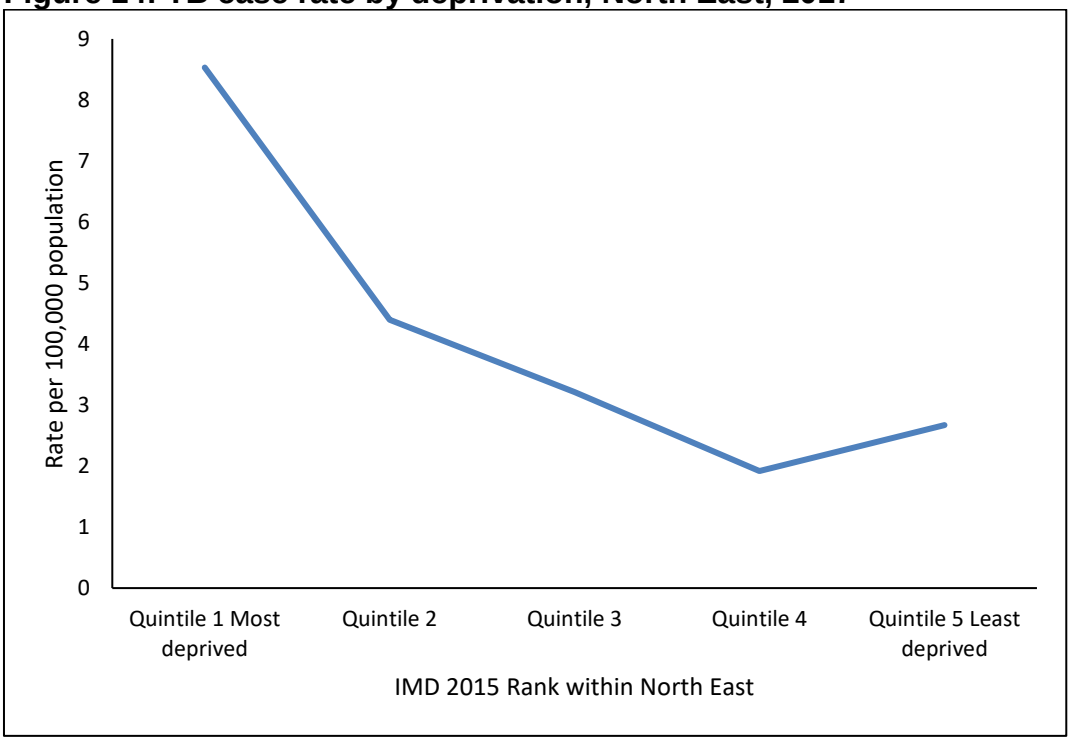
In 2017 in the North East, the proportion of UK born cases with at least 1 social risk factor was 16% (8/49) compared to those born outside the UK (14%, 7/49).
In 2017, the majority (87%, 13/15) of cases with at least 1 social risk factor had pulmonary TB, and the majority were also male (93%, 14/15).

A third (33%, 5/15) of cases with at least 1 social risk factor received DOT in 2017 compared with 3% (2/80) of cases without a social risk factor. The proportion of those with at least 1 social risk factor receiving DOT was lower in 2017 than in 2016 (35%, 6/17).

## Deprivation

During 2017, the largest proportion of TB cases lived in areas from the most deprived quintile (46, 42%). The highest TB rates were also observed in the most deprived quintile, a rate of 8.5 per 100,000 in the most deprived quintile compared to a rate of 2.7 per 100,000 in the 20% of the population living in the least deprived areas.

**Figure 14: TB case rate by deprivation, North East, 2017**



# 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 is successfully treated with a combination of highly active antiretroviral therapy (HAART) and appropriate TB antibiotic treatment [9].

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 have the opportunity to start curative TB treatment and HAART as soon as possible, and in doing so preserve their life expectancy and reduce the risk of TB and HIV transmission to others.

In 2017, data on HIV testing was available for 94% of TB cases (103/109)[4]. Of those, 89% (90/101) were offered[5] an HIV test and 11% were not offered an HIV test. Among those offered testing, the uptake was high (98%, 88/90). Cases not offered an HIV test were more common among White UK born patients compared to those born abroad (64%, 7/11 vs 36% 4/11). Of the cases not offered HIV test by age group, the 0-14-year (36%, 4/11) and 65+ year (36%, 4/11) age categories saw the highest proportion.

[4] Excludes cases identified at post mortem [5]excludes cases identified at post mortem and those where HIV status is already known

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

## TB-HIV co-infection rates

HIV status is not collected in ETS, but TB-HIV co-infection is estimated nationally by anonymously linking reports in ETS with the SOPHID and HANDD HIV datasets[6] for patients aged 15 years and older. [1] (Table 11)

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

## Table 11: Number and proportion* of TB cases with HIV co-infection, North East, 2001 to 2017

| Year | n | % |
|---|---|---|
| 2001 | 10 | 6.0 |
| 2002 | 9 | 6.3 |
| 2003 | 7 | 5.1 |
| 2004 | 10 | 7.2 |
| 2005 | 6 | 4.8 |
| 2006 | 7 | 5.5 |
| 2007 | 15 | 8.0 |
| 2008 | 7 | 4.0 |
| 2009 | 7 | 4.5 |
| 2010 | 4 | 2.8 |
| 2011 | 3 | 2.3 |
| 2012 | 1 | 0.6 |
| 2013 | 2 | 1.5 |
| 2014 | 6 | 3.8 |
| 2015 | 5 | 4.1 |
| 2016 | 4 | 3.5 |
| 2017 | 1 | 1.0 |
| Total | 104 | 4.3 |

* Proportion is calculated using the number of notified TB cases with HIV co-infection plus the number of un-notified TB isolates with HIV co-infection as the numerator, and the number of all notified TB cases (with or without HIV co-infection) plus the number of un-notified TB isolates with HIV co-infection as the denominator.

# BCG vaccination

## BCG vaccination status of TB patients

BCG vaccination status was available for 90% (99/110) of North East TB cases in 2017. Where data was available, 62% (61/99) of cases had received the BCG vaccination.

The proportion receiving BCG vaccination was greater in those born abroad than those born in the UK (41/54, 76% vs 20/45, 44%).

**Table 12: Number and proportion of TB patients with BCG vaccination, North East, 2017**

| | 0-14 years | | All ages | |
|---|---|---|---|---|
| | Number vaccinated | Proportion % | Number vaccinated | Proportion % |
| Non-UK born | 2 | 67 | 41 | 76 |
| UK born | 2 | 50 | 20 | 44 |
| **All cases** | **4** | **57** | **61** | **62** |

# Latent TB infection testing and treatment

This report, derived from the ETS surveillance system, which is a national case register and management system for cases of active TB, does not deal with the issue of 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. [10]

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 cases per 100,000 or sub-Saharan Africa) within the last 5 years and had been living in that high incidence country for 6 months or longer. Eligible individuals are primarily identified prospectively by GP practices during the new patient registration process, however some Clinical Commissioning Groups (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[7] 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]

Currently no CCGs in the North East meet the threshold for screening.

[7] 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

# Discussion

In January 2015, PHE and NHS England published the Collaborative TB Strategy for England 2015-2020, which sets out the actions required to achieve a year on year reduction in TB incidence and a reduction in the health inequalities associated with the disease. This report of TB surveillance data for North East England up until the end of 2017 provides a comprehensive overview of the epidemiology of TB in the North East England following the implementation of the strategy.

Numbers and rates of TB in the North East remain low and below the national average. However, the rates and TB burden are higher in some areas and subgroups such as urban and deprived populations. In 2017, a small decrease was seen in the TB cases born in the UK from the previous year. A greater number of TB patients were born outside the UK than in the UK. Rates of TB in the UK born remain very low compared to the non-UK born population. The most common ethnic group of TB cases remains White, followed by Black African.

HIV testing was not offered, or not recorded as offered, to 11% of TB cases notified in 2017. UK guidelines recommend all TB patients should be offered a test, regardless of age or ethnicity or where they are resident [7]. Information on symptom onset was well completed and identified longer delays in extra pulmonary cases. Less than a half of pulmonary cases had a sputum smear result. This is an important indication of infectiousness and should be done on all patients where possible.

Treatment completion at 12 months among patients with rifampicin sensitive and non-CNS/spinal/miliary or cryptic disseminated disease in the North East in 2016 was below the national figure. The most commonly reported reason for not completing treatment was due to death, with the relationship between TB and death unknown for over half the cases. The next most common reason was due to cases still being on treatment. First line drug resistance among the North East TB cases increased from 4.7% in 2016 to 9.2% in 2017.

# Conclusion and recommendations

This report updates the latest epidemiology of TB in the North East, describing those populations at increased risk of disease. This evidence can help services implement the basic elements of TB control, namely prompt identification of active cases of disease, supporting patients to successfully complete treatment, and preventing new cases of disease occurring, through effective case management and robust contact tracing. The information will also be useful to target resources effectively.

Key recommendations for the NHS and PHE derived from the data presented in this report include:

- ensuring that accurate and complete information is provided on the PHE Enhanced TB Surveillance system in a timely manner
- offering and encouraging HIV testing for all those diagnosed with TB and ensuring, where possible, that tests are done, in line with national guidance[7]
- increasing the proportion of pulmonary TB cases with a sputum smear result to better inform local infection control and prevention activity
- reporting treatment outcome for all patients, and reviewing reasons why completion is low in some areas

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# 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 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 tuberculosis (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 Yorkshire and Humber and the North East TB Control Board and North East TB Network.

## Aim of report

This report describes the recent epidemiology of TB in North East region. 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 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 cases of tuberculosis to enhanced tuberculosis surveillance systems: United Kingdom, 2000 to 2017. This is available at 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 www.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020_.pdf). Where data for these indicators is presented in this report, the indicator name is shown.

A number of TB indicators at Upper Tier Local Authority and Clinical Commissioning Group level can be found at http://fingertips.phe.org.uk/profile/tb-monitoring and will be updated with data for 2017 on 2 October 2018. [Note: data presented for TB monitoring indicators at regional level DOES 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

## Data sources

This report is based on TB case notifications made to the PHE Enhanced Tuberculosis Surveillance system (ETS) in England to the end of 2018. This 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 cases. Results for microscopy, polymerase chain reaction (PCR), histology and culture are collected in ETS. Appropriate referral of clinical specimens to the Mycobacterium Reference Laboratories is an important part of the routine work of the diagnostic laboratories in the investigation and management of TB cases.

The National Mycobacterium Reference Service (NMRS) receives these diagnostic materials and undertake characterisation using culture and 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 Whole Genome Sequencing (WGS).

## Definitions

| | |
|---|---|
| **BCG** | Bacillus Calmette-Guérin vaccination |
| **CI** | Confidence interval |
| **CCG** | Clinical Commissioning Group |
| **Cluster** | Two 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 (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: cases 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 (e.g. amikacin, capreomycin, kanamycin), fluoroquinolones (e.g. 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: cases 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 2018.

## 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 Stata, assuming a Poisson distribution.

## Population denominator

Tuberculosis rates by geographical area (Centre and local authority), 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) [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

Strain typing was performed by the National Mycobacterial Reference Service using Whole Genome Sequencing. Analysis was undertaken on strain type clusters as defined above. Analysis of clustering in North East region was carried out on cases that clustered in the North East and notified between in 2017.