



Isoniazid Resistant TB outbreak in London 2000 to 2008

Progress report for TB professionals across London

November 2008

Isoniazid Resistance TB outbreak – Jan 1995 – Sep 2008

Introduction

This report provides an update on the large outbreak of Isoniazid resistant TB which was first detected in 2000.

Background

The majority (58%) of the cases have been confirmed through restriction fragment length polymorphism (RFLP) typing, and 42% on the basis of RAPET which was initially used to rapidly identify linked cases or more recently through VNTR_MIRU typing. Typing is carried out at the Health Protection Agency Mycobacterium Reference Unit. Epidemiological data is obtained through questionnaires completed by TB clinic staff and increasingly in recent years from the London TB Register (LTBR).

Results

To date there are 343 culture proven cases, of which 299 have been diagnosed in London, and 44 diagnosed outside of London (table 1). After eight years, the outbreak still remains mostly focused in North London (table 2), although there is recent statistical evidence of migration to North East London (see appendix 1). The outbreak appears to be slowing a little (figure 1) and some statistical evidence exists to support the notion that there has been a slight downturn (appendix 1). The age of cases in the outbreak range from 1 year to 88 years, with a median age at diagnosis of 35 years. Males account for 69% of all cases with a median age at diagnosis of 37.5 years (figure 2). Females account for 29% of all cases with a median age at diagnosis of 30 years.

UK born cases account for more than half of all the outbreak cases (53%), non-UK born for 37%, and place of birth is unknown for 10% (figure 3). Over one third (34%) of UK born cases were aged between 35 and 44 years at diagnosis, whilst only 17% of non-UK born cases were in this age group. The majority of cases remain in the White and Black - Caribbean ethnic groups at 32% and 29% respectively (figure 4). This trend has not changed over time (appendix 1). The majority of non UK born cases were from Ireland and Jamaica followed by Somalia (figure 5).

There have been nine cases of Multi drug resistant TB (MDR –TB) with the last reported case in 2006.

Of the 299 cases diagnosed in London 66% are reported to have completed treatment, 13% are currently still on treatment, 10% were lost to follow up, 4% died and 1% refused treatment. The remaining 6% include patients who transferred to other clinics and overseas, relapses and where the treatment status is unknown.

Table 1**Number of Isoniazid Resistant TB Outbreak Cases by place of diagnosis and classification**

Place of diagnosis	Classification		Grand Total
	Confirmed (RFLP)	Probable (RAPET and / or MIRU)	
Outside M25	33	11	44
Inside M25	174	125	299
Grand Total	207	136	343

Table 2**Number and Proportion of Isoniazid Resistant TB Outbreak Cases by Region and PCT of Residence at Diagnosis, Jan 1999 – Sep 2008**

Region	PCT	Number of cases	% of all cases
London - North Central	Barnet	13	3.8%
	Camden	11	3.2%
	Enfield	37	10.8%
	Haringey	54	15.7%
	Islington	34	9.9%
	London - North Central Total		149
London - North East	Barking and Dagenham	1	0.3%
	City and Hackney	60	17.5%
	Newham	10	2.9%
	Redbridge	8	2.3%
	Tower Hamlets	13	3.8%
	Waltham Forest	9	2.6%
	London - North East Total		101
London - North West	Brent	3	0.9%
	Harrow	3	0.9%
	Havering	3	0.9%
	Hillingdon	4	1.2%
	Westminster	3	0.9%
	London - North West Total		16
London - South East	Bexley	1	0.3%
	Bromley	1	0.3%
	Greenwich	2	0.6%

	Lambeth	7	2.0%
	Lewisham	4	1.2%
	Southwark	3	0.9%
	London - South East Total	18	5.2%
London - South West	Croydon	1	0.3%
	London - South West Total	1	0.3%
East Midlands	Eastern Leicester	1	0.3%
	Northampton	3	0.9%
	East Midlands Total	4	1.2%
East of England	Basildon	2	0.6%
	Dacorum	1	0.3%
	Epping Forest	1	0.3%
	Great Yarmouth	1	0.3%
	Ipswich	1	0.3%
	Luton	3	0.9%
	North Hertfordshire and Stevenage	1	0.3%
	Royston, Buntingford and Bishop's Stortford	5	1.5%
	South East Hertfordshire	1	0.3%
	Southern Norfolk	2	0.6%
	Thurrock	1	0.3%
	Waveney	1	0.3%
	East of England Total	20	5.8%
South East	Cambridge City	1	0.3%
	Canterbury and Coastal	1	0.3%
	Isle of Wight	1	0.3%
	Milton Keynes	1	0.3%
	Southampton City	1	0.3%
	Surrey Heath and Woking	2	0.6%
	South East Total	7	2.0%
South West	South Gloucestershire	1	0.3%
	Taunton Deane	1	0.3%
	South West Total	2	0.6%
Yorkshire and The Humber	Scarborough, Whitby and Ryedale	1	0.3%
	Sheffield West	1	0.3%
	Wakefield West	1	0.3%
	Yorkshire and The Humber Total	3	0.9%
Wales	Wales	1	0.3%
	Wales Total	1	0.3%
Jersey	Jersey	3	0.9%
	Jersey Total	3	0.9%
Dublin	Dublin	6	1.7%
	Dublin Total	6	1.7%
Address at diagnosis unknown		12	3.5%
Total Cases		343	100.0%

Figure 1

Number of Isoniazid Resistant TB Outbreak Cases by Year and Quarter Jan 1995 – Sep 2008 (n=343)

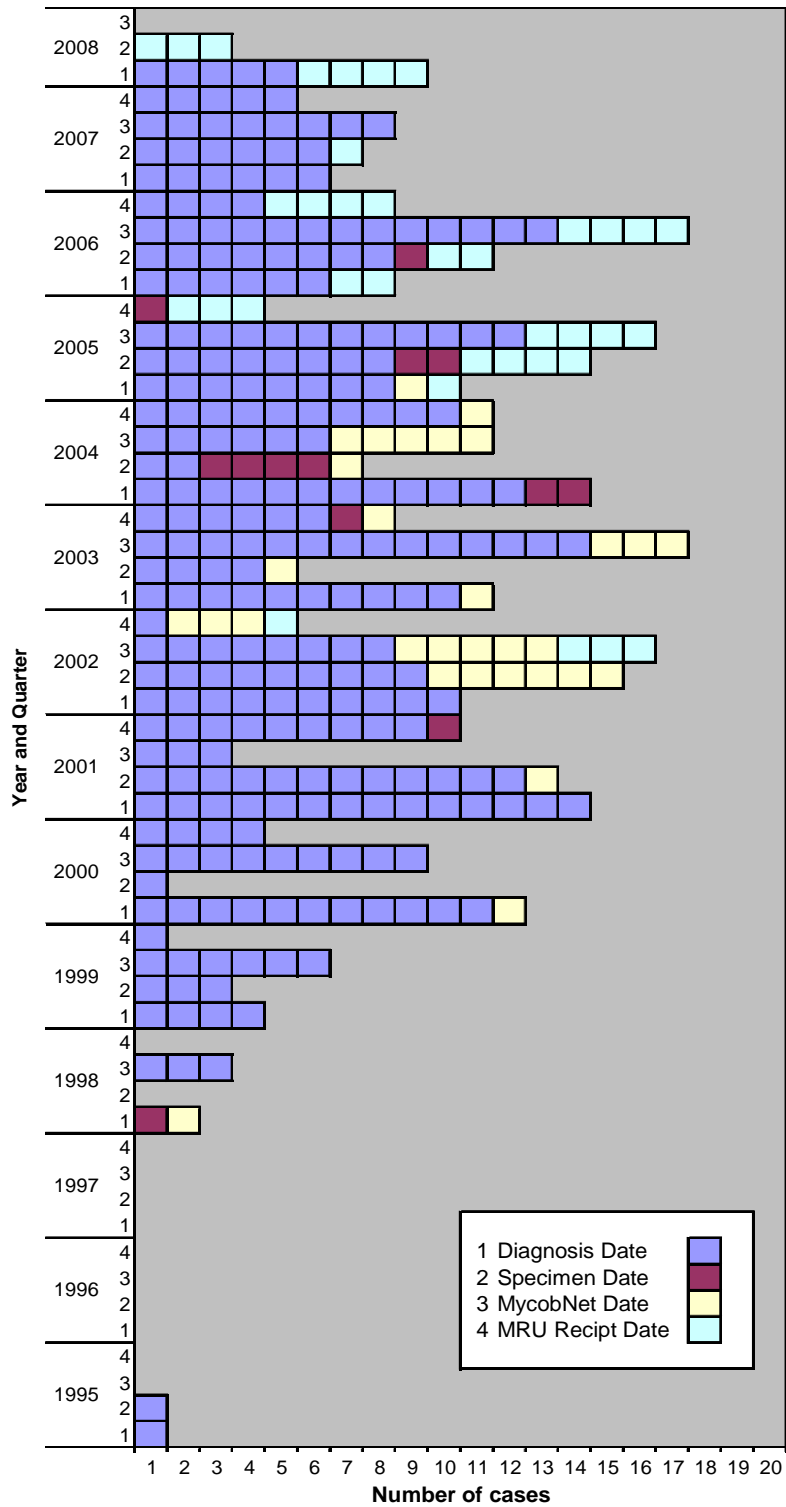


Figure 2

Number of Isoniazid Resistant TB Outbreak Cases by Age and Sex Jan 1995 - Sep 2008 (n=340)

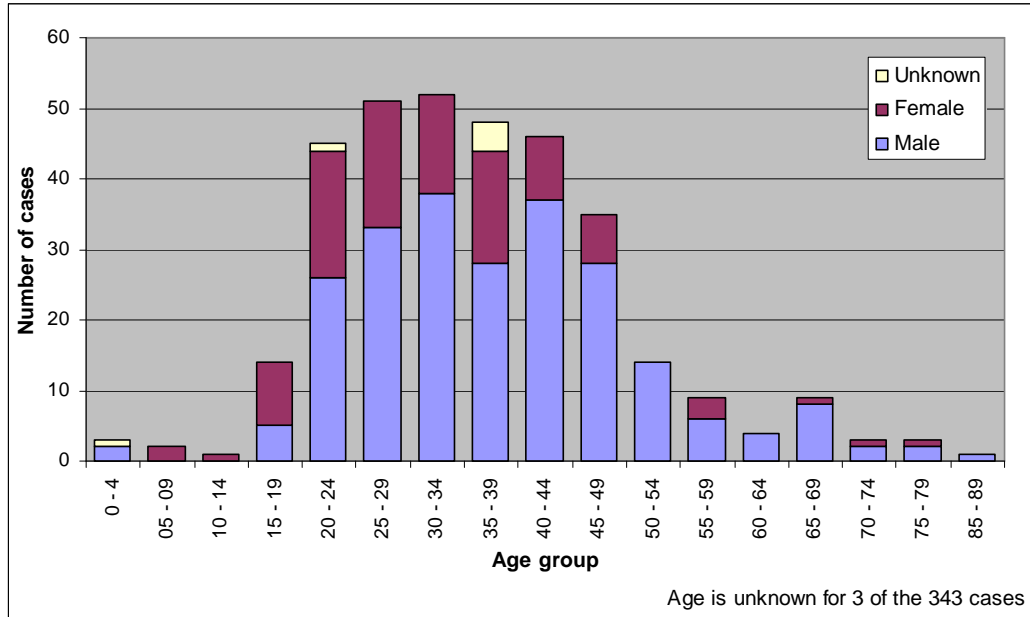


Figure 3

Number of Isoniazid Resistant TB Outbreak Cases by Age and Place of Birth, Jan 1995 - Sep 2008 (n=340)

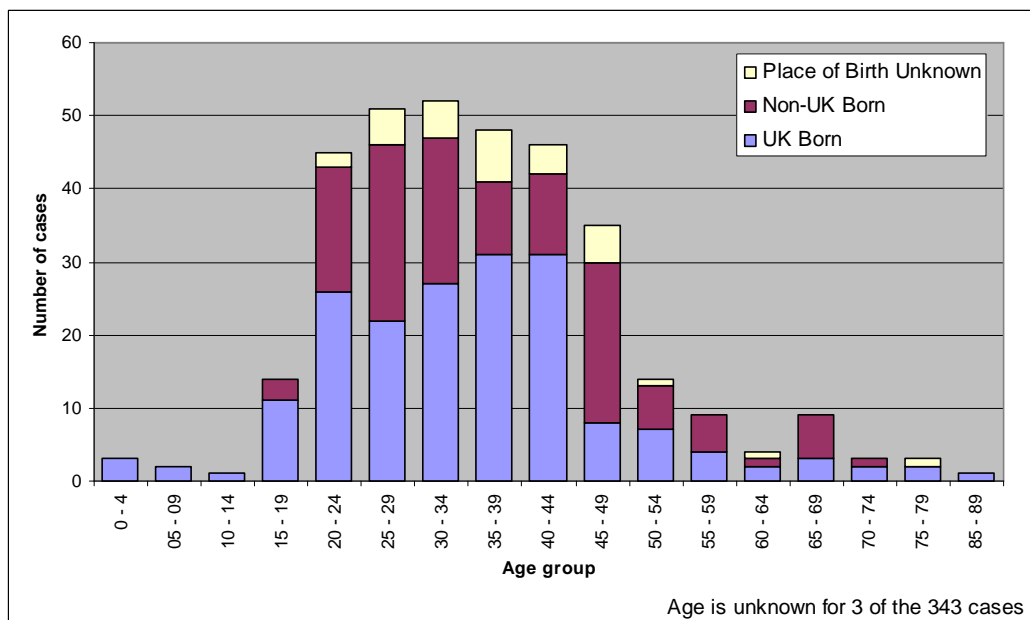


Figure 4

Number of Isoniazid Resistant TB Outbreak Cases by Place of Birth and Ethnic Group, Jan 1995 – Sep 2008 (n=343)

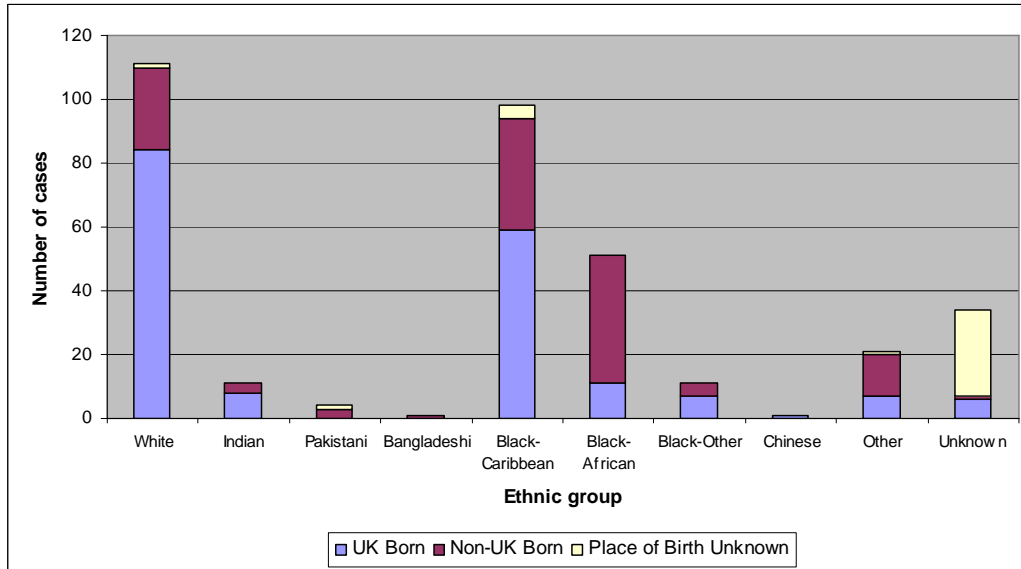
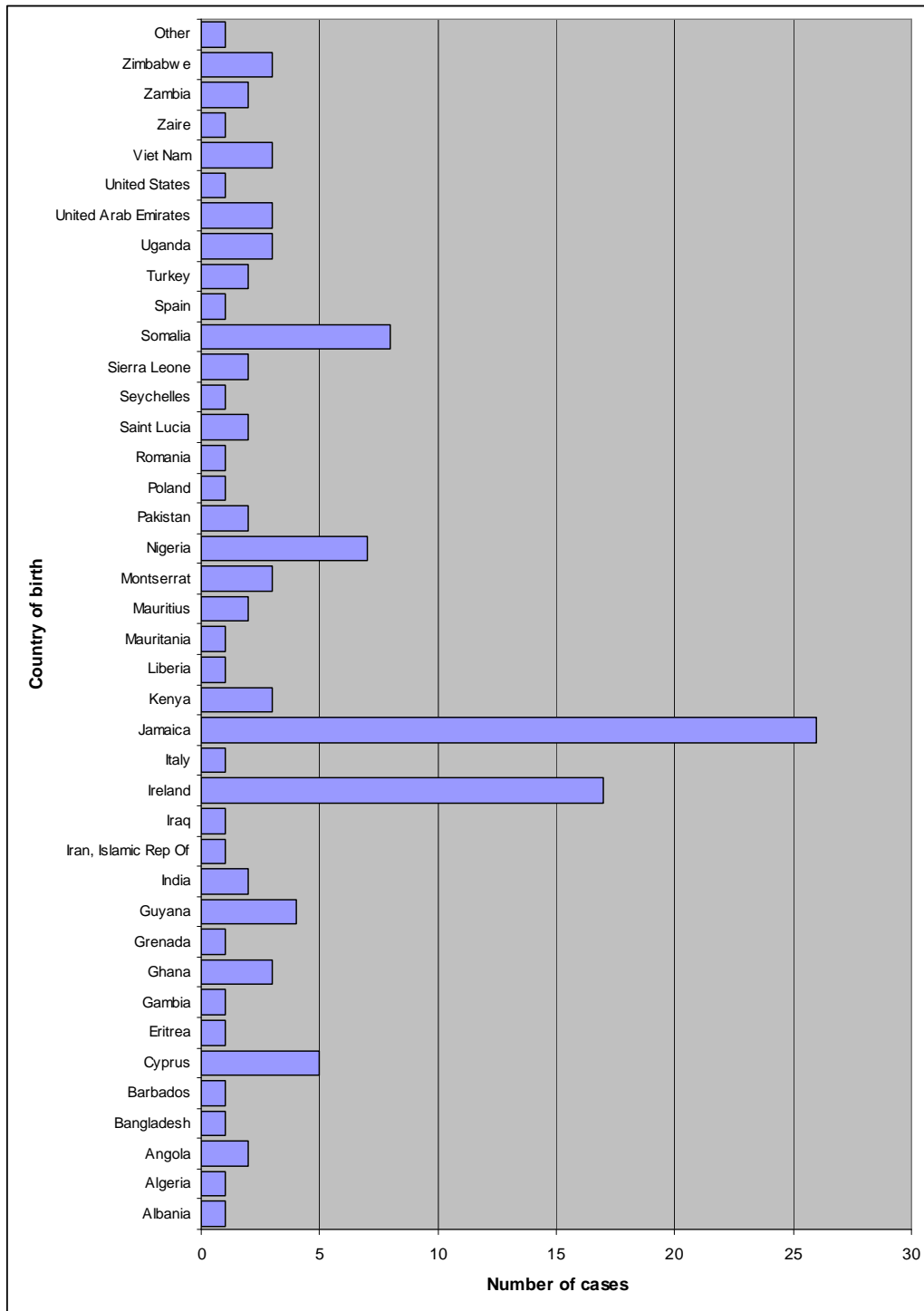


Figure 5

Number of Isoniazid Resistant TB Outbreak Cases by Country of Birth where Non-UK Born*, Jan 1995 – Sep 2008 (n=123)



*Whether UK born or not is unknown for 34 cases, and country of birth is unknown for 3 non-UK born cases.

Appendix 1 Isoniazid Resistant TB Outbreak: 12th statistical report

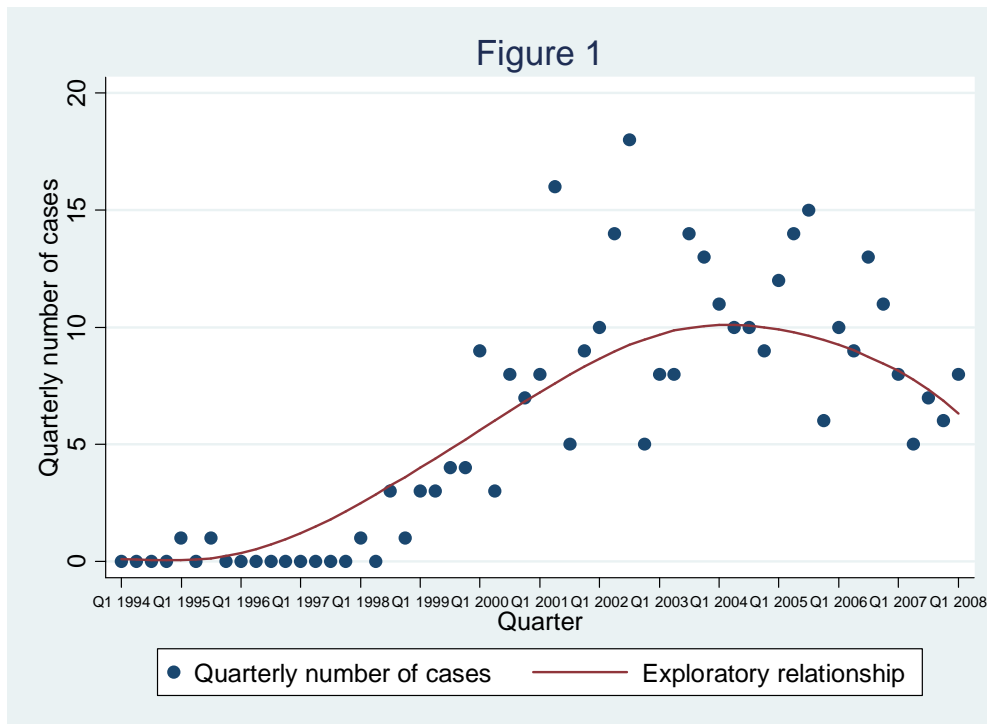
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The dataset received at HPA Centre for Infections from HPA London region, contained 343 unique cases of Isoniazid resistant TB. This analysis used the date of report, which was taken as the date of sample receipt at MRU, or if this was missing, the date when the case was entered on MycobNet. The dataset received contains 32 more cases than when the last analysis was performed in June 2007. Of the 32 new cases, one was from the 4th quarter of 2006, five were from the 2nd quarter of 2007, seven from the 3rd quarter of 2007, six from the 4th quarter of 2007, eight from the 1st quarter of 2008 and three from the 2nd quarter of 2008. Two cases appear to have been retrospectively reported from 2002 and 2005 respectively, as they were not present in previous datasets. No cases from quarter three of 2008 were in the dataset.

All cases in the database were used for analyses, whether their region of residence was stated as North London or elsewhere. One hundred and seventeen individuals were recorded on the database more than once, as they were registered at more than one address, however only unique records were used in the analyses.

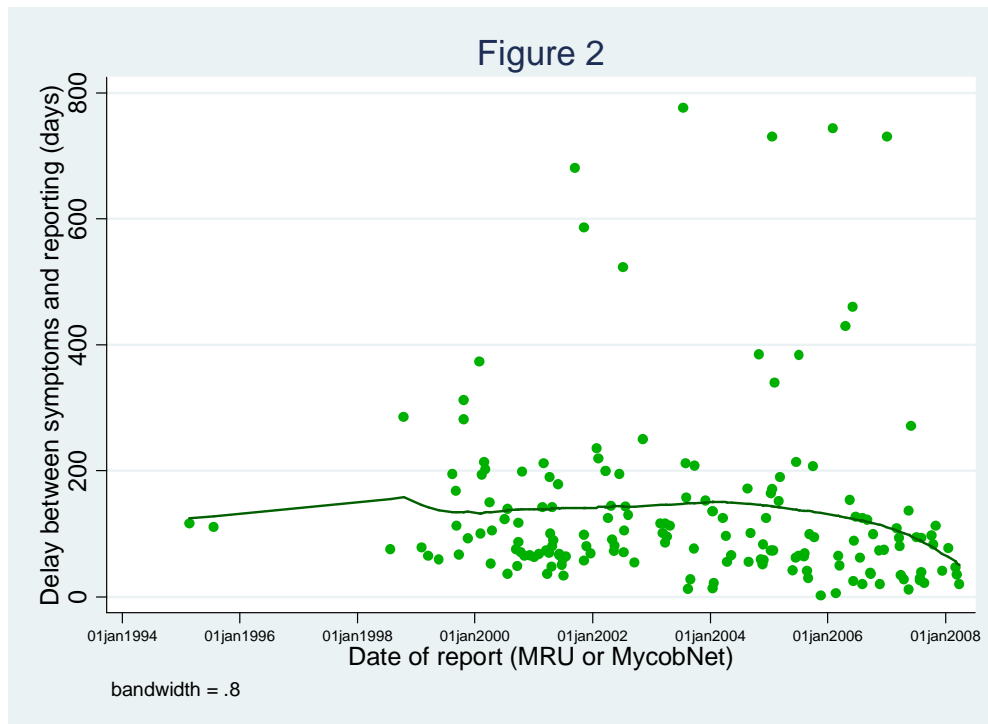
The number of reported cases by quarter from quarter 1 of 2004 to quarter 1 of 2008 is shown in Figure 1 below. The general trend in the number of quarterly cases was explored using a locally weighted smoothing technique.



There is some indication of a decrease in cases, however this could be an artefact due to an increase in the reporting delay in the last couple of years. Reporting delay was calculated as the difference between the date of symptoms and the date of MRU sample receipt or MycobNet entry (if date of MRU sample receipt was missing). However as the date of symptoms has previously been calculated from the MRU sample receipt assuming a 90 day delay if unknown, this date may be incorrect for some individuals. Only samples for which either the MRU sample receipt date or the MycobNet date were known were included in the calculation of reporting delay.

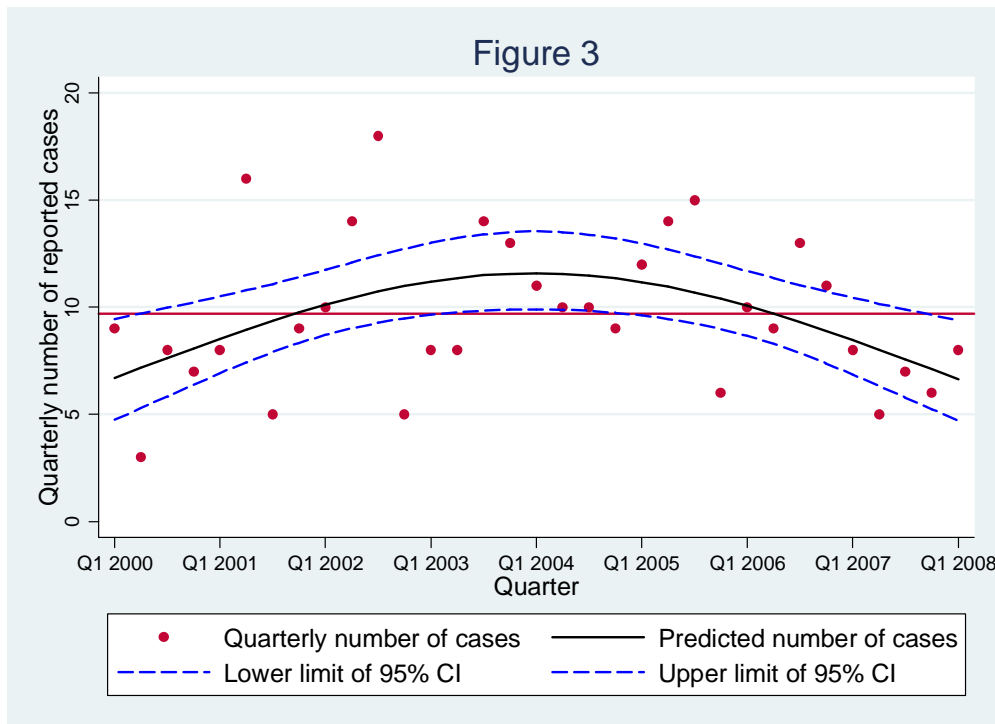
The median reporting delay was 94 days, yet this calculation was based on only 171 cases (49.9% of the total number of cases in the dataset) since 162 cases were missing a date of symptoms and six cases were missing a date of MRU or MycobNet date. Three samples had a date of symptoms which was later than the date of MRU receipt (or MycobNet date). For one case, the reporting delay was over 5 five years; this was deemed to be incorrect and this case was also excluded. Figure 2 below

shows the observed reporting delay and the trend in reporting delay over time, derived using a locally weighted smoothing technique.



The reporting delay appears constant over time, with a slight decrease since 2007. The observed decrease may be due to cases with long reporting delays not being in the dataset yet. This result should be treated with caution since only around half of cases were included in this analysis.

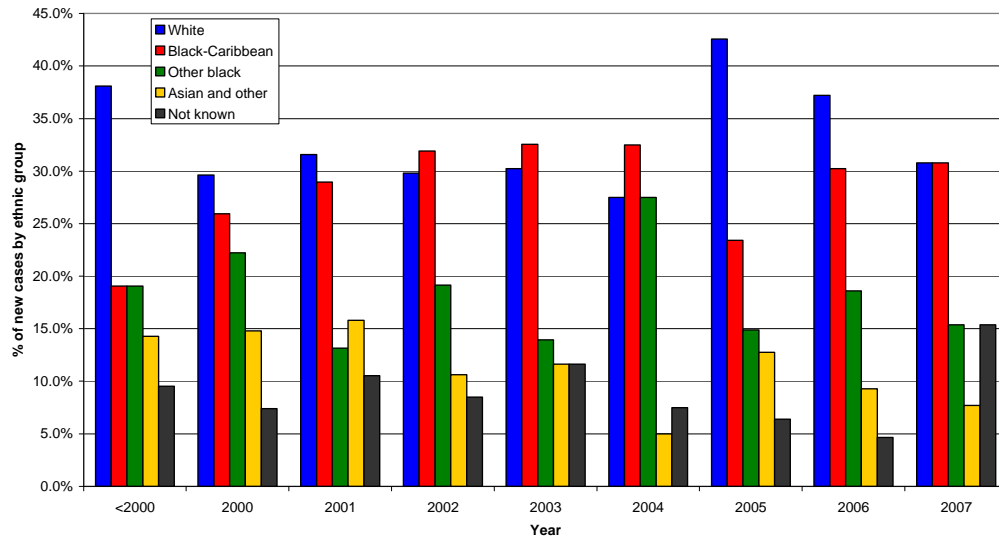
The observed decline shown in Figure 1 is less evident if only cases with a date of report after December 1999 are included. Figure 3 shows the observed quarterly number of cases since January 2000, as well as the expected quarterly number of cases obtained through a polynomial poisson regression model. The mean number of cases per quarter (9.7 cases per quarter) is also shown.



The predicted number of cases from the poisson regression model indicate that the quarterly number of cases follow an inverse *U*-shaped curve, and the regression model appears to describe the trend in quarterly cases very slightly better than a simple mean of the number of cases per quarter. The number of cases per quarter therefore appears to be decreasing, even if only those cases recorded after December 1999 are considered.

The proportion of new cases by ethnic group by year is shown in Figure 4 below. All cases with a missing ethnic group were included in the “unknown” group. Among the 11 cases from 2008, 5 had an unknown ethnic group (45.5%).

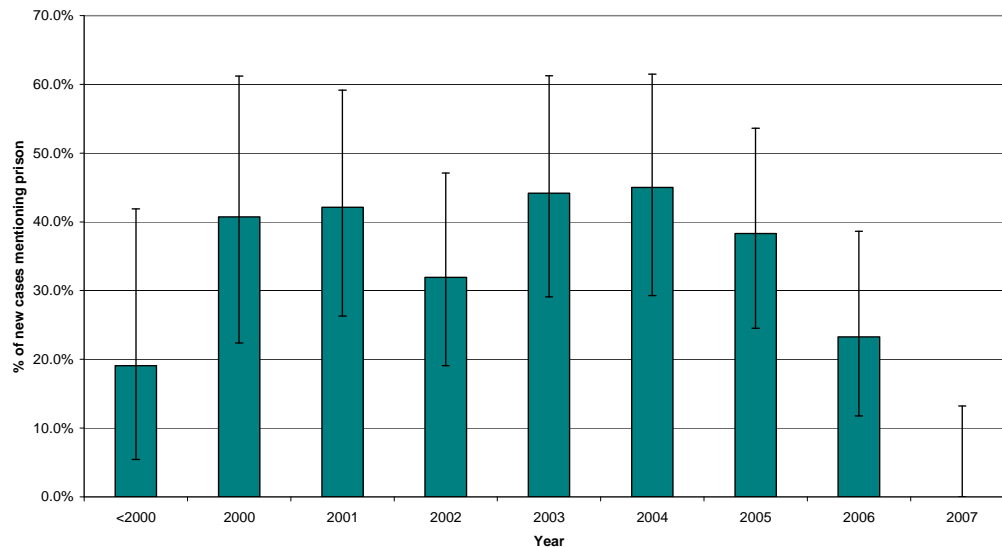
Figure 4



The proportion of new cases by ethnic group has remained relatively stable, and the differences in the proportion of new cases ethnic group by year is not statistically significant (χ^2 statistic =14.1 on 32 d.f., $p=0.997$).

The proportion of new cases with a mention of prison in the case report by year of report (with 95% confidence intervals) is shown in Figure 5.

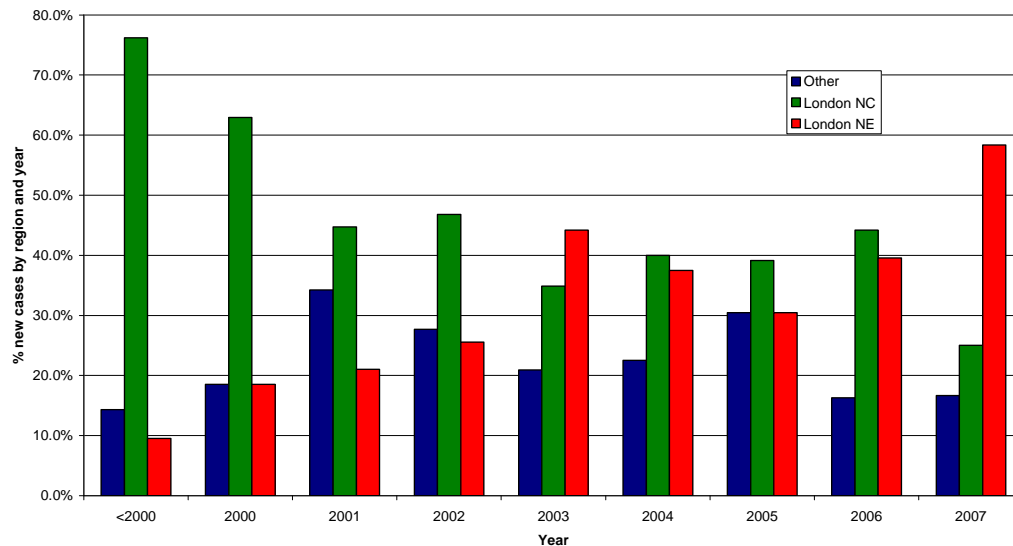
Figure 5



The difference in the proportion of cases with a mention of prison by year was statistically significant (χ^2 statistic =24.1 on 8 d.f., $p=0.002$). This was accounted for by no cases in 2007 with a mention of prison.

The proportion of new cases by year and region is shown in Figure 6.

Figure 6



The difference in the proportion of new cases by region and year is statistically significant (χ^2 statistic =31.2 on 16 d.f., $p=0.013$) At the beginning of the outbreak (before 2000), 76% of cases were from North Central London, however this proportion has since decreased while the proportion of cases from North East London has been increasing. In 2007, the majority of new cases (14/24, 58%) were from North East London, and 6 of 24 new cases (25%) were from North Central London.

Key points:

- Based on the data received, the quarterly number of cases of isoniazid resistant TB now appears to be falling, assuming there has not been a change in reporting delay over the last few years.
- There is no evidence of an increase in the reporting delay over time, however this was based on only half of all cases due to many missing values for date of symptoms.
- There is no change in the proportion of new cases by ethnic group over time.
- The significant difference in the proportion of new cases with a mention of prison by year is accounted for by no cases with a mention of prison in 2007.
- The proportion of new cases from North Central London has decreased over time, while the proportion of cases from North East London has increased. The proportion of cases from outside London has remained relatively stable.

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