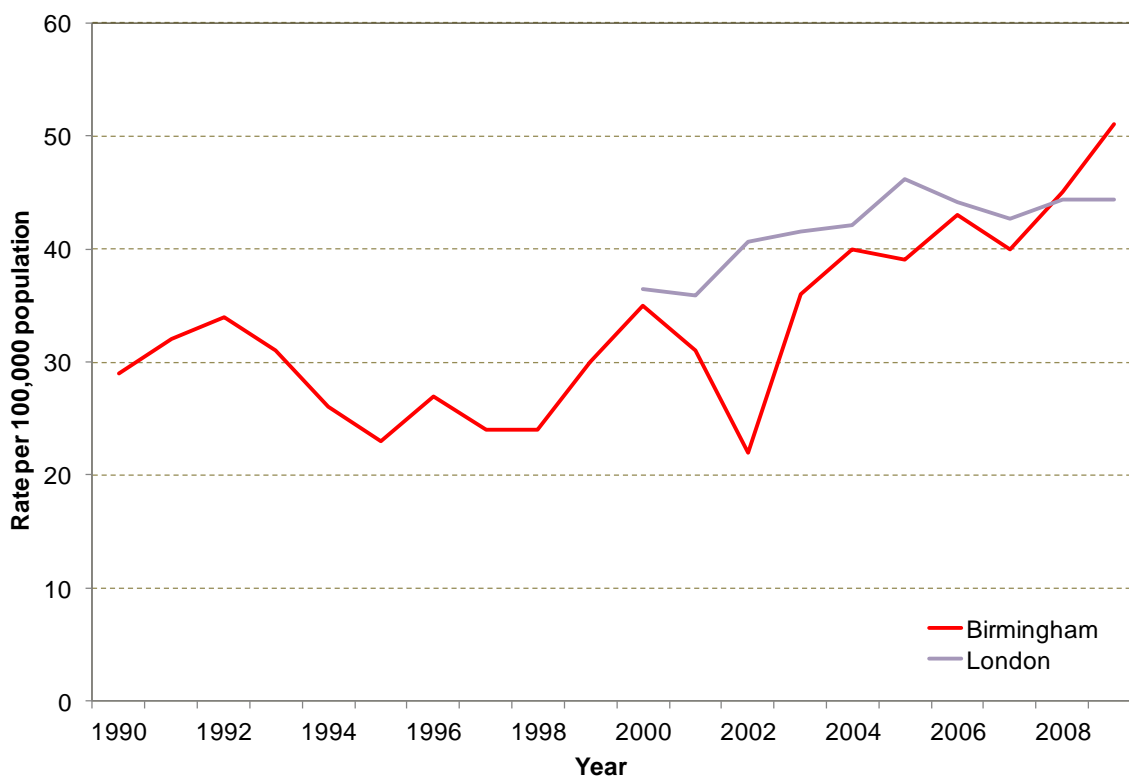


5. EVALUATING NOVEL APPROACHES TO TUBERCULOSIS CASE ASCERTAINMENT AND MANAGEMENT

5.1 Introduction

There has been a steady increase in the number of tuberculosis (TB) cases in the UK since the 1990's. This is in contrast to a decline in TB cases across most of Europe and the United States. In 2011 the incidence of TB in the UK was 14.4 per 100,000 (8963 cases), but incidence varies markedly across the country. The majority of cases occur in London but there are other high incidence areas across the UK, one of which is Birmingham and specifically the area covered by Heart of Birmingham Primary Care Trust (HOBPCT) where the incidence of TB in 2011 was 80 per 100,000.¹ The incidence of TB in Birmingham has been rising since the mid 1990's mirroring the national trend (Figure 5.1).

Figure 5.1: Trends in TB incidence rate, Birmingham and London 1990 - 2009



Source: Health Protection Agency.

Around 70% of TB cases in Birmingham occur in people born overseas. The remainder of cases are acquired in the UK. As it is a statutorily notifiable disease, when a person is diagnosed with TB in Birmingham the case is reported to the Birmingham Chest Clinic. This clinic houses the TB nursing service that covers the whole of Birmingham. Each new case of TB is allocated to a specialist nurse who undertakes contact tracing. The purpose of contact tracing is to identify active cases of TB and treat them before further spread can occur and also to identify latent cases of TB and offer eligible people chemoprophylaxis to prevent them developing and possibly spreading TB in the future.

Contact tracing conventionally this consists of asking the patient who they mix with and how much time they spend with those people. For cases of extra pulmonary TB which is usually considered non-infectious only close family members are identified and screened for active and latent TB. For cases of respiratory TB which is considered infectious close family members are screened and if more than 10% are found to be either active or latently infected wider screening is undertaken to include the index cases work place, school or other place of social aggregation. This method of screening is known as the stone in the pond method where further screening of contacts is based on the number found to be infected in each group screened, screening progresses in concentric circles until the yield is below the predetermined threshold.²

It is increasingly being recognized that a conventional approach to contact screening may miss both active and latent TB cases.³ In an effort to improve the pick-up rate of screening in Birmingham a service evaluation of the current screening programme was undertaken to determine the number of patients screened for each case notified over the past 20 years.

In order to try and improve the number of contacts identified for each new case of TB a service evaluation and improvement programme was undertaken by the Birmingham and Solihull TB service, funded by HOBPCT, to look at the use of social network analysis to investigate clusters of TB patients.⁴⁻¹³ This report contains preliminary results from the project.

5.2 Methods

All TB case notifications in Birmingham are reported to Birmingham Chest Clinic where they are entered into a database before being submitted nationally. The database contains a comprehensive set of data for all TB cases and their contacts going back to 1980. An evaluation of the number of notifications and the outcome of their contacts was made by analyzing anonymous data from this database.

Samples from all cases of TB in Birmingham and Solihull are sent to the Health Protection Agency (HPA) laboratory based at Heartlands Hospital for culture. Any sample where an isolate is cultured is typed using variable number tandem repeats (VNTR) of 24 loci. This system has been in place since 2010. These 24 loci VNTR codes are used to identify clusters of TB patients who may potentially have transmitted TB to each other, this technique has been used to study the molecular epidemiology of TB in Birmingham previously.^{14,15} As TB strains are typed the VNTR codes are loaded into the central TB database and on a monthly basis the HPA laboratory produces lists of clustered patients. These clusters are discussed at a monthly meeting at Birmingham Chest Clinic, where the TB specialist nurses, clinicians and public health team look for links between the patients and decide on possible further investigation or screening that needs to be undertaken. The definition of a cluster and the action undertaken is based on HPA guidance.¹⁶

Many clusters have obvious links between different cases, e.g. a cluster may contain a mother and her children or husband. But often no obvious links are found between cases. For these cases a TB specialist nurse was tasked to visit and interview patients using a social network questionnaire focusing on risk factors and places of possible social aggregation where cases may have met.

Data from these interviews was used to construct network diagrams to illustrate how cases and contacts are linked. Diagrams are produced using nodeXL.¹⁷ Data were analyzed using Epi Info version 7.1.1.14.¹⁸

The data analysed in this report were collected as part of routine public health management of TB cases therefore ethical approval was not required. The service evaluation was approved by the research and development department of Heart of England Foundation Trust.

5.3 Results

Between 1 January 1990 and 31 December 2012 a total of 43,968 contacts of TB patients were identified.

There were 22,191 (50.5%) females with a mean age of 25.3 years (Standard deviation (SD) 19.2 years) and 20,759 (49.5%) males with a mean age of 24.1 years (SD 19.1 years).

The mean number of contacts identified per case of respiratory TB fell from 8.7 in 1990-94 to 5.6 in 2005-09.

Outcomes were available for 40,479 (92%) cases. Overall 16,806 (42%) of contacts did not complete screening. This proportion did not vary across the four 5-year time intervals analysed. The proportion of patients given chemoprophylaxis rose from 2.6% (303 out of 11,809) in 1990-94 to 5.3% (577 out of 10,832) in 2005-09.

Amongst contacts of respiratory TB patients who were smear positive, the proportion of contacts receiving chemoprophylaxis rose from 4.3% (180 out of 4,225) in 1990-94 to 9.4% (369 out of 3,922) in 2004-09 (Table 5.1, Table 5.2, Table 5.3).

A univariate analysis of factors associated with completing screening is shown in Table 5.4. Individuals were more likely to complete screening if they were being screened as part of a school TB incident, or if the index case had respiratory TB.

The outcomes of a monthly cluster discussion meeting are summarized in Table 5.5. From the discussions at this meeting clusters were chosen for further investigation by social network analysis. Clusters for further investigation were identified based on several factors, firstly that the links between patients were not known and secondly that the cluster was growing. To date 15 clusters have been investigated. An example of a cluster diagram generated is shown in Figure 5.2. These diagrams were used to illustrate to the TB team how patients may have mixed and possibly passed TB between themselves. Contacts of the patients were also illustrated showing possible unidentified links between patients.

Table 5.1: Outcome of screening of contacts to respiratory TB patients

Time period	Did not complete screening	Well	Given BCG	Given LTBI Treatment	Given full TB treatment	Total
1990-94	4,238 (47%)	3,816 (42%)	521 (6%)	271 (3%)	162 (2%)	9,008
1995-99	3,050 (65%)	1,027 (22%)	286 (6%)	190 (4%)	153 (3%)	4,706
2000-04	3,415 (42%)	3,934 (48%)	338 (4%)	359 (4%)	155 (2%)	8,201
2005-09	3,848 (46%)	3,366 (40%)	435 (5%)	526 (6%)	229 (3%)	8,404
Total	14,551	12,143	1,580	1,346	699	30,319

Source: Birmingham and Solihull TB database.

Table 5.2: Outcome of screening of contacts to non-respiratory TB patients

Time period	Did not complete screening	Well	Given BCG	Given LTBI Treatment	Given full TB treatment	Total
1990-94	520 (19%)	2,136 (76%)	93 (3%)	32 (1%)	20 (1%)	2,801
1995-99	406 (20%)	1,501 (74%)	84 (4%)	34 (2%)	12 (1%)	2,037
2000-04	589 (24%)	1,746 (71%)	75 (3%)	37 (2%)	16 (1%)	2,463
2005-09	442 (21%)	1,486 (71%)	111 (5%)	42 (2%)	7 (0%)	2,088
Total	1,957	6,869	363	145	55	9,389

Source: Birmingham and Solihull TB database.

Table 5.3: Outcome of screening of contacts to smear positive respiratory TB patients

Time period	Did not complete screening	Well	Given BCG	Given LTBI Treatment	Given full TB treatment	Total
1990-94	2,050 (49%)	1,605 (38%)	277 (7%)	180 (4%)	113 (3%)	4,225
1995-99	1,584 (62.5%)	526 (21%)	179 (7%)	135 (5%)	109 (4%)	2,533
2000-04	1,867 (41%)	2,113 (46%)	192 (4%)	267 (6%)	117 (3%)	4,556
2005-09	1,560 (40%)	1,626 (42%)	188 (5%)	369 (9%)	179 (5%)	3,922
Total	7,061	5,870	836	951	518	15,236

Source: Birmingham and Solihull TB database.

Table 5.4: Predictors of completing screening

Risk Factor	Group	Odds ratio	95% confidence interval	p-value
Age	0-15	2.87		<0.001
	16 -64	-		-
	65 +	1.38	(1.19 - 1.60)	<0.001
Male sex		0.84	(0.79 - 0.89)	<0.001
Ethnicity	White	-		
	Black	0.56	(0.50 - 0.64)	<0.001
	ISC	0.67	(0.61 - 0.74)	<0.001
	Other	0.95	(0.80 - 1.14)	0.61
Relation to index case	1 st degree relative	-		
	Partner	1.4	(1.25 - 1.47)	<0.001
	Other relative	0.70	(0.65 - 0.76)	<0.001
	In-law	0.90	(0.81 - 0.99)	0.038
	Friend	0.82	(0.70 - 0.96)	0.014
	School	4.75	(3.62 - 6.24)	<0.001
	Other	1.52	(1.31 - 1.76)	
Index has smear positive respiratory TB		1.03	(0.96 - 1.11)	0.39
Index has respiratory TB		0.28	(0.26 - 0.30)	<0.001

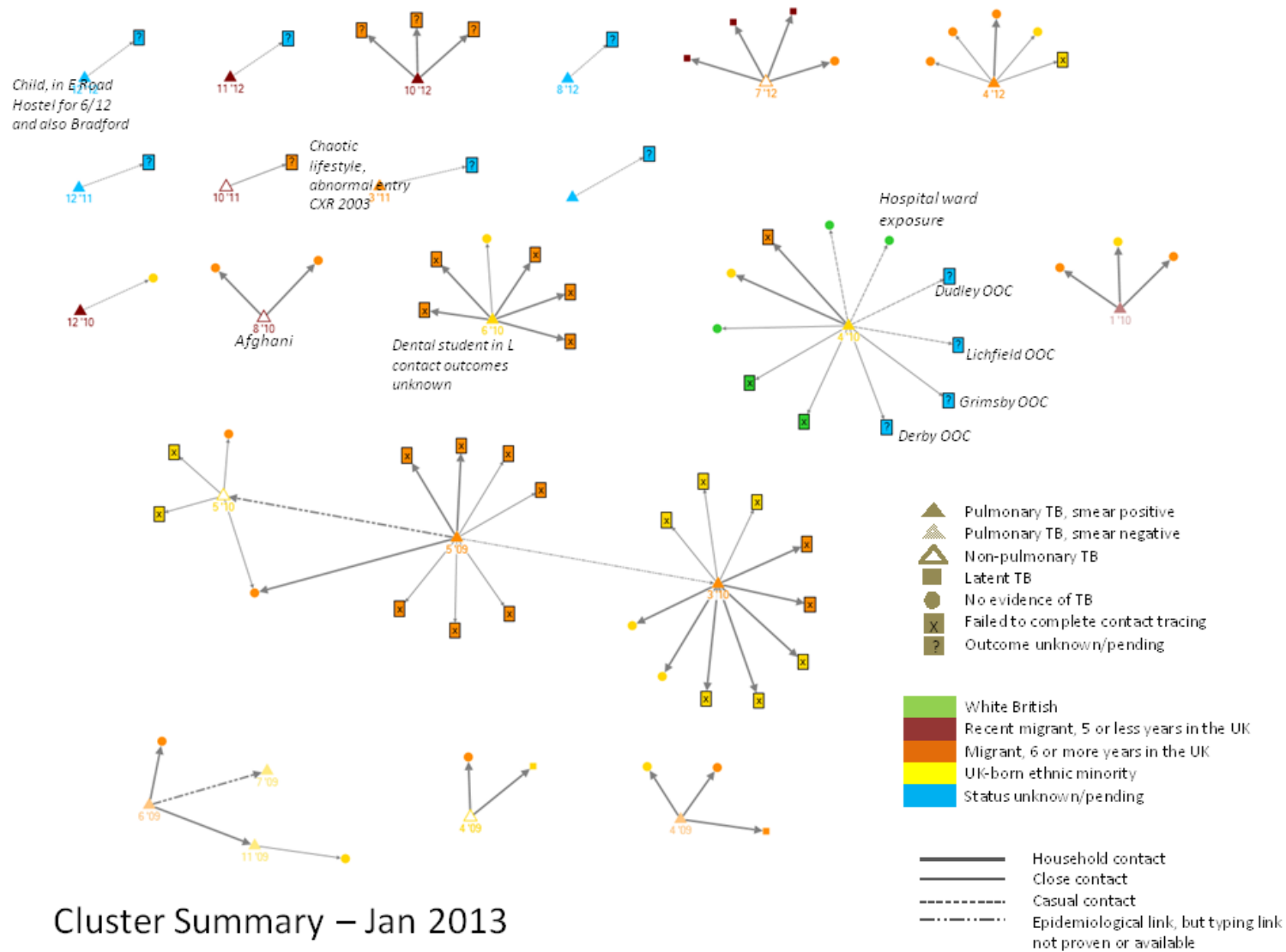
Source: Birmingham and Solihull TB database.

Table 5.5: Summary of monthly TB cluster meetings, 2012

Total number of clusters discussed	121
Number of further investigations started	48
Number new links between clustered patients (previously unsuspected links)	5
Number of extra people identified for screening	80 (to date)
Number of extra TB cases identified	2

Source: Birmingham and Solihull TB database.

Figure 5.2: An example of a cluster diagram.



5.4 Conclusions

Analysis of the contact database of the Birmingham and Solihull TB service revealed that 42% of people identified as contacts of TB patients did not complete screening. This is worrying. If we are to control TB in Birmingham it is important that all identified contacts of TB patients are assessed for both active and latent disease and treated appropriately to prevent spread of TB and morbidity from future cases. In light of our findings the TB nursing team are taking a more proactive approach in following up people who do not attend screening including increased home visits, writing to the person and contacting their general practitioner (GP). Patients who start screening but do not complete it or do not complete latent TB treatment are being visited at home and being written to by their treating clinician as well as their GP being informed. The impact of this change will be assessed after one year.

The results of the cluster investigations reported above are preliminary. The service evaluation of social network analysis is due to continue until November 2013. But the results of the first years' meetings and investigations have been useful. For example using a social network questionnaire a cluster of Eritrean patients was found to attend a single place of worship. An information session delivered at this site led to the opportunistic screening of 80 people with possible TB exposure. This was a good demonstration that a place can be key to determining the route of TB transmission.¹⁹ Despite these promising early results much still needs to be done. Birmingham has many diverse communities and questions used for one group may well be inappropriate for another. It will be important to develop culturally sensitive social network tools.

Currently we are using 24 loci VNTR typing to link TB cases, more specific techniques are becoming available and have been evaluated using whole genome sequencing. This technique may allow much more focused contact investigation and reduce time spent trying to link cases erroneously identified as clustered.^{20,21} Geographical information systems may also provide an extra layer of data to aid identifying contacts (see Chapter **Error! Reference source not found.**, Section **Error! Reference source not found.**, **Error! Reference source not found.**).

An enhanced contact tracing service may contribute to reducing the incidence of TB in Birmingham. It will be vital to provide robust data on its effectiveness to aid commissioners decide on what type of service to fund.

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5.6 Acknowledgements

We would like to acknowledge the hard work of the TB nurses in managing TB cases across Birmingham and Solihull, the laboratory staff for processing specimens in a timely fashion with a high degree of skill, the health protection unit in Birmingham specifically Helen Bagnall for provision of reports and data and the individual CCDC's who manage TB incidents.

5.7 Source of support

This service evaluation is funded by Heart of Birmingham Primary Care Trust.
The authors do not have any conflict of interest related to this manuscript.

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Version 1.0
18 March 2013

