ORIGINAL ARTICLE

Antibiotic resistant tuberculosis in the United Kingdom: 1993–1999

T Djuretic, J Herbert, F Drobniewski, M Yates, E G Smith, J G Magee, R Williams, P Flanagan, B Watt, A Rayner, M Crowe, M V Chadwick, A M Middleton, J M Watson

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See end of article for authors' affiliations

Correspondence to: Dr J Watson, Public Health Laboratory Service Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK; jwatson@phls.nhs.uk

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Background: The re-emergence of tuberculosis as a global health problem over the past two decades, accompanied by an increase in tuberculosis drug resistance, prompted the development of a comprehensive national surveillance system for tuberculosis drug resistance in 1993.
Methods: The UK Mycobacterial Resistance Network (Mycobnet), which includes all mycobacterial reference and regional laboratories in the UK, collects a minimum dataset on all individuals from whom an initial isolate of *Mycobacterium tuberculosis* complex has been isolated and submitted by source hospital laboratories. Data sought include susceptibility to first line antibiotics, demographic, geographical, and risk factor information.
Results: There were 25 217 reports of initial isolates of *M tuberculosis* complex in the UK between 1993 and 1999. All were tested for sensitivity to isoniazid, rifampicin, and ethambutol and 12 692 of the isolates were also tested for sensitivity to pyrazinamide and streptomycin. A total of 1523 (6.1%) isolates were resistant to one or more drugs, 1397 isolates (5.6%) were resistant to isoniazid with or without resistance to other drugs, and 299 (1.2%) were multidrug resistant. Although the numbers of drug resistant isolates increased over the period, the proportions remained little changed. Certain groups of people were at a higher risk of acquiring drug resistant tuberculosis including younger men, residents of London, foreign born subjects, patients with a previous history of tuberculosis and those infected with HIV.
Conclusion: Although the proportion of drug resistant tuberculosis cases appears to be stable in the UK at present, more than one in 20 patients has drug resistant disease at diagnosis and more than one in 100 has multidrug resistant disease. Tuberculosis control measures should be strengthened to minimise the emergence of drug resistance through rapid diagnosis, rapid identification of drug resistance, supervised treatment, and maintenance of comprehensive surveillance.

There has been a re-emergence of tuberculosis as a global health problem over the past two decades[1 2] accompanied by an increase in drug resistant tuberculosis strains.[3] In response to this problem and to help to inform public health policy, a system to monitor trends in drug resistant tuberculosis was developed in 1993 in the UK.

The UK Mycobacterial Resistance Network (Mycobnet) collects information on all bacteriologically confirmed cases of tuberculosis where a culture has been submitted to one of the mycobacterial reference and regional centres nationwide.[4] In this paper the nature and magnitude of drug resistance in newly diagnosed cases of tuberculosis in the UK between 1993 and 1999 using data collated by Mycobnet is presented.

METHODS

UK reference and regional laboratories collect a minimum dataset on individuals from whom an initial isolate of *Mycobacterium tuberculosis* complex (*M tuberculosis*, *M bovis*, or *M africanum*) has been isolated and submitted by source hospital laboratories. Data sought include susceptibility to first line antibiotics, demographic, geographical, and other risk factor information. An initial isolate is defined as the first positive culture from a person from whom no positive culture had been recorded during the past 12 months. First line antibiotics are isoniazid, rifampicin, ethambutol, and pyrazinamide. Monoresistance was defined as resistance to only one of the first line antibiotics or to streptomycin alone. Multidrug resistance (MDR) was defined as resistance to at least isoniazid and rifampicin. UK reference laboratories employ the resistance ratio method using solid media as well as the proportional radiometric method using the Bactec system to test for drug susceptibility.[5] Since *M bovis* isolates are intrinsically resistant to pyrazinamide,[6 7] these were excluded from estimates of pyrazinamide resistance.

The Mycobnet dataset was matched by SOUNDEX code[8] and date of birth to the national AIDS/HIV databases at CDSC to make an estimate of the association of antibiotic resistance with HIV status. Data from 1998 and 1999 only were used for analysis of drug resistance by ethnic group and previous history of tuberculosis as ethnic grouping data are very limited in the Mycobnet dataset before 1998.

The term "Oriental ethnic origin" was used to represent those ethnic groups indigenous to China and the south-east Asian area.

Analysis was performed using Epi-Info version 6.04c[9] including data from 1993 to 1999 received by November 2000. Trend analyses excluded 1993 data as it was collected retrospectively and is not strictly comparable with data for subsequent years.[4]

The proportion of isolates resistant to the first line antituberculosis drugs (either monoresistant or in combination with resistance to other first line drugs) was calculated with 95% confidence intervals. A χ^2 test was used to test the difference in proportions and χ^2 for trend was used to assess any changes in drug resistance over time.

RESULTS

All isolates

Mycobnet received 25 217 reports of initial isolates of *M tuberculosis* complex between 1993 and 1999. Fifty isolates were *M*

Table 1 Resistance to first line drugs in *Mycobacterium tuberculosis* isolates 1993–9, UK

	M tuberculosis	*M africanum*	*M bovis*	Total
Number of isolates	24876	50	291	25217
Resistance to any drug	1523 (6.1%)	4 (8%)	34 (11.7%)	1559 (6.2%)
Monoresistance*	1269 (5.1%)	3 (6%)	29 (10%)	1301 (5.2%)
Isoniazid: any resistance†	1397 (5.6%)	1 (2.0%)	34 (11.7%)	1432 (5.7%)
Rifampicin: any resistance†	332 (1.3%)	2 (4%)	6 (2.1%)	340 (1.3%)
Ethambutol any resistance†	148 (0.6%)	1 (2.0%)	0	149 (0.6%)
Pyrazinamide: any resistance†	173/20899 (0.8%)	1/48 (2.1%)	–	174 (0.8%)
Streptomycin: any resistance†	767/12950 (5.9%)	2/43 (4.7%)	2/140 (1.4%)	771 (5.9%)
MDR-TB‡	292 (1.2%)	1 (2.0%)	6 (2.1%)	299 (1.2%)

*Monoresistance: resistance to only one drug.
†Any resistance: resistance to stated drug with or without resistance to other drugs.
‡MDR-TB: multidrug resistance (resistance to at least isoniazid and rifampicin).

africanum, 291 were *M bovis*, and the remaining 24 876 were *M tuberculosis*. Of these isolates, 1432 (5.7%) were resistant to isoniazid (with or without other resistance), 340 (1.3%) to rifampicin, 149 (0.6%) to ethambutol, and 174 (0.8%) to pyrazinamide (of 20 947 tested, excluding *M bovis* and failed tests). There were 299 (1.2%) MDR isolates. Drug resistance patterns for the different species are shown in table 1.

Sex and age

Information on patient's age was available for 24 288 isolates (96.3%). Of these, 12 268 (50.5%) were from patients aged 15–44 years. A slightly higher proportion of isoniazid (significantly higher than in those aged >44 years) and multidrug resistance (significantly higher than in those aged >65 years) was observed in those aged 15–44 years than in other age groups.

Information on sex was available in 96% (24 263) of all isolates (table 2). Of these, 14 214 (59%) were men. The proportion of isoniazid resistant tuberculosis was higher in men than in women, although the difference was not significant. However, men were significantly more likely to have MDR tuberculosis (1.4% *v* 0.9%; χ^2 12.38, OR 1.57, p<0.001).

Ethnicity and place of birth

Ethnicity was reported in 13 867 (55%) of patients with initial isolates (table 2). Among the only three ethnic groups from whom substantial numbers of isolates were received, the highest proportion of isoniazid resistance and multidrug resistance was reported in isolates from people of black African origin (10.1% and 2.0%, respectively), with 7.2% and 1.4% in those originating from the Indian subcontinent, and among 4.1% and 1.4% in those of white ethnic origin. The variation in proportions of isoniazid resistance was significantly different between all three groups (χ^2 96.60, p<0.001, 2 df).

The number of isolates received from people of Oriental ethnic origin was small, but the proportion of isoniazid resistant isolates among this group was high (9.8%).

Place of birth was reported for 10 860 patients (43%) with initial isolates. People born outside the UK were significantly more likely to have isoniazid resistance than those born in the UK (9.1% *v* 4.2%, χ^2 106.08, OR 2.27, p<0.001). Similarly, 2.0% of people born outside the UK had an MDR isolate compared with 1.0% of those born in the UK (χ^2 16.93, OR 1.97, p<0.001).

Table 2 Isoniazid and multidrug resistance by age, sex, ethnic group and place of birth, 1993–9, UK

		Isoniazid resistance*		Multidrug resistance	
	All isolates	No (%)	95% CI	No (%)	95% CI
Age					
0–14	510	32 (6.3)	(4.3 to 8.7)	4 (0.8)	(0.2 to 2.0)
15–44	12268	934 (7.6)	(7.1 to 8.1)	190 (1.5)	(1.3 to 1.8)
45–64	5518	256 (4.6)	(4.1 to 5.2)	60 (1.1)	(0.8 to 1.4)
≥65	5992	157 (2.6)	(2.2 to 3.1)	32 (0.5)	(0.4 to 0.8)
Unknown	929	53 (5.7)	(4.3 to 7.4)	13 (1.4)	(0.7 to 2.4)
Sex					
M	14214	837 (5.9)	(5.5 to 6.3)	201 (1.4)	(1.2 to 1.6)
F	10049	547 (5.4)	(5.0 to 5.9)	91 (0.9)	(0.7 to 1.1)
Unknown	954	48 (5.0)	(3.7 to 6.6)	7 (0.7)	(0.3 to 1.5)
Ethnic origin					
Black African	1326	134 (10.1)	(8.5 to 11.9)	26 (2.0)	(1.3 to 2.9)
Indian subcontinent	4825	348 (7.2)	(6.5 to 8.0)	66 (1.4)	(1.1 to 1.7)
Black Caribbean	226	11 (4.9)	(2.5 to 8.5)	1 (0.4)	(0.0 to 2.4)
Oriental	377	37 (9.8)	(7.0 to 13.3)	2 (0.5)	(0.1 to 1.9)
White	6884	284 (4.1)	(3.7 to 4.6)	99 (1.4)	(1.2 to 1.7)
Other	229	16 (7.0)	(4.0 to 11.1)	5 (2.2)	(0.7 to 5.0)
Unknown	11350	602 (5.3)	(4.9 to 5.7)	100 (0.9)	(0.7 to 1.1)
UK born					
Yes	6246	264 (4.2)	(3.7 to 4.8)	64 (1.0)	(0.8 to 1.3)
No	4614	420 (9.1)	(8.3 to 10.0)	92 (2.0)	(1.6 to 2.4)
Unknown	14357	748 (5.2)	(4.9 to 5.6)	143 (1.0)	(0.8 to 1.2)

*Isoniazid resistance: with or without resistance to other drugs.

Table 3 Isoniazid and multidrug resistance by year of diagnosis, country of diagnosis, diagnosis in London, history of previous treatment, and HIV infection status, 1993–9, UK

		Isoniazid resistant*		Multidrug resistant	
	All isolates	No (%)	95% CI	No (%)	95% CI
Year					
1993	3409	157 (4.6)	(3.9 to 5.4)	19 (0.6)	(0.3 to 0.9)
1994	3253	181 (5.6)	(4.8 to 6.4)	43 (1.3)	(1.0 to 1.8)
1995	3253	197 (6.1)	(5.3 to 6.9)	49 (1.5)	(1.1 to 2.0)
1996	3632	221 (6.1)	(5.3 to 6.9)	60 (1.7)	(1.3 to 2.1)
1997	3578	193 (5.3)	(4.7 to 6.2)	45 (1.3)	(0.9 to 1.7)
1998	3832	230 (6)	(5.3 to 6.8)	50 (1.3)	(1.0 to 1.7)
1999	4260	253 (5.9)	(5.2 to 6.7)	33 (0.8)	(0.5 to 1.1)
Total	25217	1432 (5.7)	(5.4 to 6.0)	299 (1.2)	(1.1 to 1.3)
Country in which diagnosed					
England	21913	1307 (6.0)	(5.7 to 6.3)	277 (1.3)	(1.1 to 1.4)
N Ireland	354	11 (3.1)	(1.6 to 5.5)	1 (0.3)	(0.0 to 1.6)
Scotland	2148	78 (3.6)	(2.9 to 4.5)	15 (0.7)	(0.4 to 1.1)
Wales	788	35 (4.4)	(3.1 to 6.1)	5 (0.6)	(0.2 to 1.5)
Place of diagnosis					
London	9275	701 (7.6)	(7.0 to 8.1)	157 (1.7)	(1.4 to 2.0)
Outside London	15932	730 (4.6)	(4.3 to 4.9)	142 (0.9)	(0.8 to 1.0)
History of TB					
Previous	1396	217 (15.5)	(13.7 to 17.6)	131 (9.4)	(7.9 to 11.0)
No previous TB	6207	352 (5.7)	(5.1 to 6.3)	49 (0.8)	(0.6 to 1.0)
Unknown	17614	863 (4.9)	(4.6 to 5.2)	119 (0.7)	(0.6 to 0.8)
HIV infection					
Positive	910	106 (11.6)	(9.6 to 13.9)	42 (4.6)	(3.3 to 6.2)
Negative or unknown	24307	1324 (5.4)	(5.2 to 5.7)	257 (1.1)	(0.9 to 1.2)

*Isoniazid resistance: with or without resistance to other drugs.

Secular trends

The total number of initial isolates increased gradually from 3253 in 1994 to 4260 in 1999. The proportion of isolates resistant to isoniazid increased from 5.6% in 1994 to 5.9% in 1999, but this difference was not significant (table 3).

The proportion of MDR isolates decreased significantly from 1.3% in 1994 to 0.8% in 1999 (trend analysis: χ^2 6.7, p=0.009).

Geographical distribution

The proportion of isoniazid resistance was higher in residents of England than in the other areas of the UK (χ^2 587, 3 df, p<0.001) as was the proportion with MDR tuberculosis (χ^2 10.04, 3 df, p=0.01, table 3).

Compared with other English NHS regions and Scotland, Northern Ireland and Wales, patients diagnosed in London were more likely to have isolates resistant to isoniazid (7.6% *v* 4.6; χ^2 96.4, OR 1.7, p<0.001). Similarly, patients from London were more likely to have MDR isolates (1.7% *v* 0.9%; χ^2 31.44, OR 1.9, p<0.001) than those diagnosed outside London.

Site of disease

Between 1993 and 1999, 14 689 isolates (58%) were from cases who had pulmonary disease with or without non-pulmonary disease. Of these, 10 904 (74%) had an initial positive culture from a sputum specimen, of which 6031 (56%) were smear positive. Pulmonary disease was found in 62.3% of men and 54.1% of women (χ^2 162.26, p<0.001, odds ratio 1.4).

Among isolates from people with pulmonary disease, 5.8% were resistant to isoniazid, similar to the 5.4% of isolates from other cases. The proportion of MDR isolates was higher in pulmonary than in non-pulmonary cases (1.5% *v* 0.8%, χ^2 23.77, p=0.000001, odds ratio 1.9).

Overall, 42% of MDR isolates and 30% of isoniazid resistant isolates were from patients with sputum smear positive

Table 4 Isoniazid resistance by ethnic group and previous tuberculosis status, 1998 and 1999. Number (and percentage) of *M tuberculosis* complex initial isolates resistant to isoniazid (any resistance* or mono resistance†) by ethnic group and previous tuberculosis status, 1998 and 1999, UK

	Previous tuberculosis status											
	No previous tuberculosis				Previous tuberculosis				Previous tuberculosis unknown			
Ethnic group	Any	Any (%)	Mono	Mono (%)	Any	Any (%)	Mono	Mono (%)	Any	Any (%)	Mono	Mono (%)
Black African	49	8.01	39	6.37	5	9.80	0	–	22	9.40	20	8.55
Black Caribbean	7	6.80	6	5.83	0	–	0	–	3	–	3	–
ISC	99	6.07	86	5.27	20	12.05	8	4.82	31	5.95	30	5.76
Oriental	17	11.64	16	10.96	1	–	0	–	4	–	4	–
Other	7	7.53	6	6.45	1	–	0	–	7	18.92	6	13.95
Unknown	3	–	2	–	14	23.73	6	10.17	100	4.76	84	3.99
White	62	4.13	53	3.53	20	8.47	6	2.54	8	1.85	3	0.69
Total	244	5.90	208	5.03	61	11.32	20	3.71	175	5.15	150	4.42

*Any resistance: isolates resistant to isoniazid with or without resistance to drugs.
†Monoresistance: isolates resistant to isoniazid and sensitive to rifampicin, pyrazinamide, and ethambutol irrespective of sensitivity to streptomycin.
Where fewer than five cases are reported, the proportion resistant has not been calculated.

Table 5 Number (%) of isolates resistant to specified first line drugs (monoresistant or any resistance) by sex and age group, 1993–9, UK

Drug and resistance (all/monoresistance)	Isoniazid		Rifampicin		Ethambutol		Pyrazinamide		Streptomycin	
	Any*	Mono†	Any*	Mono†	Any*	Mono†	Any*	Mono†	Any*	Mono†
Sex										
Men (n=7167)	707 (9.9)	365 (5.1)	207 (2.9)	23 (0.3)	87 (1.2)	4 (0.1)	88 (1.2)	24 (0.3)	423 (5.9)	195 (2.7)
Women (n=4936)	448 (9.1)	243 (4.9)	85 (1.7)	9 (0.2)	40 (0.8)	3 (0.1)	45 (0.9)	17 (0.3)	296 (6.0)	135 (2.7)
Unknown (n=589)	41 (7.0)	27 (4.6)	7 (1.2)	1 (0.2)	2 (0.3)	0 –	4 (0.7)	2 (0.3)	29 (4.9)	17 (2.9)
Age group										
0–14 years (n=273)	29 (10.6)	14 (5.1)	4 (1.5)	0 –	2 (0.7)	1 (0.4)	3 (1.1)	2 (0.7)	35 (12.8)	21 (7.7)
15–44 years (n=7080)	807 (11.4)	420 (5.9)	195 (2.8)	25 (0.4)	77 (1.1)	4 (0.1)	77 (1.1)	24 (0.3)	531 (7.5)	245 (3.5)
45–64 years (n=2480)	213 (8.6)	114 (4.6)	59 (2.4)	2 (0.1)	34 (1.4)	1 (<0.1)	35 (1.4)	8 (0.3)	102 (4.1)	36 (1.5)
65+ years (n=2195)	105 (4.8)	63 (2.9)	29 (1.3)	4 (0.2)	12 (0.5)	1 (<0.1)	17 (0.8)	7 (0.3)	46 (2.1)	23 (1.0)
Age unknown (n=664)	42 (6.3)	24 (3.6)	12 (1.8)	2 (0.3)	4 (0.6)	0 –	5 (0.8)	2 (0.3)	34 (5.1)	22 (3.3)
Total (n=12692)	1196 (9.4)	635 (5.0)	299 (2.4)	33 (0.3)	129 (1.0)	7 (0.1)	137 (1.1)	43 (0.3)	748 (5.9)	347 (2.7)

*Any: resistance to specified drug, with or without resistance to other drugs.
†Mono: resistance to specified drug alone.

disease, compared with 25% of isolates with no resistance to isoniazid.

Previous tuberculosis

Information regarding history of previous tuberculosis was reported in 7603 (30%) of the cases, of whom 1396 were reported to have had a previous episode of tuberculosis. This group of patients exhibited a significantly higher proportion of isoniazid resistance (15.5%) and MDR (9.4%) than either those patients who had never had tuberculosis (5.7% and 0.8%, respectively), or those whose history regarding previous tuberculosis was not available (4.9% and 0.7%, respectively; χ^2 273.64, p<0.001, 2 df (isoniazid resistance); χ^2 848.25, p<0.001, 2 df (MDR), table 3).

HIV status

There were 910 (3.6%) initial isolates of *M tuberculosis* complex reported to Mycobnet between 1993 and 1999 from patients who were known to be co-infected with HIV. Most people known to be HIV seropositive (83.5%) were aged 15–44 years .

These isolates were more likely to be either isoniazid resistant (11.6% *v* 5.5%) or MDR (4.6% *v* 1.1%) than those from people of unknown or negative HIV infection status (χ^2 61.55, OR 2.28, p<0.001 (isoniazid resistance); χ^2 91.46, OR 4.52, p=0.0000 (MDR), table 3).

Isoniazid resistance, previous tuberculosis, and ethnic group

Both monoresistance to isoniazid and any resistance to isoniazid were lower in those with no previous history of tuberculosis and of white ethnic origin and highest in those of black African and Oriental ethnic origin (based on data from 1998 and 1999). Comparisons of levels of isoniazid resistance between ethnic groups in those with a previous history of tuberculosis or an unknown previous history of tuberculosis are difficult to make because of the low numbers of cases (table 4).

Monoresistance and resistance to more than one first line drug

A total of 12 692 isolates were tested for sensitivity to isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin. Isolates not tested against all five drugs and *M bovis* isolates were excluded from this analysis.

The highest level of resistance was to isoniazid and, among resistant isolates, resistance to isoniazid was most likely to be monoresistance (χ^2 260.24, df 4, p<0.001; table 5). Monoresistance to streptomycin was also relatively common. Of these 12 692 isolates, 264 (2.1%) were MDR, of which 88 (33.3%) showed no resistance to ethambutol, pyrazinamide, or streptomycin. While 22.1% of all isoniazid resistant isolates were also rifampicin resistant, 88.3% of rifampicin resistant isolates were also resistant to isoniazid. Combined resistance to isoniazid and streptomycin was found in 396 (3.1%) of the 12 692 isolates, of which 257 (64.9%) showed no resistance to ethambutol, rifampicin, or pyrazinamide.

DISCUSSION

Drug resistant tuberculosis in countries with good national control programmes such as the UK and others in Western Europe[10 11] is not commonly a major public health problem although, with increasing migration, there is a need to remain vigilant.

The overall level of drug resistance in the UK remained stable and low during the mid to late 1990s. A small but significant decrease in the proportion of MDR tuberculosis was observed, but this finding may be partly due to an increase in the number of MDR cases in 1995 and 1996 resulting from two major outbreaks of hospital acquired MDR tuberculosis in HIV

positive patients.[12 13] The small increase in the proportion of isoniazid resistant isolates between 1994 and 1999 was not statistically significant.

Certain groups of people appear to be at a higher risk of acquiring drug resistant tuberculosis. Men have higher levels of drug resistance generally, and a significantly higher proportion of multidrug resistance. These findings could either be due to the fact that men are less compliant with drug treatment or because of other risk factors associated with the male sex (homelessness, alcohol misuse, and HIV infection).

Resistance was higher among patients resident in London than in the rest of the UK, as reported previously.[4] Factors that may contribute to this problem in the capital are an increase in tuberculosis case numbers, immigration from countries with a high incidence of resistant tuberculosis, co-infection with HIV, and social problems such as overcrowding and poverty.[14] The NHS Executive report on tuberculosis control in London suggests that the high demand on health services may not be met adequately in the city.[15]

A universal approach to supervised drug taking in the initial treatment stage for sputum smear positive cases in areas with a high prevalence of MDR tuberculosis, one component of the directly observed therapy-short course (DOTS) strategy, is proving to be an effective approach in controlling the emergence of MDR tuberculosis elsewhere in the world.[16] Supervised drug taking for all sputum smear positive cases in London may result in a decreased incidence of tuberculosis and MDR disease. The use of rapid molecular methods for identification of mycobacterial species and determination of rifampicin resistance could also support case management in London.[17] Determination of rifampicin resistance in smear positive sputum samples has been shown to be cost effective in areas of high prevalence.[18 19]

Demographic data derived from Mycobnet must be interpreted with caution as completion rates of some variables are low—for example, the ethnic group of 45% of patients is unknown and place of birth is unknown in 57% of patients. Nonetheless, these data suggest a higher proportion of drug resistance among foreign born patients and those of black African, Oriental, and Indian subcontinent ethnic origin. Levels of drug resistance in these groups of people could therefore reflect either the prevalence in the country of origin[20] or resistance within specific communities in the UK.[21 22] A higher prevalence of HIV infection among some groups of foreign born patients may also have contributed to increased resistance. Matching against clinical tuberculosis enhanced surveillance data (using the national surveillance system developed recently that collects more detailed information on individual cases)[23] will improve the quality of this information in future.

The level of drug resistance in people with a previous history of tuberculosis is almost three times higher than in those known to have no previous history. The management of these patients may be more difficult and should concentrate on the use of rapid diagnostic tests for identification of *Mycobacterium* spp and rifampicin resistance, the administration of adequate and strictly supervised treatment, and the completion of treatment. Potential side effects of second and third line drugs and social, cultural, and psychological effects of prolonged isolation for a small number of cases may present considerable problems for the individual concerned.

The higher levels of resistance to isoniazid (both monoresistance and any resistance) in ethnic minority groups suggest that the recommendation by the British Thoracic Society[24] that ethambutol be included as a fourth drug in the initial phase of treatment for all non-white patients is sensible. However, the fact that 4% of even previously untreated white patients may be resistant to isoniazid suggests that consideration should be given to the inclusion of the fourth drug in the management of all patients with tuberculosis.

Patients with HIV infection are at increased risk of drug resistant tuberculosis.[25] This is probably not due to any increased susceptibility to MDR strains compared with fully sensitive strains of *M tuberculosis* but may reflect an increased spread of infection within institutional settings such as hospitals[12 13 26–28] accompanied by the rapid progression to active disease and longer duration of illness on average in those with drug resistant disease.

Levels of drug resistance are similar in those reported not to have previously had tuberculosis and those whose previous history was unknown. Most of those in the second category are therefore unlikely to have been treated previously. Similarly, among those whose HIV status was unknown, levels of drug resistance were similar to those known to be HIV seronegative. Reports of isolates from patients with unknown HIV status and HIV seronegative cases have been grouped together, but may include a small number of HIV seropositive cases which were not ascertained.

As almost nine out of 10 isolates resistant to rifampicin were MDR, the use of rapid molecular techniques to identify rifampicin resistance in cases with risk factors for MDR is likely to prove highly effective in facilitating early detection of MDR cases.[18]

The analysis of resistance to tuberculosis drugs in laboratory isolates using Mycobnet assesses the magnitude of the problem in the UK and indicates potential demographic risk factors. However, Mycobnet has limitations characteristic of any routine surveillance system such as incompleteness of information and reporting bias. Its information is useful for descriptive purposes, generating hypotheses and suggesting areas for further research, and ongoing monitoring of drug resistance. Regular matching of Mycobnet data in the future with data from the PHLS Enhanced Surveillance of Tuberculosis will make it possible to link clinical, demographic and microbiological information on all cases and, subsequently, to relate these further to treatment outcome.[28]

Drug resistant *M tuberculosis* is difficult to treat, creates a financial burden to health services,[18 19] and poses a potential threat to the national tuberculosis control programme. Action for improving its control and prevention should be directed towards those who are at higher risk such as younger male patients, people who are resident in London, those who are foreign born, patients with a previous history of tuberculosis, and those infected with HIV. Molecular DNA/RNA amplification assays and molecular rifampicin resistance detection should be arranged for these patients to assure rapid diagnosis and prompt adequate treatment.[17] In addition, direct observation of treatment should be arranged for all sputum smear positive patients in high risk groups.

Supervised treatment can be provided in a variety of settings and is most likely to succeed if tailored to the individual patient's needs.

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Authors' affiliations

T Djuretic, J Herbert, J M Watson, Public Health Laboratory Service Communicable Disease Surveillance Centre, London NW9 5EQ, UK
F Drobniewski, M Yates, Mycobacterium Reference Unit, Public Health Laboratory Service, College Hospital (Dulwich), London SE22 8QF, UK
E G Smith, Regional Centre for Mycobacteriology, Public Health Laboratory Service, Birmingham Heartlands Hospital, Bordesley Green East, Birmingham B9 5ST, UK

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