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The association between HIV and anti-tuberculosis drug resistance in England and Wales

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ABSTRACT

In the UK, HIV is considered to be a risk factor for anti-tuberculosis drug resistance. Evidence on the association is, however, inconclusive and there is little population level data. This study investigated the association in England and Wales during 1999-2005.

National tuberculosis surveillance data for adults were matched to HIV/AIDS reports. Unmatched cases were assumed to be HIV-negative. Separate analyses were conducted on new tuberculosis cases and those with a previous diagnosis. Logistic regression was used for univariable and multivariable analyses.

There were 1657 previously diagnosed cases (80 HIV-positive) and 18,130 new cases (1156 HIV-positive). Isoniazid resistance was found in 8.1% of previously diagnosed cases and 6.6% of new cases, and multidrug resistance (MDR) in 2.8% and 0.7% respectively. There was no evidence of an association between HIV and anti-tuberculosis drug resistance among previously diagnosed cases. Among new cases, there was no overall association between HIV and isoniazid resistance or MDR after adjusting for confounding factors. White HIV-positive patients were more likely to have MDR, but numbers were small.

In contrast to some previous studies, this large up-to-date study provides little evidence that HIV co-infected tuberculosis patients in England and Wales are at increased risk of first-line anti-tuberculosis drug resistance.

INTRODUCTION

The proportion of tuberculosis patients co-infected with HIV has been increasing alongside the increasing incidence of tuberculosis in England and Wales [1,2]. Anti-tuberculosis drug resistance makes tuberculosis more difficult to treat and may prolong the infectious period of the disease, resulting in increased transmission [3]. It also adversely affects clinical outcomes [4]. A recent survey of global anti-tuberculosis drug resistance highlighted that the relation between HIV and drug resistant tuberculosis is not well understood, and there is a need for more population level data on this association [5].

Anti-tuberculosis drug resistance may be initial (i.e. in those with no previous tuberculosis treatment) or acquired (in those who have been previously treated) [5]. Infection with HIV could influence anti-tuberculosis drug resistance through behavioural/environmental or biological mechanisms. For example, certain HIV-positive population groups, such as injecting drug users, may have behavioural risk factors that make them less likely to adhere to tuberculosis treatment, resulting in the development of resistant strains (acquired resistance) which are then transmitted within that community (resulting in initial resistance). Since immunocompromised patients are more likely to develop disease and to do so more rapidly than immunocompetent patients [6], extensive transmission of drug resistant strains may occur. HIV-positive patients might also be more likely to frequent settings in which they could be exposed to drug resistant strains of tuberculosis, such as hospitals [7], and may be more susceptible to drug resistant tuberculosis strains which are possibly less virulent [8]. Furthermore, HIV infection may impair the absorption of some anti-tuberculosis drugs, thus contributing to the development of resistance [9]. Drug interactions and adverse reactions may also be more likely among HIV co-infected patients [9] and could lead to treatment interruptions thus promoting the development of resistance.

In the UK, HIV is considered to be a risk factor for anti-tuberculosis drug resistance [10,11]. The current evidence on the association between HIV and anti-tuberculosis drug resistance is, however, inconclusive. During the late 1980s and early 1990s, a number of tuberculosis outbreaks occurred involving the transmission of multidrug resistant (MDR) strains among HIV-positive persons in specific settings in the United States (US) including hospitals and correctional facilities [12,13]. There is also evidence of an association in Europe and countries of the former Soviet Union [14-18]. By contrast, there is little evidence of an association in Africa [19-21], although the recent emergence of extensively drug resistant (XDR) tuberculosis, particularly in areas with high levels of HIV infection [22], is of concern. Two earlier studies in the UK found that during the early to mid 1990s, HIV-positive patients were more likely to have isoniazid resistance and MDR, but these studies were based on univariable analysis only and did not separate new and previously diagnosed cases [23,24]. Conaty *et al* found an increased risk of initial isoniazid resistance among HIV-positive patients during 1993-1994 but no association during 1999-2000, and an association with initial MDR in the combined periods. There was no evidence of any association between HIV and acquired drug resistance [25].

This study investigates the association between HIV and first-line anti-tuberculosis drug resistance in England and Wales during 1999-2005.

METHODS

In England and Wales, demographic and clinical information on tuberculosis cases (individuals with disease due to *Mycobacterium tuberculosis* complex; *M.tuberculosis*, *M.bovis* or *M.africanum*) is collected through the Enhanced Tuberculosis Surveillance (ETS) system. Drug susceptibility testing results are reported through the UK Mycobacterial Surveillance Network (MycobNet) and are matched to case reports annually. The ETS system does not collect information on HIV status, therefore, this information was obtained by matching the ETS case reports (for 1999-2005) with the national HIV/AIDS reports database (for 1979-2006) using in-house matching software based on soundex surname code [26], forename initial, date of birth, sex, ethnic group and country of birth. Matching was not carried out on cases aged below 15 years as HIV in children is reported separately. Tuberculosis cases that were not matched to HIV/AIDS reports were considered to be HIV-negative (although it is recognised that they are more accurately described as 'not known to be HIV-positive'). Cases who were diagnosed with HIV more than one year after the date of tuberculosis diagnosis were excluded since it was unknown whether they were infected with HIV at the time of tuberculosis diagnosis.

Five mycobacterial reference laboratories in England and Wales carry out anti-tuberculosis drug susceptibility testing on initial isolates (the first isolate from a patient in a 12 month period). Isolates are tested for resistance to the four first-line drugs (isoniazid, rifampicin, ethambutol and pyrazinamide), and some second line drugs. Reference laboratories use the resistance ratio or the proportion method, and are subject to quality assurance systems.

Data were analysed using Stata 10.0. Proportions were calculated among cases with known information on that variable. Data were compared using the X^2 or Fisher's exact test as appropriate. For linear variables, the X^2 test for trend was used. Separate analyses were conducted on new tuberculosis patients and those with a previous diagnosis because of the inherent difference between initial and acquired drug resistance. The proportion of resistant cases at start of treatment was calculated as R/(R+S) where R=resistant and S=susceptible. Cases with *M.bovis* were excluded from calculations of pyrazinamide resistance since they are usually intrinsically resistant to it. For the calculation of MDR (resistance to at least isoniazid and rifampicin), R=cases resistant to both isoniazid and rifampicin, S=cases susceptible to isoniazid or rifampicin or both. Logistic regression was used for univariable and multivariable analyses. Multivariable models were built using a forward-fitting approach, and interactions were assessed using the likelihood ratio test. The association of HIV with isoniazid resistance and MDR was examined in detail due to the clinical importance of these two types of resistance. Although rifampicin mono-resistance is also of importance, levels are very low [27].

RESULTS

The study population

During 1999-2005, 27,164 culture-confirmed tuberculosis cases aged 15 years and over were reported in England and Wales, 117 of which were excluded because they were diagnosed with HIV more than one year after their tuberculosis diagnosis. Drug susceptibility testing (DST) results (for at least isoniazid and rifampicin) were available for 92.1% (24,912/27,047) of the remaining cases who were thus eligible for inclusion in the study. Among this study population, 6.1% were known to be HIV-positive, the median age was 36 years (inter-quartile range (IQR): 27-54 years),

56.9% were male, 42.5% were reported in London, and 70.8% were non-UK born. The majority of cases belonged to the Indian/Pakistani/Bangladeshi (36.7%), white (26.3%), and black African (22.6%) ethnic groups.

Among those with missing DST results, the proportion of cases who were HIV-positive was similar (6.6%), the sex ratio was similar (56.2% were male), the median age was higher (44 years, IQR:30-66 years), a slightly lower proportion were reported in London (39.1%) and were non-UK born (61.7%), and a higher proportion were white (38.7%).

HIV co-infection among tuberculosis cases
Among cases with a previous tuberculosis diagnosis, 4.8% were known to be HIV-positive, and the proportion of co-infected cases increased over the study period (p=0.003). Levels of HIV co-infection were highest in the 15-44 year age group (8.7%), those reported in London (7.9%), black Africans (23.4%), and recent entrants to the UK i.e. those who had entered the UK less than two years prior to being diagnosed with tuberculosis (15.4%) (table 1).

There was a similar pattern among new tuberculosis cases; 6.4% were HIV-positive, and there was strong evidence of increasing levels of co-infection during the study period (p<0.001). Again, levels of HIV co-infection were highest in the 15-44 year age group (8.2%), those reported in London (7.3%), black Africans (21.1%), and recent entrants to the UK (12.3%). In addition, females had higher levels of co-infection (7.1%) (table 1).

Anti-tuberculosis drug resistance among tuberculosis cases
Levels of resistance to the first line anti-tuberculosis drugs are given in table 2. Isoniazid resistance was found in 8.1% of those with a previous diagnosis, and 6.6% of new cases, and MDR in 2.8% and 0.7% respectively.

Association between HIV and anti-tuberculosis drug resistance among cases with a previous tuberculosis diagnosis
There was no evidence of an association between HIV and any type of drug resistance among cases with a previous tuberculosis diagnosis (table 2). Due to the small numbers of HIV-positive drug resistant cases, no further analyses were conducted on this group.

Association between HIV and anti-tuberculosis drug resistance among new tuberculosis cases
Among new tuberculosis cases, HIV-positive individuals were more likely to be resistant to rifampicin (odds ratio (OR):2.03, 95% confidence interval (CI):1.29-3.18, p=0.002), and to have MDR tuberculosis (OR:1.86, 95% CI:1.06-3.26, p=0.029). There was only weak evidence of an increased risk of pyrazinamide resistance (OR:2.04, 95% CI:1.01-4.10, p=0.047) and any first-line drug resistance (OR:1.24, 95% CI:1.00-1.54, p=0.047). There was no evidence that the level of resistance to isoniazid or ethambutol was different among HIV-positive cases compared to HIV-negative cases (table 2).

Table 3 shows that isoniazid resistance increased linearly with year of reporting (p=0.031), and was more common in younger age groups (p<0.001), those reported in London (p<0.001), non-white ethnic groups (p<0.001), and those born abroad (p=0.002). There was no evidence that sex (p=0.098) or site of disease (p=0.307) were associated with isoniazid resistance. After adjusting for age, ethnic group and place of residence (there was little evidence to keep any other factors in the model),

there remained no evidence of an association between HIV and isoniazid resistance (adjusted odds ratio (aOR): 1.02, 95% CI:0.80-1.30, p=0.895).

On univariable analysis, MDR was more common in younger age groups (p<0.001), those reported in London (p=0.009), non-white ethnic groups (except black Caribbeans) (p<0.001), and those born abroad (p<0.001). There was no evidence that year of reporting (p=0.165), sex (p=0.382) or site of disease (p=0.322) were associated with MDR (table 4).

After adjusting for age group, ethnic group, and time since entry into the UK (there was little evidence to keep any other factors in the model), overall there was no evidence that HIV-positive patients had an increased risk of MDR (aOR:0.91, 95% CI:0.47-1.76, p=0.775) (table 4). There was, however, evidence of an interaction between HIV and ethnic group in the model (likelihood ratio test for interaction p=0.006); there was an increased risk of MDR among white HIV-positive patients (aOR:6.30, 95% CI:1.70-23.40) although the numbers of cases were small (3/166 vs.10/4478). Meanwhile, among black Africans there was no increased risk (aOR:0.71, 95% CI:0.33-1.53; 11/869 vs. 40/3242). There were no HIV-positive MDR cases in the other ethnic groups. The three white HIV-positive MDR cases were all male and were reported in broadly the same area of England. However, they were reported during different years and there was no evidence to suggest that they were associated.

Table 1. Number and proportion of tuberculosis cases co-infected with HIV according to case characteristics and previous tuberculosis diagnosis status*, England and Wales, 1999-2005

Case characteristic	Previously diagnosed cases				New cases			
	Total	HIV-positive		P-value†	Total	HIV-positive		P-value†
	n	n	%		n	n	%	
Total	1657	80	4.8		18130	1156	6.4	
Year								
1999	219	5	2.3		2163	50	2.3	
2000	226	6	2.7		2231	81	3.6	
2001	210	8	3.8		2435	127	5.2	
2002	263	16	6.1	0.003‡	2656	188	7.1	<0.001‡
2003	240	12	5.0		2687	239	8.9	
2004	238	16	6.7		2805	238	8.5	
2005	261	17	6.5		3153	233	7.4	
Age group								
15-44 years	744	65	8.7		12082	987	8.2	
45-64 years	356	12	3.4	<0.001	3424	158	4.6	<0.001
65+ years	557	3	0.5		2624	11	0.4	
Sex								
Male	945	44	4.7	0.697	10258	596	5.8	<0.001
Female	710	36	5.1		7845	558	7.1	
Place of reporting								
Outside London	1072	34	3.2	<0.001	10506	603	5.7	<0.001
London	585	46	7.9		7624	553	7.3	
Ethnic group								
White	687	13	1.9		4644	166	3.6	
Black Caribbean	29	1	3.5		568	14	2.5	
Black African	261	61	23.4	<0.001	4111	869	21.1	<0.001
Indian/Pakistani/Bangladeshi	525	2	0.4		6572	25	0.4	
Other	136	3	2.2		2009	63	3.1	
Place of birth/time since entry								
UK born	670	10	1.5		4999	139	2.8	
Born abroad, entry <2 years ago	162	25	15.4	<0.001	2469	304	12.3	<0.001
Born abroad, entry 2+ years ago	557	32	5.7		7974	547	6.9	
Born abroad, year of entry missing	157	11	7.0		1781	128	7.2	
Site of disease								
Extra-pulmonary	398	16	4.0		6170	328	5.3	
Pulmonary sputum smear positive	713	38	5.3	0.619	6287	401	6.4	<0.001
Other pulmonary	545	26	4.8		5628	427	7.6	

** Cases with missing information on previous tuberculosis diagnosis status are not shown*
† P-value for overall differences between groups
‡Test for trend p-value

Table 2. Anti-tuberculosis drug resistance among previously diagnosed and new tuberculosis cases by HIV status, England and Wales, 1999-2005

	Type of resistance	All cases	HIV-negative	HIV-positive	OR (95% CI)*	P-value
		Resistant/Total (%)	Resistant/Total (%)	Resistant/Total (%)		
Previously diagnosed cases	Isoniazid	135/1657 (8.1)	131/1577 (8.3)	4/80 (5.0)	0.58 (0.21-1.61)	0.297
	Rifampicin	62/1657 (3.7)	57/1577 (3.6)	5/80 (6.3)	1.78 (0.69-4.57)	0.232
	Ethambutol	20/1656 (1.2)	19/1576 (1.2)	1/80 (1.3)	1.04 (0.14-7.85)	0.972
	Pyrazinamide†	17/1650 (1.0)	16/1570 (1.0)	1/80 (1.3)	1.23 (0.16-9.39)	0.842
	Any first-line drug	153/1655 (9.2)	146/1575 (9.3)	7/80 (8.8)	0.94 (0.42-2.08)	0.876
	MDR	47/1657 (2.8)	45/1577 (2.9)	2/80 (2.5)	0.87 (0.21-3.66)	0.853
New cases	Isoniazid	1195/18130 (6.6)	1108/16974 (6.5)	87/1156 (7.5)	1.17 (0.93-1.46)	0.186
	Rifampicin	183/18130 (1.0)	161/16974 (0.9)	22/1156 (1.9)	2.03 (1.29-3.18)	0.002
	Ethambutol	63/18123 (0.3)	57/16968 (0.3)	6/1155 (0.5)	1.55 (0.67-3.60)	0.309
	Pyrazinamide†	74/18016 (0.4)	65/16864 (0.4)	9/1152 (0.8)	2.04 (1.01-4.10)	0.047
	Any first-line drug	1288/18077 (7.1)	1189/16924 (7.0)	99/1153 (8.6)	1.24 (1.00-1.54)	0.047
	MDR	125/18130 (0.7)	111/16974 (0.7)	14/1156 (1.2)	1.86 (1.06-3.26)	0.029

MDR – multidrug resistance, OR - odds ratio, CI - confidence interval

**HIV-positive cases compared to HIV-negative cases*
†Cases with M.bovis are excluded from calculations of pyrazinamide resistance since they are usually intrinsically resistant

Table 3. Univariable and multivariable analyses for isoniazid resistance among new tuberculosis cases, England and Wales, 1999-2005

Case characteristic	Resistant/Total (%)	Univariable analysis		Multivariable analysis	
		OR (95% CI)	P-value	aOR (95% CI)	P-value
HIV status					
Negative	1108/16974 (6.5)	1	0.186	1	0.895
Positive	87/1156 (7.5)	1.17 (0.93-1.46)		1.02 (0.80-1.30)	
Year					
(linear variable)	-	1.03 (1.00-1.06)	0.031*		
Age group					
15-44 years	957/12082 (7.9)	1	<0.001	1	<0.001
45-64 years	177/3424 (5.2)	0.63 (0.54-0.75)		0.70 (0.59-0.83)	
65+ years	61/2624 (2.3)	0.28 (0.21-0.36)		0.34 (0.26-0.44)	
Sex					
Male	704/10258 (6.9)	1	0.098		
Female	490/7845 (6.2)	0.90 (0.80-1.02)			
Place of reporting					
Outside London	534/10506 (5.1)	1	<0.001	1	<0.001
London	661/7624 (8.7)	1.77 (1.58-1.99)		1.52 (1.34-1.72)	
Ethnic group					
White	193/4644 (4.2)	1	<0.001	1	<0.001
Black Caribbean	91/568 (16.0)	4.40 (3.37-5.74)		3.11 (2.36-4.08)	
Black African	324/4111 (7.9)	1.97 (1.64-2.37)		1.22 (1.00-1.50)	
Indian/Pakistani/Bangladeshi	400/6572 (6.1)	1.49 (1.25-1.78)		1.18 (0.99-1.42)	
Other	168/2009 (8.4)	2.10 (1.70-2.61)		1.40 (1.12-1.76)	
Place of birth/ time since entry					
UK born	275/4999 (5.5)	1	0.002		
Born abroad, entry <2 years ago	182/2469 (7.4)	1.37 (1.13-1.66)			
Born abroad, entry 2+ years ago	562/7974 (7.0)	1.30 (1.12-1.51)			
Born abroad, year of entry missing	116/1781 (6.5)	1.20 (0.96-1.50)			
Site of disease					
Extra-pulmonary	427/6170 (6.9)	1	0.307		
Pulmonary sputum smear positive	415/6287 (6.6)	0.95 (0.83-1.09)			
Other pulmonary	350/5628 (6.2)	0.89 (0.77-1.03)			

OR - odds ratio, aOR – adjusted odds ratio, CI - confidence interval

**Test for trend p-value*

Table 4. Univariable and multivariable analyses for MDR among new tuberculosis cases, England and Wales, 1999-2005

Case characteristic	MDR/Total (%)	Univariable analysis		Multivariable analysis	
		OR (95% CI)	P-value	aOR (95% CI)	P-value
HIV status					
Negative	111/16974 (0.7)	1	0.029	1	0.775
Positive	14/1156 (1.2)	1.86 (1.06-3.26)		0.91 (0.47-1.76)	
Year					
(linear variable)	-	1.07 (0.97-1.17)	0.165*		
Age group					
15-44 years	108/12082 (0.9)	1	<0.001	1	0.010
45-64 years	12/3424 (0.4)	0.39 (0.21-0.71)		0.52 (0.27-0.99)	
65+ years	5/2624 (0.2)	0.21 (0.09-0.52)		0.35 (0.14-0.90)	
Sex					
Male	66/10258 (0.6)	1	0.382		
Female	59/7845 (0.8)	1.17 (0.82-1.66)			
Place of reporting					
Outside London	58/10506 (0.6)	1	0.009		
London	67/7624 (0.9)	1.60 (1.12-2.27)			
Ethnic group					
White	13/4644 (0.3)	1	<0.001	1	0.323
Black Caribbean	3/568 (0.5)	1.89 (0.54-6.66)		1.40 (0.39-5.01)	
Black African	51/4111 (1.2)	4.47 (2.43-8.24)		2.02 (0.88-4.64)	
Indian/Pakistani/Bangladeshi	39/6572 (0.6)	2.13 (1.13-3.99)		1.33 (0.61-2.90)	
Other	16/2009 (0.8)	2.86 (1.37-5.96)		1.39 (0.56-3.45)	
Place of birth/ time since entry					
UK born	19/4999 (0.4)	1	<0.001	1	0.028
Born abroad, entry <2 years ago	37/2469 (1.5)	3.99 (2.29-6.95)		2.23 (1.08-4.63)	
Born abroad, entry 2+ years ago	53/7974 (0.7)	1.75 (1.04-2.97)		1.19 (0.59-2.38)	
Born abroad, year of entry missing	11/1781 (0.6)	1.63 (0.77-3.43)		1.24 (0.53-2.91)	
Site of disease					
Extra-pulmonary	35/6170 (0.6)	1	0.322		
Pulmonary sputum smear positive	46/6287 (0.7)	1.29 (0.83-2.01)			
Other pulmonary	44/5628 (0.8)	1.38 (0.88-2.16)			

MDR – multidrug resistance, OR - odds ratio, aOR – adjusted odds ratio, CI - confidence interval

**Test for trend p-value*

DISCUSSION

This study provides national data on the association between HIV and first-line anti-tuberculosis drug resistance in England and Wales during 1999-2005. In contrast to previous studies from the UK and some other western countries [12-18, 23-25], this large up-to-date study provides little evidence that HIV co-infected patients are at increased risk of drug resistant tuberculosis. Among cases with a previous tuberculosis diagnosis, there was no evidence of an association though numbers were small. Among new tuberculosis cases, there was no overall association between HIV and isoniazid resistance or MDR after adjusting for confounding factors. White HIV-positive patients were more likely to have MDR, but numbers were very small.

The analysis used seven consecutive years of national surveillance data which provided a large and representative dataset. One of the main limitations of the study is that in order to obtain information on HIV status it was necessary to match tuberculosis cases to HIV/AIDS reports. It is likely that the number of co-infected cases has been underestimated. Although HIV is known to be an important risk factor for the development of tuberculosis disease [6], there is currently no policy in the UK to test all tuberculosis cases for HIV. It is therefore probable that there are a number of tuberculosis cases with undiagnosed HIV. Furthermore, since no information is available on individuals with negative HIV test results, we do not know what proportion of patients were tested. Misclassification of HIV status may underestimate any association, but it is possible that patients with drug resistant tuberculosis are more likely to be tested for HIV which may result in an overestimation of the association between HIV and anti-tuberculosis drug resistance.

The lack of DST results for 10% of cases is likely to be due to limitations of the process for matching ETS cases reports with MycobNet isolates rather than differential testing. In addition, the characteristics of these excluded cases were reasonably similar to those of the study population, thus the exclusion of these cases is unlikely to have resulted in any substantial bias. Meanwhile, any misclassification of drug resistance will most likely be due to random laboratory or data input errors, or limitations of the matching procedure. Such misclassification is likely to be minimal and would not be influenced by HIV status. Any resulting bias would thus be non-differential. Information on previous tuberculosis diagnosis is generally self-reported and is thus subject to recall bias. This is unlikely to be a serious concern due to the nature of tuberculosis treatment i.e. patients are generally unlikely to forget having been previously treated. However, as the analyses were stratified by previous history of tuberculosis, cases with missing data on this variable could not be included in the analysis which may have introduced some bias, and will have reduced the power of the study.

There was no evidence of an association between HIV and isoniazid resistance in this study. Earlier studies in the UK found an increased risk of isoniazid resistance among HIV-positive cases during the 1990s [23,24], but because these studies did not analyse new and previously diagnosed cases separately, it is difficult to compare the results with those of the present study. Conaty *et al* found an increased risk of initial isoniazid resistance among HIV-positive patients in England and Wales during 1993-1994 but no association during 1999-2000 [25]. An outbreak of isoniazid resistant tuberculosis began during 1999-2000 [28], and has not been associated with HIV infection.

In this study, there was no overall association between HIV and initial MDR after adjusting for confounding factors. An earlier UK study [25], as well as several studies

in western Europe [15-17] found an association between HIV and initial MDR tuberculosis. The reason for the differing finding in the present study could be related to the different time periods studied, lack of adjustment for confounders in previous studies [17], or possibly the differing demographics of tuberculosis cases. Meanwhile, although there is well documented evidence of the transmission of MDR tuberculosis among HIV positive patients in the US, this occurred during outbreaks in specific settings [12,13].

The finding of an association between HIV and MDR tuberculosis only in the white ethnic group suggests a behavioural rather than biological explanation. The ETS system does not collect information on behavioural factors such as problem drug use, imprisonment, and homelessness so these could not be adjusted for in this analysis. Such factors are known to play an important role in the epidemiology of tuberculosis [29], and may be confounders of the observed association. The collection of information on these factors is an important consideration for future surveillance. Meanwhile, further investigation, including the use of strain typing data, may help determine the cause of the association in the white ethnic group and inform appropriate public health interventions. That the association between HIV and anti-tuberculosis drug resistance seems to vary in different parts of the world may support the suggestion of a behavioural explanation in the present study. Associations have been most commonly observed in countries with a low incidence of both tuberculosis and HIV e.g. western Europe and the US, and in these areas both diseases tend to be concentrated in population sub-groups including those with unique risk factors such as problem drug use [29,30]. By contrast, in Africa where both diseases are much more widespread in the general population, there is little evidence of an association [19-21]. This is also consistent with the finding of no increased risk among HIV-positive black Africans in the present study.

CONCLUSION

Overall, this study provides little evidence that HIV co-infected tuberculosis patients are at increased risk of initial or acquired drug resistant tuberculosis. Although there is some evidence of an increased risk of initial MDR tuberculosis among white HIV-positive patients, the risk is still very low (<2%), and may be due to behavioural factors. Routine HIV testing of tuberculosis patients would help inform clinical care and allow a better understanding of the impact of HIV co-infection on the epidemiology of tuberculosis.

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Competing interests

None.

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None.

Ethics approval

The Health Protection Agency has Patient Information Advisory Group approval to hold and analyse national surveillance data for public health purposes under Section 60 of the Health and Social Care Act 2001. The HIV surveillance system uses

surname soundex codes in place of patient surnames. Strict confidentiality of all data is maintained.

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