Eur Respir J 2004; 23: 741–746
DOI: 10.1183/09031936.04.00114004
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European Respiratory Journal
ISSN 0903-1936

Nontuberculous mycobacteria in non-HIV patients: epidemiology, treatment and response

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Nontuberculous mycobacteria in non-HIV patients: epidemiology, treatment and response. M.T. Henry, L. Inamdar, D. O'Riordain, M. Schweiger, J.P. Watson. ©ERS Journals Ltd 2004.

ABSTRACT: Recent international guidelines published in 1997 and 1999 have proposed diagnostic and treatment criteria for disease caused by nontuberculous mycobacteria (NTM).

In this paper, the epidemiological data, diagnostic criteria, treatment regimens and outcomes from 117 HIV-negative patients who had a positive culture for NTM between 1995–1999 are reviewed. The authors wished to identify factors associated with improved outcome in these patients.

A total of 71 patients were believed to have a clinical disease caused by NTM, as defined by international criteria. A total of 72% patients were found to have had pulmonary disease. There was a rise in infections between 1995–1999, with a peak in infections in 1997. The most striking rise was in *Mycobacterium avium* intracellulare complex infections (1995: 33% infections; 1996: 36% infections; 1997: 41% infections; 1998: 61% infections; 1999: 57% infections). There was a link between deprivation and number of positive NTM isolates (34.4% isolates occurred in the areas of lowest Carstairs deprivation index *versus* 20.6% isolates from areas of least deprivation). There was a significant association between appropriate therapy, defined by American Thoracic Society and British Thoracic Society guidelines, and successful outcome (74%) in contrast to those who received inappropriate treatment prior to the publication of these guidelines.

Nontuberculous mycobacteria infections remain a significant problem in non-HIV patients. Adherence to published guidelines may improve patient outcomes.

Eur Respir J 2004; 23: 741–746.

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Keywords: Epidemiology
nontuberculous mycobacterium
response-to-treatment guidelines

Received: October 12 2003
Accepted after revision: January 23 2004

Although nontuberculous mycobacteria (NTM) were observed soon after Koch's discovery of *Mycobacterium tuberculosis*, the clinical significance of this group of NTM was not appreciated until the 1950s when they were classified as "atypical mycobacteria," on the basis of their *in vitro* characteristics. Since this time many large series of both HIV-positive and -negative patients, suffering from both pulmonary and extrapulmonary diseases attributable to what are now described as "nontuberculous mycobacteria," have been described [1–6]. NTM and the pulmonary diseases they cause remain a challenge for microbiologists and pulmonary physicians.

The increase in HIV prevalence in developed countries has contributed to a rise in NTM infections. However, increasing vigilance and awareness of these bacteria as human pathogens, improvements in methods of detection and culture, and increasing contact between humans and NTM have also contributed to the apparent increase in disease burden [7]. There is also evidence that the prevalence of NTM infections is increasing, particularly though not exclusively, in non-HIV patients with underlying lung disease [5, 8–11]. In response to this increase in the burden of disease, the American Thoracic Society (ATS) and the British Thoracic Society (BTS) have issued guidelines on the diagnosis and management of NTM infections [12, 13]. Both sets of guidelines highlight the difficulty in distinguishing patients with clinical disease related to NTM from those in whom the isolation of single clinical specimens raises a clinical suspicion of disease. Both bodies suggest similar therapeutic regimens for individual NTM, in both pulmonary and extrapulmonary disease. Success rates with these regimens are often poor, with failure to eradicate the organisms or recurrence of disease after cessation of therapy. The incidence of NTM infections in non-HIV patients in a large urban centre in the UK, over a 5-yr period, was reviewed by the present authors. Epidemiological factors associated with disease and factors associated with recurrence of clinical infection were also reviewed. Diagnostic criteria and treatment regimens used by clinicians prior to publication of evidence-based guidelines were scrutinised. Subsets of patients whose treatment regimens were consistent with subsequent guidelines were compared with those patients whose treatment regimens were not consistent with the guidelines to evaluate the likely benefit of adherence to the ATS and BTS guidelines on treatment of NTM disease.

Methods

Subjects and design of the study

The present authors reviewed the case records of 117 HIV-negative patients coded as suffering from NTM, atypical mycobacteria or opportunist mycobacteria in Leeds, a large

urban community in the UK with a population of 715,000 including 35,000 (4.8%) from ethnic minorities born outside the European Union (EU) and 12,000 (1.7%) born outside the UK but within the EU [14]. A standard proforma was used to extract information from case notes including age, sex, occupation, background respiratory disease status, Bacille Calmette-Guérin (BCG) status, and conditions other than HIV which were likely to impair immune defences, *e.g.* diabetes mellitus, leukaemia, lymphoma, rheumatoid arthritis, corticosteroid and immunosuppressant drug use (defined as "non-HIV immunocompromised patients"). The number and type of histological or microbiological samples which were culture positive for NTM and the number of these samples, which had a positive smear were all recorded. Samples were inoculated onto a solid Lowenstein-Jensen medium. A liquid culture system, mycobacterial growth indication tubes, was not introduced until 1999. The treatment regimens instituted were also analysed along with the success or failure of treatment regimes defined as clinical deterioration associated with failure to eradicate the NTM or recurrence of disease confirmed on culture within 2 yrs of cessation of treatment. *In vitro* sensitivity tests for individual drugs were performed by the Mycobacterium Reference Units for the UK. The data identifying each individual's NTM sample profile, antibiotic sensitivities and follow-up samples for evidence of recurrence of infection were all extracted for analysis.

In 2001 and 2002 a telephone questionnaire was applied to the same patients or relatives of patients, verified above, to identify potential epidemiological factors which may have contributed to the development of NTM infection, *e.g.* a weekly use of natural bottled spring water, exposure to pet birds, particularly psitticine birds and pigeons, and a patient's occupation [7, 8]. Data was also collected on a patient's outcome including retreatment or death. For each city ward in Leeds Health Authority, a deprivation score, the Carstairs Index, was calculated using the 2001 census [15]. Population-weighted densities were calculated by ward as this measure was considered to reflect more accurately the density at which the average person lives compared with the area-based population densities.

The diagnostic criteria used to support the treatment of NTM clinical infection in this group of patients as opposed to colonisation of secretions [16] in the absence of clinical disease were compared with subsequently published ATS or BTS diagnostic criteria for NTM. These criteria include the following.

American Thoracic Society. In symptomatic patients with infiltrate, nodular or cavitary disease, or a high resolution computed tomography scan which shows multifocal bronchiectasis and/or multiple small nodules, the following apply: 1) three positive sputum/bronchial wash cultures with negative acid-fast bacillus (AFB) smear or two positive cultures and one positive AFB smear in the last 12 months; 2) if only one bronchial wash available then a positive culture with a 2+ to 4+ AFB smear or 2+ to 4+ growth on solid media; 3) if sputum or bronchial wash are nondiagnostic then a transbronchial or lung biopsy yielding nontuberculous mycobacteria or biopsy showing mycobacterial histopathological features and one or more sputums, or bronchial washings, are positive for nontuberculous mycobacteria even if in low numbers [12].

British Thoracic Society. Pulmonary disease: *M. kansasii, M. avium* intracellulare complex infections*, M. malmoense, M. xenopi.* Pulmonary disease is diagnosed when positive cultures develop from specimens of sputum obtained at least 7 days apart in a patient whose chest radiograph suggests mycobacterial infection and who may or may not present with symptoms and signs [13].

Likewise antibiotic treatment regimens were compared with the BTS management guidelines for NTM infection [12, 13].

Statistical methods

Much of the data provided is presented as summary statistics. Relative success of treatment regimens in the different NTM subgroups were compared using the Chi-squared test and Fisher's exact test, and were considered significant when the p-value was <0.05.

Results

Between 1995–1999, 117 non-HIV positive patients had clinical specimens taken by clinicians in Leeds, which were subsequently found on culture to have a growth of NTM. A total of 71 patients, from the initial 117, were felt by the clinicians involved to have had clinically relevant disease and their decisions, when reviewed retrospectively, were supported by diagnostic criteria laid down by the ATS relating to NTM. Forty-nine patients were diagnosed as suffering from clinically relevant pulmonary disease and 22 patients were felt to have clinically relevant extrapulmonary disease. Table 1 outlines the demographic characteristics of the patients involved.

The incidence of NTM infections increased over this period of time. Figure 1 illustrates the annual incidence of NTM infections between 1995 when 6 (0.8 out of 100,000) clinically relevant infections were diagnosed, to a peak of 22 (3.07 out of 100,000) infections in 1997 and 14 (1.95 out of 100,000)

Table 1. – Characteristics of 71 patients suffering from nontuberculous mycobacterial infections in Leeds 1995–1999

Characteristic	Patients n			Total patients %
	Total	Pulm.	Extrapulm.	
Total	71			
Pulm.	51			72
Extrapulm.	20			28
Lymph node	14			20
Skin	5			7
Locomotor	1			1
White	69			96
Non-White	3			4
Year of culture				
1995	6	6	0	8
1996	14	12	2	20
1997	22	12	10	31
1998	15	9	6	21
1999	14	12	2	20
Exposure to psitticine birds				
Yes	9			13
No	62			87
Socio-economic status				
I	2			3
II	13			18
III	22			31
IV	22			31
V	12			17
Immunocompromised	19			27
Immunocompetent	52			73

Pulm.: pulmonary; Extrapulm.: extrapulmonary.

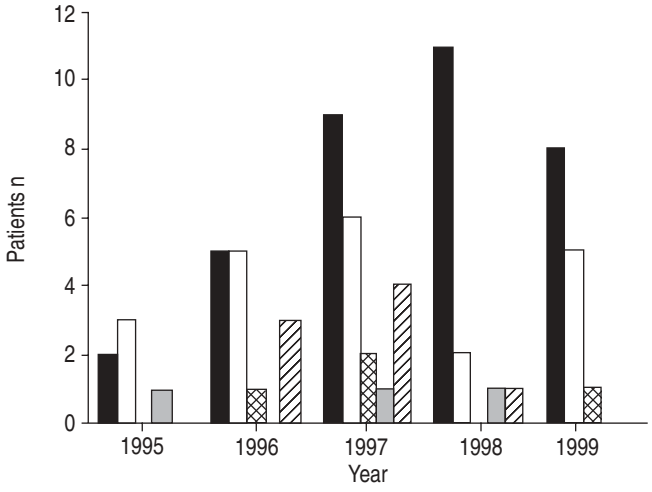

Fig. 1. – Incidence of nontuberculous mycobacterial infections in Leeds 1995–1999 subdivided by subtype and year. ■: *Mycobacterium avium* intracellulare complex; □: *Mycobacterium malmoense*: ■ *Mycobacterium kansasii*; ■: *Mycobacterium xenopi*; ▨: others.

infections in 1999. The mean age of patients in the 3 yrs with lowest incidence, 1995, 1996 and 1999, was 53.4 yrs. This compares with a mean age of 41.6 yrs for 1997 and 1998. There was a notable increase in the proportion of *M. avium* intracellulare complex (MAC) infections over this period of time (33% of the total in 1995, 36% in 1996, 41% in 1997, 61% in 1998 and 57% in 1999). The peak high incidence of MAC disease in 1997 related to five cases (62.5%) of MAC lymph node disease in children, whereas in 1998, the high incidence seemed to relate to a peak (8 out of 11: 73%) in the number of respiratory infections. Other notable increases included a peak in *M. marinum* skin infections in 1997 (17%). Otherwise there did not appear to be a trend in the incidence of individual opportunistic infections over this 5-yr period. There was also an increase in incidence in NTM infections as a proportion of total number of recorded mycobacterial infections over this period (8% in 1995, 14% in 1996, 18% in 1997, 15% in 1998 and 14% in 1999).

Among the 117 patients who had positive cultures during the review period within Leeds, it was possible to map the Carstairs deprivation index of 102 of these cases [15]. A total of 34.4% of cases lived in the most deprived areas (Carstairs Index 3.9–9.5), 23.5% in areas with a Carstairs Index of 0.3–3.9, 21.5% in areas with a Carstairs Index of -2.4–0.3 and 20.6% of cases lived in the areas of least deprivation (Carstairs Index -7.2– -2.4). There was no apparent relationship between individual NTM and deprivation index. Subgroup analysis did not identify any difference between pulmonary and extra-pulmonary disease as regards antigen exposure or deprivation index.

Fourteen patients received treatment inappropriately for NTM infection. These patients received treatment without fulfilling ATS criteria for diagnosis of clinical infection. From these 14 patients, 10 were treated after a single positive sputum culture and/or a degree of clinical suspicion. Only three of these patients had a sample sent from a sterile site before treatment. A total of 50% of this group of patients (n=7) died or deteriorated and 50% improved or recovered. The average length of inappropriate antibiotic therapy was 12 months. In contrast, amongst those patients who were diagnosed and treated with appropriate antibiotics in accordance with the ATS diagnostic criteria, 28 patients had only a single clinical sample sent for culture and 26 of these patients had a diagnosis made on the basis of culture from a sample from a sterile site (predominmantly lymph node biopsies), smear positivity and a strong clinical suspicion including MAC lymph-node disease in children and dermatological disease (*M. marinum*-fish tank granuloma) [17, 18]. Thirty five per cent of this group died or deteriorated over the following 2 yrs, the remaining 65% improved or recovered.

A review of predisposing pulmonary conditions in the group of patients with a secure diagnosis of NTM disease showed that 37% had no underlying lung disease. The pattern of underlying lung disease and species of NTM infection in each disease subtype is outlined in table 2.

There did not appear to be a pattern of species specificity for particular respiratory disease subtypes apart from an apparent increase in *M. malmoense* infections in chronic

Table 2. – Treatment regimens used for nontuberculous mycobacterial pulmonary infections

	Total n	Treatment Appropriateness			Died of disease recurrence		Received ⩾2 antibiotics to which NTM were sensitive			Died or disease recurrence	
			n	%	n	%		n	%	n	%
Mycobacterium avium complex	22	Yes	13	59	4	31	Yes	5	23	1	20
		No	9	41	7	78	No	17	77	8	53
						p=0.08					p=0.3
Mycobacterium malmoense	18	Yes	8	44	2	25	Yes	9	50	3	33
		No	10	56	8	80	No	9	50	6	66
						p=0.05					p=0.35
Mycobacterium Kansasii	3	Yes	1	33	0	0	Yes	2	67	0	0
		No	2	66	1	50	No	1	33	1	100
Mycobacterium xenopi	3	Yes	1	33	0	0	Yes	1	33	0	0
		No	2	66	1	50	No	2	67	1	50
Others		Yes	0	0	0	0	Yes	0	0	0	0
Rapidly growing Mycobacterium	3	No	3	100	2	66	No	3	100	2	67
Total	49	Yes	23	47	6	24	Yes	17	35	4	23
		No	26	53	19	76	No	32	65	19	59
						p=0.001					p=0.03

The appropriateness of treatment was defined using American Thoracic Soiciety and British Thoracic Society criteria [12, 13]. Death or disease recurrence occurred within 2 yrs of treatment cessation. NTM: nontuberculous mycobacteria.

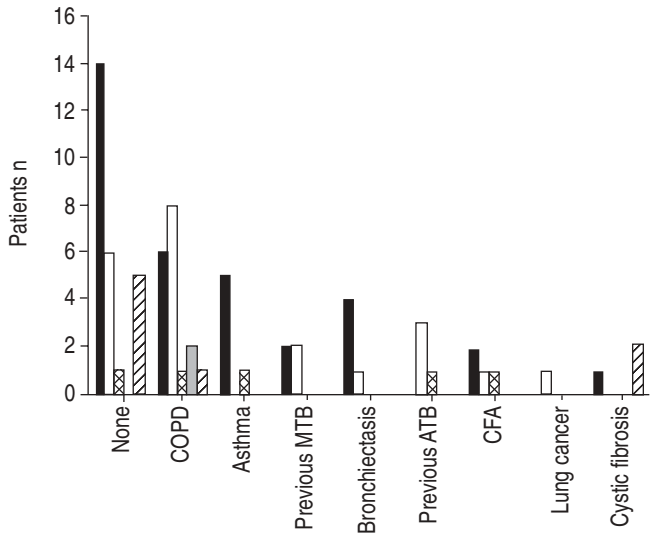

Fig. 2. – Underlying lung disease in patients subgrouped according to individual nontuberculous mycobacteria. ■: *Mycobacterium avium* intracellulare complex; □: *Mycobacterium malmoense*: ■: *Mycobacterium kansasii*; ■: *Mycobacterium xenopi*; ▨: others. COPD: chronic obstructive pulmonary disease; MTB: *Mycobacterium tuberculosis*; ATB: atypical mycobacteria; CFA: cryoptogenic fibrosing alveolitis.

obstructive pulmonary disease (COPD) patients and, not surprisingly, a lack of any underlying lung disease in *M. marinum* disease patients. The mortality rate among COPD patients (n=20) suffering from NTM infections was 55%, among bronchiectasis patients (n=6) was 66% and among cystic fibrosis patients (n=3) was 100% within 2 yrs of diagnosis, perhaps reflecting severity of the underlying condition rather than an independent association with NTM infection. In contrast the mortality among asthma patients with NTM infections (n=6) was 0% within 2 yrs of diagnosis.

The BTS has outlined specific antibiotic regimens, which should be used, and the duration of treatment for first and recurrent pulmonary NTM infections. These recommendations are based on the best available evidence [3, 12, 13, 19–23]. It has been suggested that success of treatment may be related to the adherence to correct antibiotic regimens [24, 25]. Suggested treatments for pulmonary nontuberculous mycobacterial pathogens include the following.

M. avium *complex*, M. malmoense, M. xenopi, *pulmonary disease*

Rifampicin+ethambutol±isoniazid±clarithromycin or ciprofloxacin. Treatment for 2 yrs. If recurrent disease treat indefinitely or until sputum clear for 12 months.

M. kansasii *pulmonary disease*

Rifampicin+ethambutol±isoniazid±clarithromycin or ciprofloxacin. Treatment for 9 months. If recurrent disease treat indefinitely or until sputum clear for 12 months.

*Pulmonary disease due to rapidly growing mycobacteria (*e.g. M. chelonae, M. szulgai*)*

Rifampicin+ethambutol+clarithromycin. Treatment time not specified, probably indefinite [12].

The 49 patients with clinically significant NTM pulmonary disease during this period were divided into those who received appropriate antibiotic treatment regimens and those who received inappropriate regimens as defined above. They either received the wrong combination of antibiotics and/or treatment for an inappropriately short period of time or both. Table 2 outlines the treatment regimens given for these patients. The striking feature of the treatment that these patients received was that 53% of these patients were treated using antibiotic regimens that would now be considered suboptimal or inappropriate. The rate of disease recurrence and/or mortality amongst the patients who received inappropriate treatment was 76% and significantly higher than those who received appropriate therapy (ranging from 50% amongst *M. kansasii* patients to 80% amongst *M. malmoense* patients). These figures compare strikingly with a recurrence and/or death rate of 26% among patients who received effective and appropriate therapeutic antibiotic regimens. The odds ratio for recovery from NTM pulmonary disease was 7.7 (95% CI: 2.1–27.4) among those who received appropriate therapy compared to those who did not. During the study and follow-up period, there were 19 patients who received inappropriate treatment who had an unsuccessful outcome. Eighteen of these patients received incorrect antibiotics according to the regimens outlined above. All 19 patients were treated for too short a period of time and 11 patients received both incorrect antibiotics and were treated too briefly. This group of patients was further subdivided into those who were treated from the outset with at least two antibiotics to which they were subsequently shown to be sensitive and those who were not. Table 2 demonstrates a significantly better outcome in patients who received at least two antibiotics to which their NTM isolate was sensitive. The odds ratio of a favourable outcome in this group was 4.7 (95% CI: 1.3–17.8).

In general, standard *in vitro* drug sensitivity of NTM isolates is of little use in predicting clinical efficacy particularly in those receiving repeat treatment [26]. The single exception to this is *in vitro* sensitivity of *M. kansasii* to rifampicin and ethambutol. Likewise, synergy between antibiotics *in vivo* maybe important in cases where resistance to the individual antibiotics has been reported [21, 27]. Susceptibility

Table 3. – *In vitro* antibiotic sensitivities received from UK Mycobacterium Reference Units for the individual nontuberculous mycobacteria isolated in Leeds between 1995–1999

Isolates sensitive %	Rifampicin	Rifabutin	Isoniazid	Ethambutol	Clarithromycin/azithromycin	Ciprofloxacin
Mycobacterium avium complex	11	13	0	20	93	7
Mycobacterium malmoense	32	62	0	61.5	87.5	12
Mycobacterium kansasii	82	82	0	75	100	42
Mycobacterium xenopi[#]	67	0	0	33	100	100
Mycobacterium marinum	80	75	0	80	100	25
Others	0	33	0	33	33	0

[#]: n=3.

testing of the MAC for first-line antituberculousis drugs is not recommended but there may occasionally be a case for testing against clarithromycin. [12, 13, 21, 26–28]. All clinically significant isolates of *M. kansasii* should be tested against rifampicin. In the case of rifampicin resistance, sensitivities to isoniazid, ethambutol, clarithromycin and ciprofloxacin may be important [12, 28]. Antibiotic sensitivity of all rapidly growing isolates should be available [12, 28].

Table 3 outlines the antibiotic sensitivities for all 117 NTM isolates in Leeds in 1995–1999. It is interesting that none of the isolates were sensitive to isoniazid. A recent study from the BTS Research Committee comparing rifampacin and ethambutol with rifampicin, ethambutol and isoniazid for the treatment of *M. malmoense* patients concluded that better regimens incorporating rifampicin, ethabutol and other second line antituberculous drugs are needed [23]. There are ongoing studies comparing clarithromycin or ciprofloxacin in addition to rifampicin and ethambutol in *M. avium* complex or *M. malmoense* pulmonary infections. Notwithstanding the fact that there is, as yet, no clinical *in vitro* evidence to support the use of one over the other, table 3 shows a clear superiority of clarithromycin (or azithromycin) over ciprofloxacin in *in vitro* sensitivity testing in the samples tested.

Discussion

The incidence of NTM infections has increased particularly among immunosuppressed patients. However, as this study demonstrates, there may also be a rising incidence of non-immunosuppressed persons with clinical NTM disease. While one could speculate that this rise may reflect increased surveillance for NTM infection amongst patients with chronic respiratory disease, particularly after 1997 when the first definitive investigation and treatment guidelines were published [12], during the period of this review the authors were unable to identify any increase in screening for NTM infection amongst either the pulmonary physicians, paediatricians, surgeons or any other group involved in the treatment of these patients. In particular there were no new consultant appointments with an interest in this area and there was no change in policy for tuberculosis (TB) screening or culture methods in Leeds during this time. There was no increase in number of biological samples tested for TB or NTM infection over this period. Neither was there any policy for increased surveillance for NTM disease amongst pulmonary radiologists, microbiologists or public health doctors during this period. The peak in 1997 is likely to have been related to a higher incidence of MAC lymph-node disease in children than usual. The peak of MAC infection in 1998 does appear to relate to a peak in respiratory infections that year. Higher incidences of clinical disease related to NTM and in particular MAC over these 2 yrs have been reported in other series in similar climates and populations [32], and in UK in communicable disease reports over that period.

The majority of pulmonary NTM disease occurred in patients with underlying lung disease in this study. However, 41% of patients in this study who developed significant NTM pulmonary infections had no underlying lung disease. MAC infections in non-HIV patients without pre-existing lung disease have been described in the literature in recent years with increasing frequency [4, 9, 22, 29]. In this study, 66% of patients with pulmonary NTM infection without underlying lung disease suffered MAC pulmonary infections. This group also accounts for 20% of all clinical NTM infections between 1995–1999. This is similar to the 18% of 119 patients described by PRINCE *et al.* [9] as having MAC pulmonary infection without predisposing conditions. The clinical implications of this finding as described previously are that these patients have a long delay before diagnosis is made and a high recurrence rate.

The overall incidence of NTM infections and in particular MAC infections increased in Leeds between 1995 (0.8 out of 100,000) and 1999 (1.95 out of 100,000) with a peak in 1997 (3.07 out of 100,000). This is considerably higher than a comparable report (0.62 out of 100,000) in a predominantly (>99%) indigenous Caucasian population in southwest Ireland, an area of similar climate, recently reported, although this group did report a steady rise in NTM infections in a HIV-negative population. They also reported a peak in infections in 1997, which were predominantly MAC infections [30]. The present figures are similar to those published in north Australia (3.9 out of 100,000) and the USA (2.1 out of 100,000) areas with a more mixed racial population similar to that of Leeds [31, 32]. The rise in NTM infections in the present study population is proportionally larger than the rise in cases of TB over the same period of time.

There is an established geographical variation in nontuberculous mycobacterial infections throughout the UK with *M. Kansasii* infection predominating generally in England and Wales, *M. malmoense* infections in Scotland, and *M. xenopi* in the south east of England [11]. MAC has been reported as accounting for up to 60% of isolates in the USA [33]. MAC accounted for 48% of NTM infections in non-HIV patients in Leeds. No epidemiological link was established with the high incidence of MAC infections in Leeds. While no link was established between race, exposure to psitticine birds, sex or immune status in HIV-negative patients and the incidence of opportunistic infections, there was a clear link between lower socio-economic status and NTM infection in this study. This mirrors previous studies, which demonstrated a greater incidence of tuberculosis independent of race in the more deprived areas of the city [34].

The BTS have provided evidence-based recommendations for the treatment of pulmonary and extra-pulmonary NTM infections [13]. Prior to the publication of evidence-based guidelines in 1997 and 1999, there was a lack of consensus reflecting an absence of large clinical trials and as a result treatment of such infections was less regimented, as evidenced by the number of different regimes used to treat pulmonary infections in this study. While this is a retrospective review of treatment, it is felt that the data presented strongly support an association between correct evidence based regimens and outcome. The physicians treating patients described in this report did so prior to the publication and dissemination of the ATS and BTS guidelines. While 53% of the treatment regimens used between 1995–1999 would now be considered inappropriate, 76% of these patients suffered recurrence of disease or died within 2 yrs of cessation of treatment. In comparison only 24% of patients who were treated using regimens subsequently supported by evidence-based BTS guidelines died or suffered disease recurrence within the same period. The authors feel that this evidence supports the appropriateness of the BTS guidelines for the treatment of NTM in non-HIV patients [13].

The BTS and ATS guidelines for pulmonary NTM treatment provide evidence-based guidance on treatment of NTM infections. The best regimens available, used in clinical trial settings, would suggest that 90% clinical response rates for *M. kansasii* treatment, 70% for MAC, 90% for *M. malmoense* and 45% for *M. xenopi* pulmonary infections can be achieved by adhering to evidence regimens [2–6, 19–21, 23]. In this reterospective review, carried out in a less controlled clinical trial setting, MAC pulmonary infections treated with appropriate regimens achieved a successful outcome in 69% of cases and *M. malmoense* in 75% of cases. *In vitro* sensitivities suggests that the addition of clarithromycin or azithromycin to these regimens either in

addition or in place of isoniazid is liable to be more successful than the addition of ciprofloxacin, which has been suggested as a possible alternative in the BTS guidelines. In this study between 7–42% of MAC and *M. malmoense* isolates were sensitive to ciprofloxacin as opposed to between 87–100% of isolates which were sensitive to clarithromycin/azithromycin. The numbers of *M. kansasii* and *M. xenopi* treated with appropriate regimens are too small to make valid comments on.

In summary this survey provides descriptive epidemiology of a series of conditions that continue to be a significant problem in the UK. The results support a link with lower socio-economic class and nontuberculous mycobacteria disease. The importance of adherence with recently published evidence based guidelines for the treatment of nontuberculous mycobacteria pulmonary disease is highlighted by the marked contrast in outcomes between those patients who received appropriate treatment regimens and those who did not. Continued vigilance amongst populations at risk and strict adherence to published international treatment guidelines should improve outcomes in these conditions.

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