

# The changing epidemiology of mycobacterial isolates in Northern Ireland: a 12-year study



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## INTRODUCTION

Changing trends in the epidemiology of mycobacterial infections have been reported globally<sup>1</sup>. Many developed countries have reported a rise in infections caused by non-tuberculous mycobacteria (NTM) with a corresponding fall in cases of *Mycobacterium tuberculosis* (MTb) infection.

Over 170 species of NTM have been identified, though nearly all are environmental commensals and only a minority are implicated in human infection. There is significant geographic variation in the incidence and predominant species of pathogenic species of NTM, relating to a complex interplay of environmental conditions (such as climate and proximity to the coast), social dynamics (including urbanisation and living conditions) and host factors (particularly impaired immunity and pre-existing lung disease)<sup>2</sup>.

This project aimed to characterise the epidemiological profile of mycobacterial isolates, identifying trends in species and geographical factors that would inform service planning and research priorities.

## METHODS

Since 2007, mycobacterial isolates from all patient specimens in all five Health and Social Care Trusts (HSCT) have been identified in the NI Mycobacterial Reference Laboratory. All positive mycobacterial isolates between 2007-2019 were analysed by species, tissue source and referring HSCT. Non-pathogenic NTM (such as *M. goodii*) were excluded from analysis. Annual population data was obtained from the NI Statistics and Research Agency. Statistical analysis was performed using simple linear regression.

### References:

1. Hoefsloot W, van Ingen J, Andrejak C et al. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: an NTM-NET collaborative study. *Eur Respir J*. 2013 Dec;42(6):1604-13.
2. Prevots DR, Marras TK. Epidemiology of human pulmonary infection with nontuberculous mycobacteria: a review. *Clin Chest Med*. 2015;36(1):13-34

## RESULTS

2193 mycobacterial isolates were captured in the study period. In 2007, numbers of mycobacterial isolates were comparable between MTb and pathogenic NTM (3.2 versus 3.6 per 100,000). The 3-year average incidence of MTb has since fallen from 2.9 to 2.5 per 100,000 (R squared 0.50, p=0.015). In contrast, the incidence of pathogenic NTM isolates has almost doubled from 3.4 to 6.5 (R squared 0.96, p<0.0001). By 2019, three times as many NTM isolates were isolated from patient specimens than MTb (Fig. 1).

Isolates of MTb versus pathogenic NTM per 100,000 in Northern Ireland

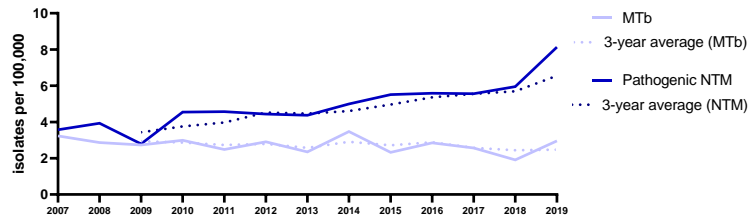


Figure 1: the rising incidence of NTM isolates per 100,000 population

The Belfast Health and Social Care Trust (BHSCT) accounted for the largest number of NTM isolates per 100,000 every year (Fig. 2). This may be related to a higher population density (1803 persons/square mile) than the other HSCTs (64-227 persons/square mile), as well as representation of specimens sent from regional/tertiary-level services. BHSCT isolation rates remained steady between 2011 and 2017 (~8 per 100,000), but have risen further in the last two years. Nevertheless, all HSCTs reported a rise in the incidence of NTM isolation during the study period.

Pathogenic NTM isolates by Health and Social Care Trust over time

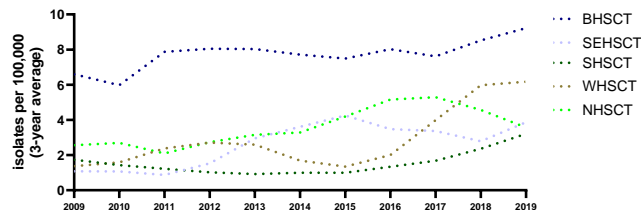


Figure 2: BHSCT accounts for the greatest number of NTM isolates per 100,000 population

Eighteen different species of pathogenic NTM were identified throughout the study period. *M. avium* complex (comprising *M. avium* and *M. intracellulare*) accounted for more than half (55.4%) of all NTM isolates during the study period. Comparable numbers of *M. chelonae* (8.7%), *M. fortuitum* (7.9%), *M. malmoense* (6.1%) and *M. abscessus* (5.4%). The remaining 12 other species accounted for around 10% of isolates.

Whereas the rates of isolation for most NTM species have not significantly changed over time, yearly *M. avium* complex (MAC) isolates have increased by three-fold over the study period (R squared 0.83, p<0.001) (Fig. 3). Of these specimens, 91.5% were from pulmonary specimens (sputum, BAL, pulmonary tissue biopsy), with the remaining 8.5% from a diverse range of extra-pulmonary tissue sites.

Changes in NTM species over time

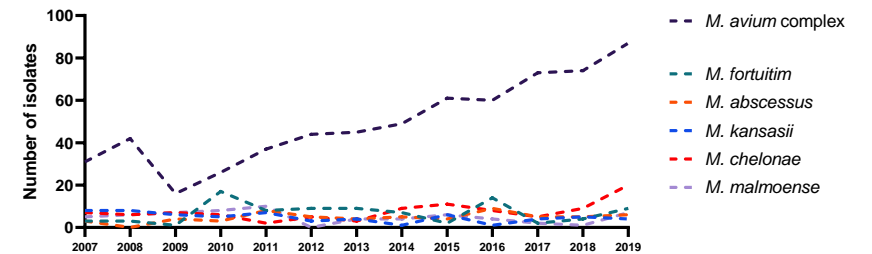


Figure 3: *M. avium* complex species account for the rise in NTM isolates

## DISCUSSION AND NEXT STEPS

In the last 12 years, NTM have overtaken MTb as the leading cause of mycobacterial isolates from patient specimens in NI. The BHSCT continues to account for the largest proportion of NTM isolates, although rates are rising across all other Trusts. This may be related to a growing population of susceptible patients, comprised mainly of those with immunocompromise and/or pre-existing lung disease. Clinicians in respiratory and general (internal) medicine should expect to encounter more cases of NTM infection.

These figures correlate with studies elsewhere that describe a rise in NTM pulmonary disease (NTM-PD), largely driven by increasing MAC infection<sup>1</sup>. Antimicrobial courses for NTM-PD are typically 18-months duration and are limited due to drug resistance, intolerances and toxicity. Therefore NTM-PD represents an emerging infectious disease for which we need improved treatment strategies. To better anticipate service needs and identify research priorities, further work should characterise the environmental, social and patient factors behind the rise in NTM isolates.