Poster #: 574

Pulmonary Nontuberculous Mycobacteria Infections: Pre-Index Comorbidity and Utilization Patterns at a Large US Health Plan

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ABSTRACT

Objective: Nontuberculous mycobacteria (NTM) lung infections are difficult to diagnose since symptoms, such as coughing and fatigue, are also features of other respiratory diseases. These overlapping symptoms may mask the infection, delaying diagnosis. The incidence of NTM lung infection is growing among patients over 65. NTM lung infections may occur in patients with underlying disease and can accelerate the deterioration of lung function associated with these diseases. NTM lung infections are challenging to diagnose and treat, which can lead to prolonged treatment with multiple antibiotics. Comorbidities and resource utilization occurring prediagnosis as a function of time vs. a matched control group were examined.

Methods: Using Medicare medical and pharmacy claims between January 1, 2007, and May 31, 2014, NTM lung infection patients (defined by ≥2 separate medical claims for NTM lung infection [ICD-9-CM 031.0]) (n = 738) and matched controls (n = 5166) were identified; first diagnosis served as the index date. Both groups had ≥18 months of continuous enrollment pre-index. Demographic and treatment characteristics and pre-index utilization patterns were examined. Differences in pre-index comorbidities were generated as odds ratios (OR) by ICD-9-CM chapters.

Results: Comorbidities analyses showed NTM lung infection patients have significantly higher OR vs. controls for 3 ICD-9-CM chapters 3 months prediagnosis: Respiratory System (RR = 35.3); Symptoms, Signs, and Ill-defined Conditions (RR = 16.3); Infectious and Parasitic Diseases (RR = 11.4). Scores are higher as early as 3rd quarter prediagnosis. Pre-index healthcare resource utilization was significantly higher across all categories for NTM lung infection patients vs. matched controls (all $P < .0001$).

Conclusions: Comorbidity results indicate physicians are applying broad diagnoses in the respiratory, infectious disease, and ill-defined condition areas prior to NTM lung infection diagnosis. These patterns are evident ≤9 months prior to diagnosis, suggesting a delay in identifying NTM lung infection and may account for why these patients are utilizing more resources than matched controls during that period. Findings suggest healthcare providers would benefit from better diagnostic support including use of administrative claims data and/or predictive models.

INTRODUCTION

- Pulmonary nontuberculous mycobacteria (PNTM) infections are difficult to diagnosis, which may lead to prolonged diagnostic time and increased healthcare resource utilization.
- Symptoms of PNTM, such as coughing, sputum production, dyspnea, weight loss, and fatigue are common of other respiratory comorbidities such as bronchiectasis, chronic obstructive pulmonary disease (COPD) associated with smoking, and cystic fibrosis (CF).[1-3]
- There are a large number of identified NTM species with a wide spectrum of virulence and a variable host susceptibility for NTM. It is unlikely that a single set of diagnostic criteria would be useful or accurate for all NTM species in all clinical circumstances.[4]
- NTM lung infections are increasing among patients ≥65 years old,[1] and can exacerbate deterioration of lung function, compounding respiratory problems for patients with serious comorbid conditions.[2]

OBJECTIVE

- To examine the comorbidities and resource utilization occurring during the 18 months preceding diagnosis of PNTM as a function of time in the Medicare population vs. a matched control group at a large US health plan

METHODS

Study Design

- Medical and pharmacy claims between January 1, 2007, and May 31, 2014, were used to identify Medicare patients with PNTM infection (n = 738) and matched controls (n = 5166).
- Medicare members with PNTM infection were defined by:
  - Identifying ≥2 separate medical claims for PNTM infection (ICD-9-CM 031.0) with claim for first diagnosis serving as the index date; and
  - ≥18 months of continuous enrollment pre- and post-diagnosis
- Matched control members were identified by the following criteria:
  - Between the age of ≥18 years and ≤89 years at index date with Medical and Pharmacy coverage; and
  - ≥18 months of continuous enrollment pre- and post-diagnosis
- Medicare PNTM and control patients were matched on gender, age, and line of business.

Outcome Measures

- Demographic and treatment characteristics
  - Total numbers and percentages were calculated for 2 demographic characteristics and 11 treatment characteristics, which included:
    - Average age
    - Gender (% males)
    - Presence of guideline antibiotics (%)
    - Average days' supply of antibiotics
    - Count of patients treated per guidelines (2 distinct FDA-approved antibiotics for NTM treatment for at least 180 days) (%)
    - Claim for amikacin (%)
    - Count of lung surgeries (%)
    - Count of patients with ≥1 sputum tests (%)
    - Average number sputum tests post-diagnosis
    - Count of patients with ≥3 negative sputum tests and no positive test (%)
    - Average number of days between index date and 1st sputum test
    - Average number of days between 1st and last negative sputum test
- Pre-diagnosis comorbidities:
  - The Tabular List of Diseases from the ICD-9-CM was used to identify other diagnoses that the Medicare PNTM patients and matched controls had during the 18-month pre-index period.
  - An odds ratio (OR) was calculated for each ICD-9-CM category. An OR represents the likelihood that a patient with PNTM infection will be diagnosed with a specific disease compared with a matched control.

$$\text{Odds Ratio} = \frac{(\#\text{ of PNTM patients with condition X})/(\text{total }\#\text{ of PNTM patients} - \#\text{ of PNTM patients with condition X})}{(\#\text{ of controls with condition X})/(\text{total }\#\text{ of controls} - \#\text{ of controls with condition X})}$$

- Pre-diagnosis Healthcare Resource Utilization
  - The mean (SD) was calculated for each of the 8 utilization categories, which included:
    - Inpatient stays – count of distinct admit dates (excluded facility transfers that are contiguous to a stay)
    - Length of stay (LOS) – measured in days per month
    - Emergency room (ER) visits – count of distinct service dates at an Emergency Department
    - Outpatient visits – count of distinct service dates and distinct providers for claims where place of treatment is listed as outpatient (includes office visits)
    - Specialist visits – subset of Outpatient visits where the provider is a specialist as specified on the claim line
    - Laboratory tests – count of distinct service dates for claims where place of service is Laboratory
    - Other (e.g., ambulance)
    - Pharmacy utilization (fills) – count of distinct service dates (fill date) and NDC code

RESULTS

Demographic and Treatment Characteristics

- Approximately 35% of patients with PNTM infection had >1 sputum test post-diagnosis, with the average number of tests post-diagnosis being 1.
- Most patients with PNTM infection did not have their first negative sputum test until 3.5 months after their diagnosis.
- About 10% achieved 3 or more negative sputum cultures after diagnosis, with 178 days between the first and third negative tests.

Table 1. Demographic and Treatment Characteristics for PNTM Patients and Matched Controls in the Medicare Population

	Medicare Population	
	PNTM	Controls
Sample size	**n = 738**	**n = 5,166**
Demographic Characteristics		
Age, mean (SD)	74.0 (8.7)	73.8 (8.5)
Gender (male), %	299 (40.5%)	2,093 (40.5%)
Treatment Characteristics		
Patients with a claim for a Guideline antibiotic[a], n (%)	373 (50.5%)	12 (0.2%)
Number of fills for an antibiotic within 270 days of post-index period[b], mean (SD)	1.3 (1.3)	0.1 (0.3)
Average (SD) days' supply	83.3 (103.0)	1.1 (7.7)
Patients treated per guidelines, n (%)	160 (20.0%)	2 (0.3%)
Patients with a claim for amikacin[c], n (%)	18 (2.3%)	1 (0.1%)
Patients with lung surgeries during post-index period, n (%)	14 (1.8%)	4 (0.5%)
Patients with ≥1 sputum test[d], n (%)	290 (36.3%)	51 (6.4%)
Distinct sputum tests post-index, average (SD)	1.0 (2.0)	0.0 (0.2)
Patients with ≥3 negative sputum cultures and no positive cultures, n (%)	70 (8.8%)	4 (0.5%)
Days between index date and first negative culture[e], average (SD)	101.2 (119.8)	NA
Days between first and last negative culture[e], average (SD)	177.5 (147.7)	NA

[a]Presence of antibiotic between index date and up to 270 days post-index. [b]Average number of claims 270 days post-index (includes index date). [c]Presence of medical claim during 270 days post-index (includes index date). [d]Medical claim for sputum test up to 545 days post-index. [e]Calculated only for patients who achieved 3 or more negative sputum cultures.

Pre-diagnosis Comorbidities

- Patients with PNTM infection had significantly higher Odds Ratio (OR) prior to their diagnosis than matched controls for 3 ICD-9-CM chapters: Respiratory System (OR = 35.3), Symptoms, Signs, and Ill-Defined Conditions (OR = 16.3), and Infectious and Parasitic Diseases (OR = 11.4) (all $P < .001$).
- The pattern of a rise in the OR for these 3 chapters was observed for the patients with PNTM infection as early as the third quarter preceding the diagnosis. The strongest signal is the previous quarter to the diagnosis, as it should be, as the providers are about to generate the correct diagnosis.
- Figures 2-4 graphically depict the OR scores for PNTM patients over the course of the 18 months prior to diagnosis.

Figure 2. Odds ratio for respiratory diseases by quarter for Medicare patients with PNTM infection pre-diagnosis vs. controls without PNTM infection (Q6 being the furthest data point prior to index date, Q1 the closest)

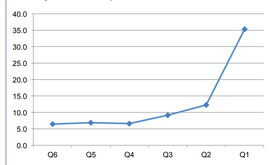


Figure 3. Odds ratio for symptoms, signs, and ill-defined conditions by quarter for Medicare patients with PNTM infection pre-diagnosis vs. controls without PNTM infection

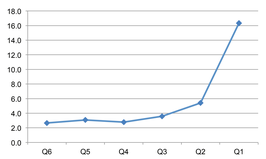
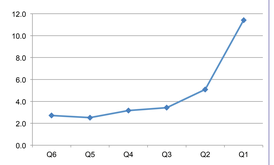


Figure 4. Odds ratio for infectious and parasitic diseases by quarter for Medicare patients with PNMT infection pre-diagnosis vs. controls without PNTM infection



Pre-diagnosis Healthcare Resource Utilization

- Patients with PNTM infection had significantly higher utilization across all 8 categories ($P < .0001$ for each category) than the matched controls **(Table 2)**.

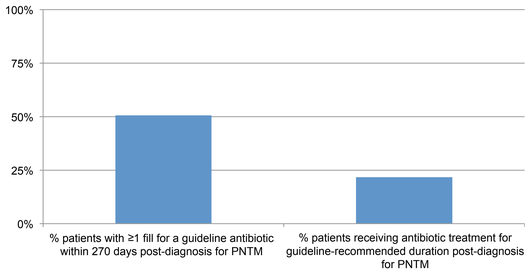
Table 2. Pre-diagnosis Healthcare Resource Utilization for PNTM Patients and Matched Controls in the Medicare Population

	Medicare Population	
	PNTM	Controls
Sample size	**n = 738**	**n = 5,166**
Category	Mean (SD)	Mean (SD)
Inpatient Stays *(count of admission dates/month)*	0.06 (0.08)	0.02 (0.04)
Inpatient Length of Stay *(sum of days in a hospital/month)*	0.24 (0.36)	0.06 (0.17)
Emergency Room visits *(count of service dates at an Emergency Room/month)*	0.19 (0.29)	0.09 (0.34)
Outpatient visits *(count of service dates at an outpatient setting/month)*	2.60 (1.75)	1.34 (1.19)
Specialists visits *(count of service dates with a specialist/month)*	1.10 (0.96)	0.57 (0.70)
Laboratory Tests *(count of service dates for laboratory claims/month)*	0.38 (0.45)	0.20 (0.29)
Other *(count of all other place of treatment not captured in other categories (e.g., ambulance)/month)*	0.71 (1.64)	0.25 (0.86)
Pharmacy fills *(count of fill dates and NDC codes/month)*	3.69 (2.73)	2.60 (2.34)

Treatment Utilization Post-Diagnosis

- 20% of patients with PNTM infection had claims consistent with 2007 ATS/IDSA guideline standards of combination therapy.
- 51% had claims for any guideline antibiotic with ≥1 fill in the post-index period. Single antibiotic treatment is against the guideline recommendations **(Figure 5).**

Figure 5. Percentage of PNTM infection patients receiving guideline antibiotic fills during post-diagnosis period



CONCLUSIONS

- Prior to the index date, comorbidity results indicate physicians are applying broad diagnoses in the respiratory, infectious disease, and ill-defined conditions areas. These comorbidity patterns are evident 9 months prior to a PNTM diagnostic code, suggesting a delay in reaching a diagnosis.
- Patients with PNTM are using significantly greater healthcare resources in the period preceding their diagnosis. Ordering a sputum mycobacterial test earlier may help in preventing misdiagnosis or a delay in diagnosis.
- Post-diagnosis, only about half of patients diagnosed with PNTM infection have claims for any guideline-recommended antibiotic, with only 20% of claims indicating a combination of antibiotics which aligns with the actual recommendation. Even fewer receive appropriate sputum testing **(Figure 5)**.
- Based on these findings, including the post-diagnosis data points on substandard-to-guidelines antibiotic use and sputum testing, healthcare providers would benefit from more information about PNTM care. This includes education about the role and timing of mycobacterial sputum testing in PNTM to achieve faster, more confident diagnoses as well as its importance in post-diagnosis follow-up in monitoring response to therapy. An emphasis on the value of adhering to antibiotic treatment guidelines is also recommended.

REFERENCES

1. Adjemian J, Olivier KN, Seitz AE, Holland SM, Prevots DR. *Am J Respir Crit Care Med.* 2012;185(8):881-886.
2. Lee MR, Yang CY, Chang KP, et al. *PLoS One.* 2013;8(3):e58214.
3. Young JD, Balagopal A, Reddy NS, Schlesinger LS. *J Respir Dis.* 2007;28(1):7-18.
4. Griffith DE, Aksamit T, Brown-Elliott BA, et al. *Am J Respir Crit Care Med.* 2007;175(4):367-416.
5. Dufour R, Tarr A. *Comprehensive Health Insights, The Incidence and Burden of Nontuberculous Mycobacteria in a US Health Plan.* 10 June 2015;1-31.

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DISCLOSURES

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