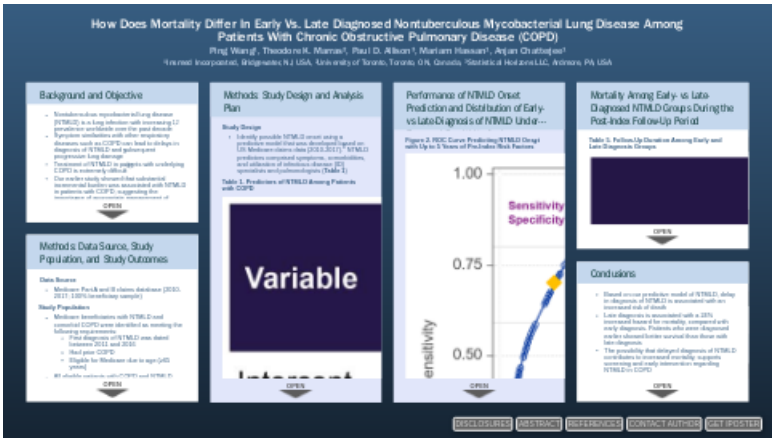
How Does Mortality Differ In Early Vs. Late Diagnosed Nontuberculous Mycobacterial Lung Disease Among Patients With Chronic Obstructive Pulmonary Disease (COPD)



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BACKGROUND AND OBJECTIVE

- Nontuberculous mycobacterial lung disease (NTMLD) is a lung infection with increasing prevalence worldwide over the past decade[1,2]
- Symptom similarities with other respiratory diseases such as COPD can lead to delays in diagnosis of NTMLD and subsequent progressive lung damage[3]
- Treatment of NTMLD in patients with underlying COPD is extremely difficult[4,5]
- Our earlier study showed that substantial incremental burden was associated with NTMLD in patients with COPD, suggesting the importance of appropriate management of NTMLD[6]
- Screening for NTM infection in patients with COPD[7] is recommended, while the consequence of delayed diagnosis of NTMLD remains unclear

Objective

- To study the associations between early vs late NTMLD diagnosis and mortality among patients with comorbid COPD

METHODS: DATA SOURCE, STUDY POPULATION, AND STUDY OUTCOMES

Data Source

- Medicare Part A and B claims database (2010-2017; 100% beneficiary sample)

Study Population

- Medicare beneficiaries with NTMLD and comorbid COPD were identified as meeting the following requirements:
  - First diagnosis of NTMLD was dated between 2011 and 2016
  - Had prior COPD
  - Eligible for Medicare due to age (≥65 years)
- All eligible patients with COPD and NTMLD (cases) were matched 1:3 to patients with COPD without NTMLD (controls) by age, sex, and duration of COPD
- The index date (defined as the date of the first diagnosis of NTMLD) of a case was assigned to the matched controls
- All cases and matched controls had 5-year pre-index continuous coverage of Medicare Parts A and B
- Patients with bronchiectasis were excluded from the study

Study Outcomes

- Over the post-index follow-up period, mortality was compared between early vs late NTMLD diagnosis, classified according to a predictive model to identify time of probable NTMLD onset among patients with preexisting COPD:
  - Proportions of patients who died
  - Annual mortality rate
  - Time to death

Definitions

Bronchiectasis[10]: A case of BE was defined as a beneficiary who had either ≥2 ambulatory encounters with a diagnostic code for BE (ICD-9-CM 494.0, 494.1, or ICD-10-CM J47.0, J47.1, J47.9) that were dated ≥30 days apart, or ≥1 ambulatory encounter with a BE diagnosis and a computed tomography scan of the thorax (CPT-4 71250, 71260, or 71270) within 60 days prior to the encounter, or ≥1 hospitalization with a principal or secondary diagnosis for BE.

COPD[10]: A case of COPD was defined as a beneficiary who had either ≥2 ambulatory encounters with a diagnostic code for COPD (ICD-9-CM 491.0, 491.1, 491.8, 491.9, 491.20, 491.21, 491.22, 492.0, 492.8, 496, or ICD-10-CM J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, or J44.9) that were dated ≥30 days apart or ≥1 hospitalization with a principal or secondary diagnosis for COPD.

NTMLD: A case of NTMLD was defined as a beneficiary who had ≥2 medical encounters with a diagnostic code for NTMLD (ICD-9-CM 031.0 or ICD-10-CM A31.0) from a physician's office visit (diagnostic code must be assigned by a physician), or a hospital inpatient stay or a hospital outpatient visit that were dated ≥30 days apart but within 365 days.

METHODS: STUDY DESIGN AND ANALYSIS PLAN

Study Design

- Identify possible NTMLD onset using a predictive model that was developed based on US Medicare claims data (2010-2017).[8] NTMLD predictors comprised symptoms, comorbidities, and utilization of infectious disease (ID) specialists and pulmonologists (**Table 1**)

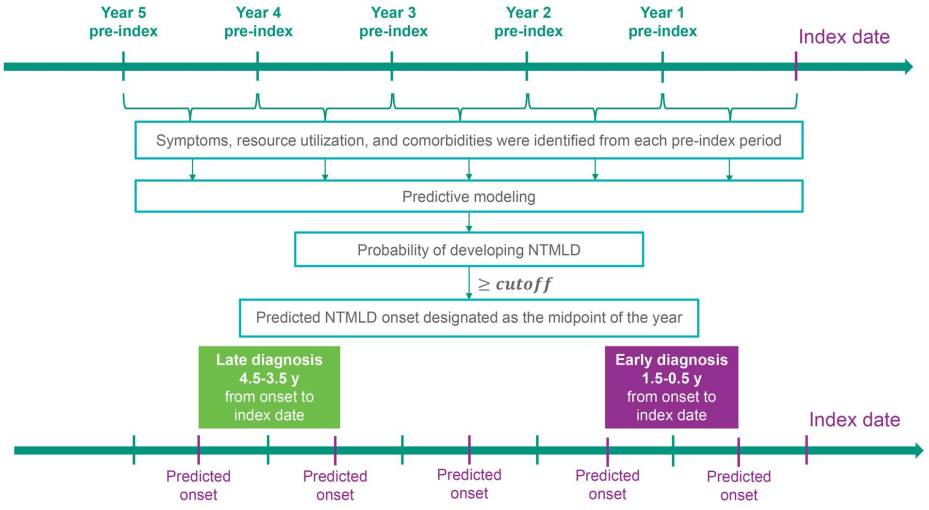
Table 1. Predictors of NTMLD Among Patients with COPD

Variable	Maximum likelihood estimates	Pr > χ^2	OR	95% CI
Intercept	3.3304	<.0001		
≥2 vs <2 ID specialist visits	0.4191	<.0001	2.31	1.95-2.74
≥4 vs <4 PUL visits	0.7698	<.0001	4.66	4.21-5.17
Hemoptysis vs no hemoptysis	0.6591	<.0001	3.74	2.97-4.69
Cough vs no cough	0.4537	<.0001	2.48	2.24-2.74
Emphysema vs no emphysema	0.3322	<.0001	1.94	1.73-2.18
Tuberculosis vs no tuberculosis	1.9119	<.0001	45.78	25.27-82.91
Lung cancer vs no lung cancer	0.3857	<.0001	2.16	1.81-2.58
Idiopathic interstitial lung disease vs no idiopathic interstitial lung disease	0.5317	<.0001	2.90	2.50-3.35
Underweight vs overweight/normal weight	0.4509	<.0001	2.46	2.13-2.85
Pneumonia vs no pneumonia	0.5612	<.0001	3.07	2.76-3.42

Predictors were learned using multivariate logistic regression with forward stepwise selection based on symptoms, comorbidities and resource utilization identified during 1-year period prior to the index date.[8]

- The 1- to 5-year pre-index predictors were used to determine probabilities of NTMLD onset. The earliest timepoint at which the probability crossed a predefined threshold was considered the timepoint for NTMLD onset (**Figure 1**)

Figure 1. Visual Representation of Study Design



- Patients from the true positives (TPs) were grouped based on the interval between the predicted NTMLD onset and the index date (0.5-, 1.5-, 2.5-, 3.5-, and 4.5-year groups)
- The 0.5 to 1.5-year groups were considered early diagnosis and the 3.5 to 4.5-year groups were late diagnosis
- Mortality was compared between the early and late NTMLD diagnosis groups during the post-index follow-up period

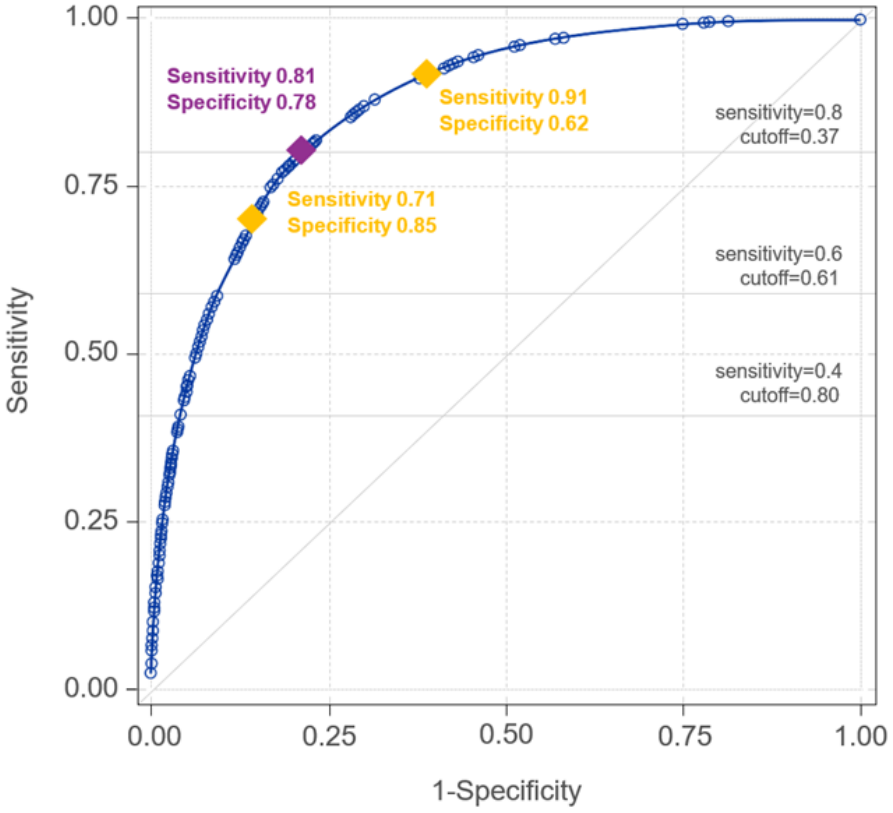
Analysis Plan

- Descriptive analysis of patient characteristics: age, sex, race/ethnicity, and clinical characteristics during the 1-year pre-index period
- The consequences of delayed diagnosis of NTMLD in patients with COPD were analyzed as follows:

- Post-index mortality was compared between early and late diagnosis NTMLD with proportion of death, annual mortality rate, and Kaplan-Meier survival estimator; odds ratio (OR), mortality rate ratio (RR), and hazard ratio (HR) after controlling for confounding factors were also reported
- Categorical variables were presented as the number and percentage of patients; continuous variables were summarized as means and standard deviations, medians, and quartiles
- Univariate analysis included McNemar's test for categorical variables and Wilcoxon signed-rank test for continuous variables; an α of 0.05 was defined as statistically significant
- Multivariate analysis included logistic regression, Poisson regression, and Cox proportional hazards model to control for confounding comorbidities during the 1-year pre-index period
- Sensitivity analysis with ±10% change in sensitivities was compared with the base analysis

PERFORMANCE OF NTMLD ONSET PREDICTION AND DISTRIBUTION OF EARLY- VS LATE-DIAGNOSIS OF NTMLD UNDER BASE AND SENSITIVITY ANALYSES SCENARIOS

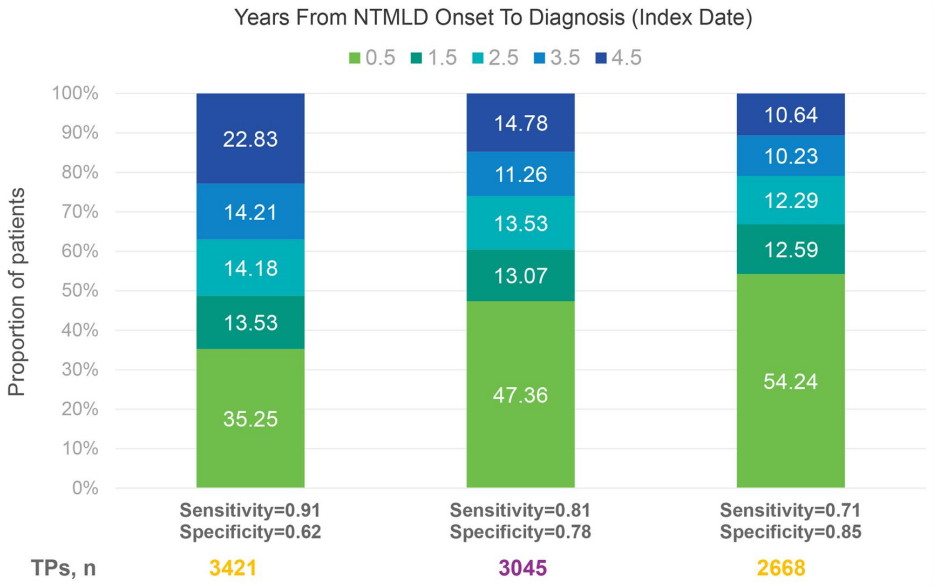
Figure 2. ROC Curve Predicting NTMLD Onset with Up to 5 Years of Pre-Index Risk Factors[a]



[a]Assume an average of 5 years from symptom onset to diagnosis of NTMLD.[9]

- The ROC curve (**Figure 2)** was generated using up to 5 years of pre-index data based on the assumption of an average of 5 years from symptom onset to diagnosis of NTMLD[9]
- We have chosen the cutoff with sensitivity of 0.81 and specificity of 0.78 as our base analysis scenario and the cutoffs with sensitivity 0.91, specificity 0.62 and sensitivity 0.71, specificity 0.85 as our sensitivity analysis scenarios

Figure 3. Distribution of Early- vs Late-Diagnosis NTMLD Under Base and Sensitivity Analysis



- In the base analysis, a total of 3045 patients who were later diagnosed with NTMLD were predicted to have NTMLD onset (they are also referred to as TPs). The early diagnosis group (patients diagnosed within 0.5-1.5 years of NTMLD onset) included 1840 (60.43%) patients, and the late diagnosis group (patients diagnosed within 3.5-4.5 years of NTMLD onset) included 793 (26.04%) patients (**Figure 3**)
- In the sensitivity analysis scenarios, increased sensitivity/decreased specificity identified 3421 TP patients (48.79% early diagnosis and 37.04% late diagnosis), and decreased sensitivity/increased specificity identified 2668 TP patients (66.83% early diagnosis and 20.88% late diagnosis) **(Figure 3**)

Table 2. Risk Factors Among Early to Late Diagnosis Groups (Base Analysis: Sensitivity, 0.81; Specificity, 0.78)

	Years from NTMLD onset to diagnosis (index date)		
n (%)	Early diagnosis 0.5-1.5 (n=1840)	2.5 (n=412)	Late diagnosis 3.5-4.5 (n=793)
≥2 Specialist ID visits	472 (25.7)	59 (14.3)	101 (12.7)
≥4 Specialist PUL visits	1440 (78.3)	325 (78.9)	639 (80.6)
Hemoptysis	294 (16.0)	48 (11.7)	94 (11.9)
Cough	1273 (69.2)	281 (68.2)	551 (69.5)
Emphysema	752 (40.9)	178 (43.2)	357 (45.0)
Pulmonary tuberculosis	236 (12.8)	14 (3.4)	35 (4.4)
Malignant neoplasm of bronchus and lung	314 (17.1)	78 (18.9)	129 (16.3)
Idiopathic interstitial lung disease	625 (34.0)	112 (27.2)	228 (28.8)
Underweight or abnormal weight loss	492 (26.7)	88 (21.4)	136 (17.2)
Pneumonia	1383 (75.2)	270 (65.5)	487 (61.4)

- Compared with the late diagnosis group, the early diagnosis group had a higher percentage of patients with claims for more frequent ID specialist visits, pulmonary tuberculosis, underweight or abnormal weight loss, and pneumonia during the year in which risk factors were scored for NTMLD onset prediction (**Table 2**)

Patient Demographics and Clinical Characteristics

Table 3. Patient Demographics

	Years from NTMLD onset to diagnosis (index date)			
	Early diagnosis 0.5-1.5 (n=1840)	2.5 (n=412)	Late diagnosis 3.5-4.5 (n=793)	All (N=3045)
Age at COPD diagnosis, mean (SD), years	72.3 (6.3)	71.2 (6.3)	70.0 (5.5)	71.6 (6.1)
Age at index date, mean (SD), years	78.8 (6.0)	78.8 (5.8)	78.2 (5.5)	78.7 (5.8)
Sex, n (%)				
Female	1030 (56.0)	241 (58.5)	403 (50.8)	1674 (55.0)
Race/ethnicity, n (%)				
White	1694 (92.1)	379 (92.0)	738 (93.1)	2811 (92.3)
Black	65 (3.5)	12 (2.9)	17 (2.1)	94 (3.1)
Asian	34 (1.9)	<11 (1.5)	15 (1.9)	55 (1.8)
Hispanic or Native American	17 (0.9)	<11 (1.9)	12 (1.5)	37 (1.2)
Unknown or other	30 (1.6)	<11 (1.7)	11 (1.4)	48 (1.6)

- Patient demographics were similar in all diagnosis groups; women had slightly higher proportions in the early diagnosis and 2.5-year groups than in the late diagnosis group (56%-59% vs 51%; **Table 3**)

Table 4. Patient Clinical Characteristics During the 1-Year Pre-Index Period

	Years from predicted NTMLD onset to diagnosis (index date)			
Characteristic	Early diagnosis 0.5-1.5 (n=1840)	2.5 (n=412)	Late diagnosis 3.5-4.5 (n=793)	All (N=3045)
Charlson comorbidity index, mean (SD)	2.9 (1.6)	2.95 (1.6)	3.0 (1.6)	2.95 (1.6)
Nonpulmonary comorbid conditions, n (%)				
Diabetes[a]	487 (26.5)	109 (26.5)	235 (29.6)	831 (27.3)
High blood pressure[a]	1530 (83.2)	337 (81.8)	664 (83.7)	2531 (83.1)
Overweight and obesity[a]	149 (8.1)	30 (7.3)	63 (7.9)	242 (8.0)
Chronic kidney disease[a]	370 (20.1)	90 (21.8)	172 (21.7)	632 (20.8)
Total cardiovascular diseases[a]	1734 (94.2)	385 (93.5)	757 (95.5)	2876 (94.5)
Moderate or severe liver disease[a]	15 (0.8)	<11 (0.5)	<11 (0.6)	22 (0.7)
Cancer, excluding lung[a]	447 (24.3)	92 (22.3)	209 (26.4)	748 (24.6)
Dementia[a]	220 (12.0)	44 (10.7)	112 (14.1)	376 (12.4)
Rheumatoid arthritis[a]	115 (6.3)	30 (7.3)	78 (9.8)	223 (7.3)
Transplant of kidney, heart, or liver[a]	<11 (0.5)	-	<11 (0.9)	17 (0.6)
Gastroesophageal reflux disease[a]	766 (41.6)	170 (41.3)	369 (46.5)	1305 (42.9)
Malnutrition[a]	509 (27.7)	104 (25.2)	208 (26.2)	821 (27.0)
Underweight or abnormal weight loss	480 (26.1)	90 (21.8)	156 (19.7)	726 (23.8)
Pulmonary comorbid conditions, n (%)				
Dyspnea	1399 (76.0)	303 (73.5)	627 (79.1)	2329 (76.5)
Asthma[a]	468 (25.4)	113 (27.4)	237 (29.9)	818 (26.9)
Idiopathic pulmonary fibrosis[a]	52 (2.8)	15 (3.6)	30 (3.8)	97 (3.2)
Simple and mucopurulent chronic bronchitis[a]	752 (40.9)	175 (42.5)	399 (50.3)	1326 (43.6)
Lung transplant	<11 (0.4)	<11 (0.7)	<11 (0.5)	15 (0.5)
Smoking history	755 (41.0)	141 (34.2)	344 (43.4)	1240 (40.7)
Hemoptysis	296 (16.1)	45 (10.9)	108 (13.6)	449 (14.8)
Cough	1262 (68.6)	263 (63.8)	520 (65.6)	2045 (67.2)
Emphysema	752 (40.9)	163 (39.6)	347 (43.8)	1262 (41.4)
Pulmonary tuberculosis[a]	241 (13.1)	44 (10.7)	69 (8.7)	354 (11.6)
Malignant neoplasm of bronchus and lung	308 (16.7)	89 (21.6)	161 (20.3)	558 (18.3)
Idiopathic interstitial lung disease[a]	607 (33.0)	113 (27.4)	229 (28.9)	949 (31.2)
Pneumonia	1348 (73.3)	238 (57.8)	496 (62.5)	2082 (68.4)

[a] Comorbidities included in all 3 multivariate regression analyses.

- For nonpulmonary conditions (**Table 4**), underweight or abnormal weight loss was more prevalent in the early- vs late-diagnosis group (26.1% vs 19.7%)
- For pulmonary conditions (**Table 4**), simple and mucopurulent chronic bronchitis was less prevalent in the early- vs late-diagnosis group (40.9% vs 50.3%); pulmonary tuberculosis and pneumonia were more prevalent in the early- vs late-diagnosis group (13.1% vs 8.7% and 73.3% vs 62.5%)

MORTALITY AMONG EARLY- VS LATE-DIAGNOSED NTMLD GROUPS DURING THE POST-INDEX FOLLOW-UP PERIOD

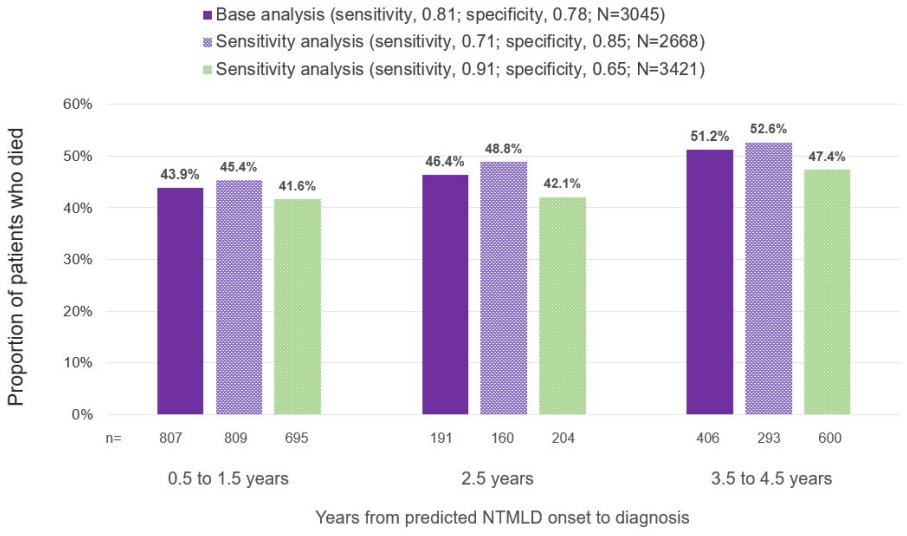
Table 5. Follow-Up Duration Among Early and Late Diagnosis Groups

Years to death or data cutoff (December 31, 2017)	Years from predicted NTMLD onset to diagnosis (index date)			
	Early diagnosis 0.5-1.5 (n=1840)	2.5 (n=412)	Late diagnosis 3.5-4.5 (n=793)	All (N=3045)
Mean (SD)	2.6 (1.7)	2.6 (1.7)	2.4 (1.6)	2.5 (1.7)
Median (Q1, Q3)	2.2 (1.3, 3.8)	2.1 (1.2, 3.8)	2.0 (1.1, 3.3)	2.1 (1.2, 3.7)

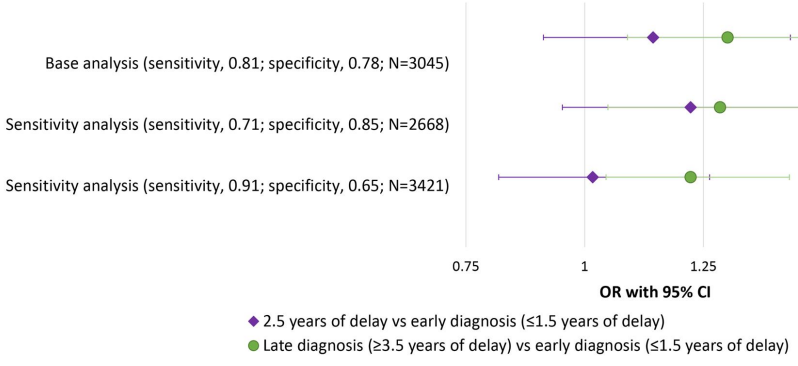
Proportion of Patients with Death and ORs Associated with Late Diagnosed NTMLD

Figure 4. Proportion of Patients Who Died (A) and Odds Ratios Associated with Late-Diagnosed NTMLD After Multivariate Analysis Adjustment (B) During Follow-Up in Patients in Early- vs Late-Diagnosed NTMLD Groups (Base and Sensitivity Analysis)

A. Proportion of patients who died (univariate analysis)



B. Odds ratios associated with late diagnosed NTMLD (multivariate logistic regression analysis[a])



[a] Odds ratio (OR) derived from multivariate logistic regression analysis controlling for age, sex, and comorbidities during 1-year pre-index period.

List of comorbidities controlled for in the multivariate analysis: diabetes mellitus, high blood pressure, overweight and obesity, chronic kidney disease, total cardiovascular diseases, moderate or severe liver disease, cancer (excluding lung cancer), dementia, rheumatoid arthritis, transplant of kidney or heart or liver, gastroesophageal reflux disease, malnutrition, pulmonary tuberculosis, asthma, simple and mucopurulent chronic bronchitis, IPF, IILD.

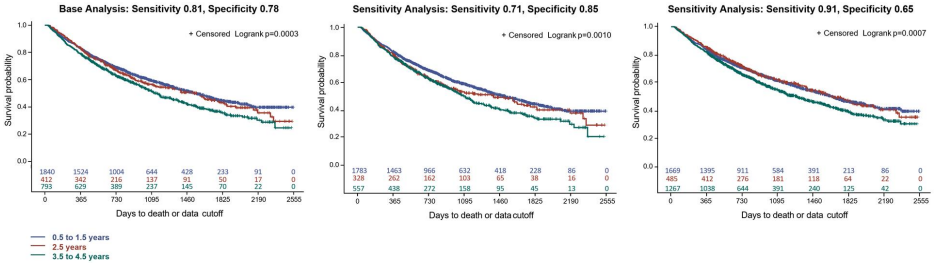
- A trend for increased proportions of death in the early to late diagnosed NTMLD groups was observed by univariate analysis in both the base analysis and the 2 sensitivity analysis scenarios (**Figure 4A**); in the base analysis, the proportion of death in the early diagnosis group was 43.9% vs 52.8% in the late diagnosis group

- A significantly higher likelihood for death was associated with late diagnosis of NTMLD, after controlling for confounding age, sex, and pre-index comorbidities by multivariate logistic regression analysis (**Figure 4B**); compared with patients in the early diagnosis group, patients in the late diagnosis group were 1.3 times more likely to die during follow-up in the base analysis (OR [95% CI], 1.30 [1.09-1.55]; P = 0.0036); a similar increased likelihood for death associated with late diagnosis relative to early diagnosis was also observed in the sensitivity analyses (OR, 1.22-1.29)

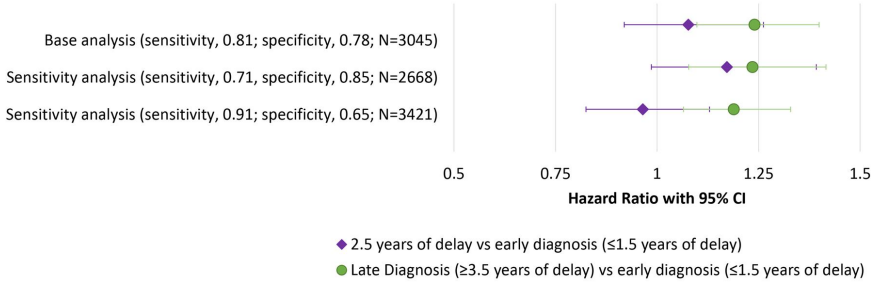
Time to Death and HRs Associated with Late-Diagnosed NTMLD

Figure 5. Time to Death (A) and Mortality Hazard Ratios Associated with Late Diagnosed NTMLD After Multivariate Analysis Adjustment (B) During Follow-Up in Patients in Early- vs Late-Diagnosed NTMLD Groups (Base and Sensitivity Analysis)

A. Kaplan-Meier survival curves (univariate analysis[a])



B. Hazard ratio of death associated with late diagnosed NTMLD (multivariate Cox proportional hazards analysis[b])



[a] *P* values based on a log-rank test for mortality between diagnosis groups.
[b] Hazard ratios (HR) derived from multivariate Cox proportional hazards regression analysis after controlling for age, sex, and comorbidities during the 1-year pre-index period.

For men and women respectively, the HRs associated with late diagnosis relative to early diagnosis were 1.24 (1.05-1.46) and 1.24 (1.05-1.48).

Within each delayed diagnosis group (early diagnosis, 2.5 years of delay, late diagnosis), men still had higher risk of mortality than women, HRs relative to women were 1.34 (1.16-1.54), 1.29 (0.97-1.72), 1.33 (1.09-1.62).

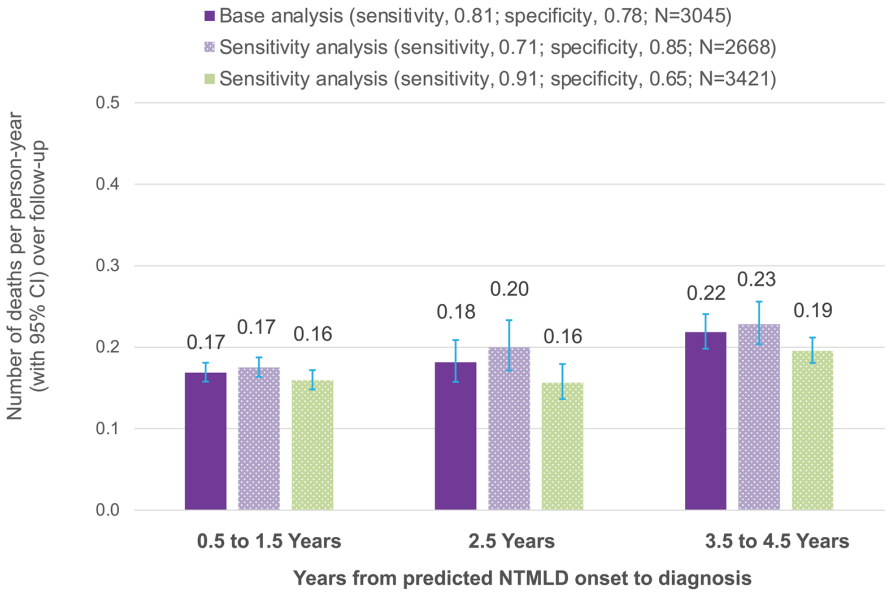
List of comorbidities controlled for in the multivariate analysis: diabetes mellitus, high blood pressure, overweight and obesity, chronic kidney disease, total cardiovascular diseases, cancer, dementia, rheumatoid arthritis, transplant of kidney or heart or lung or liver, gastroesophageal reflux disease, pulmonary tuberculosis, asthma, simple and mucopurulent chronic bronchitis, IPF, IILD.

- A significantly shorter time to death was observed among patients in the late diagnosed group compared with patients in the early diagnosed group by univariate analysis in both the base and sensitivity analyses (**Figure 5A**)
- A significantly higher HR of death was associated with late diagnosis of NTMLD, adjusted for age, sex, and confounding pre-index comorbidities by multivariate Cox proportional hazards regression analysis (**Figure 5B**); compared with patients in the early diagnosis group, patients in the late diagnosis group had a 24% increased hazard of all-cause death in the base scenario (HR [95% CI], 1.24 [1.10-1.40]; *P*=0.0005). A similar increased hazard of all-cause death associated with late diagnosis NTMLD relative to early diagnosis was also observed in the sensitivity analyses (HR, 1.19-1.24)

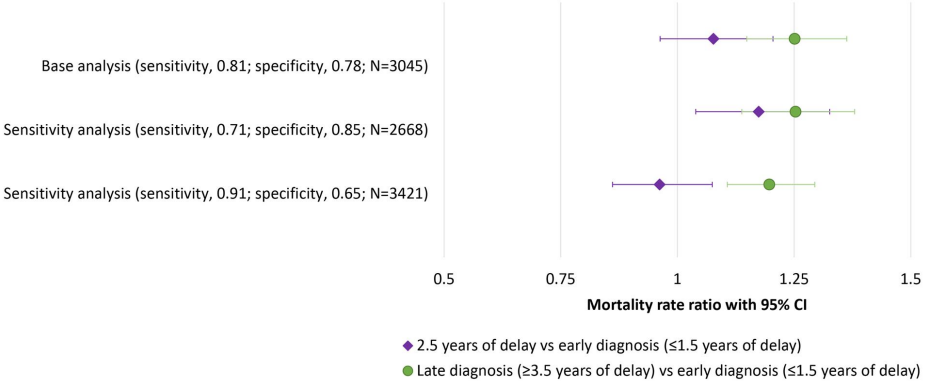
Annual Mortality Rates and RRs Associated with Late Diagnosed NTMLD

Figure 6. Annual Mortality Rate (Deaths Per Person-Year) (A) and Mortality RRs Associated with Late-Diagnosis NTMLD After Multivariate Analysis Adjustment (B) During Follow-Up in Patients in Early- vs Late-Diagnosis NTMLD Groups (Base and Sensitivity Analysis)

A. Annualized mortality rate (univariate analysis)



B. Mortality rate ratio associated with late-diagnosis NTMLD (multivariate Poisson regression analysis[a])



[a] Mortality rate ratio (RR) derived from Poisson regression analysis controlling for 1-year pre-index comorbidities; RR is a ratio of mortality rate between the two groups being compared.

List of comorbidities controlled for in the multivariate analysis: diabetes mellitus, high blood pressure, overweight and obesity, chronic kidney disease, total cardiovascular diseases, cancer, dementia, rheumatoid arthritis, transplant of kidney or heart or lung or liver, gastroesophageal reflux disease, pulmonary tuberculosis, asthma, simple and mucopurulent chronic bronchitis, IPF, IILD.

- A trend for increased annual mortality rates from early to late diagnosed NTMLD groups was observed by univariate analysis in the base analysis and the 2 sensitivity analysis scenarios (**Figure 6A**)
- A significantly higher mortality RR was associated with late diagnosed NTMLD, adjusted for age, sex, and confounding pre-index comorbidities by multivariate Poisson regression analysis (**Figure 6B**); compared with patients in the early diagnosis group, patients in the late diagnosis group had 1.25 times the annual rate of all-cause death in the base scenario (RR [95% CI], 1.25 [1.11-1.41]; *P*=0.0003). A similar increased all-cause mortality RR associated with late diagnosed NTMLD relative to early diagnosis was also observed in the sensitivity analyses (RR, 1.20-1.25)

CONCLUSIONS

- Based on our predictive model of NTMLD, delay in diagnosis of NTMLD is associated with an increased risk of death
- Late diagnosis is associated with a 24% increased hazard for mortality, compared with early diagnosis. Patients who were diagnosed earlier showed better survival than those with late diagnosis
- The possibility that delayed diagnosis of NTMLD contributes to increased mortality, supports screening and early intervention regarding NTMLD in COPD

Abbreviations:
CCI, Charlson comorbidity index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; ICD-9-CM, *International Classification of Diseases 9th Revision, Clinical Modification*; ICD-10-CM, *International Classification of Diseases 10th Revision, Clinical Modification*; ID, infectious disease; NTMLD, nontuberculous mycobacterial lung disease; IPF, idiopathic pulmonary fibrosis; IILD, idiopathic interstitial lung disease; OR, odds ratio; PUL, pulmonologist; Q, quarter; ROC, receiver operating characteristic; RR, rate ratio; TP, true positives.

DISCLOSURES

- This study was supported by Insmed Incorporated, Bridgewater, NJ, USA
- The authors would like to thank Evo Alemao, PhD, formerly an employee of Insmed, for his contributions to the study design and data analyses
- All authors contributed to and approved the presentation
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ABSTRACT

How Does Mortality Differ in EARLY VS. Late Diagnosed Nontuberculous Mycobacterial LUNG Disease Among Patients with Chronic Obstructive Pulmonary Disease (COPD)

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OBJECTIVES: Nontuberculous mycobacterial lung disease (NTMLD) is a rare lung disease that can add substantial incremental burden to respiratory diseases such as COPD. Symptom similarities with other respiratory diseases can lead to diagnostic delay of NTMLD and progressive lung damage. We sought to study associations between early versus late NTMLD diagnosis and mortality using a predictive model to identify time of probable NTMLD onset among COPD patients.

METHODS: A predictive model was developed using US Medicare claims data (2010-2017) to identify possible NTMLD onset. NTMLD predictors comprised symptoms, comorbidities, utilization of infectious disease specialist and pulmonologist pre-index (first NTMLD diagnostic claim). The 1-to-5-year pre-index predictors were used to determine probabilities of NTMLD onset. Earliest timepoint at which the probability crossed a predefined threshold was considered the timepoint for NTMLD onset. Patients were grouped based on interval between NTMLD onset and index date (0.5-,1.5-,2.5-,3.5-,4.5-year groups). The 0.5- to 1.5-year groups were considered early diagnosis and 2.5- to 4.5-year were late diagnosis. Mortality post-index was compared with death proportions, rates and KM-estimates.

RESULTS: The predictive model identified 2668 true positive patients (by a threshold with sensitivity 0.71 and specificity 0.75) grouped into 0.5- to 4.5-years as: 1447(54%), 336(13%), 328(12%), 273(10%), 284(11%). Accordingly, the mean (SD) follow-up from index to death or data cutoff were 2.6(1.8), 2.5(1.7), 2.5(1.7), 2.2(1.6), 2.4(1.6) years; proportion of patients deceased were 45%, 46%, 49%, 55%, 50%; annual mortality rates were 0.17, 0.18, 0.20, 0.25, 0.21 deaths per person-year; time to death was shorter in late diagnosis groups (P=0.002); survival years (95% CI) when 50% of patients had died were 4.1(3.6-4.5), 4.0(3.5-4.9), 3.8(2.5-4.7), 2.7(2.1-3.2), 3.2(2.7-4.0).

CONCLUSIONS: Delayed NTMLD diagnosis, determined by our methods, is associated with mortality. An incremental mortality burden is observed in patients with predicted late diagnosis compared to patients with early diagnosis.

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