

Population-Based Incidence and Prevalence (2013-2015) of Nontuberculous Mycobacterial Lung Disease in Incident Cohorts of Bronchiectasis and Chronic Obstructive Pulmonary Disease

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INTRODUCTION

- The incidence and prevalence of nontuberculous mycobacterial lung disease (NTMLD) is increasing in the United States (US).¹
 - In 2015, the incidence and prevalence of NTMLD per 100,000 people were 4.73 and 11.70, respectively.¹
 - Between 2008 and 2015, the average annual increases in overall incidence and prevalence of NTMLD in the US were 6.6% and 8.7%, respectively.¹
- NTMLD is associated with declines in lung function² and increased mortality³ and often occurs in the setting of structural lung diseases such as chronic obstructive pulmonary disease (COPD) and bronchiectasis (BE).⁴
 - Chronic pulmonary diseases, including COPD and BE, have been identified among prevalent comorbidities in patients with NTMLD.⁵
 - However, the risk of NTMLD in patients with incident BE or COPD is not well understood, and the reporting on NTMLD incidence and prevalence in BE and COPD patient cohorts has been limited.

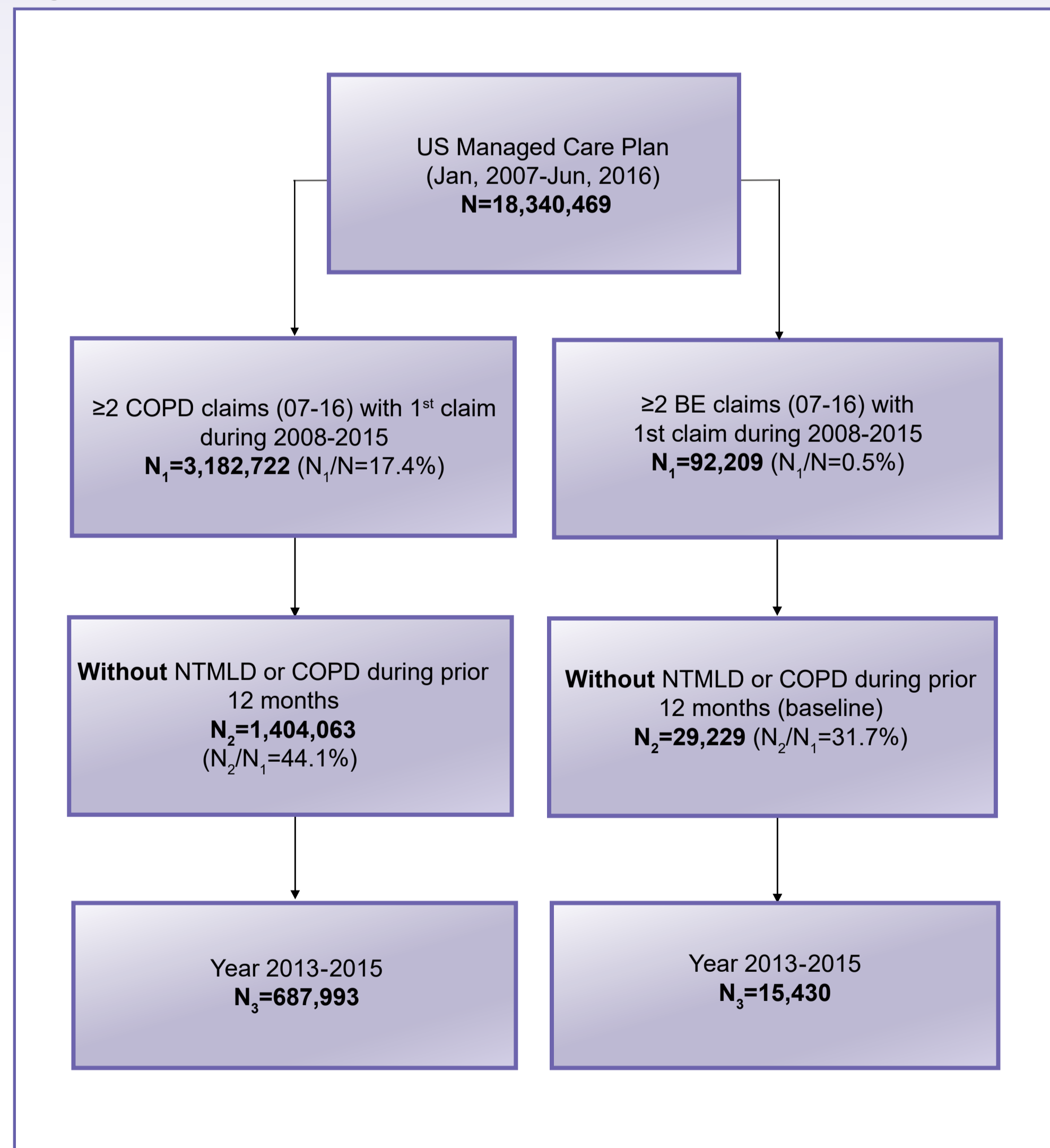
OBJECTIVE

- The objective of this study was to estimate incidence and prevalence of NTMLD in patients diagnosed with BE or COPD between 2013 and 2015.

METHODS

- Individuals with ≥ 2 medical claims for BE or COPD between 2012 and 2015 were identified from a large national US managed care claims database (2007-2016; **Figure 1**).
- All patients included in the incident BE or COPD cohort had at least 12 months (baseline) continued healthcare insurance coverage prior to the first available physician claim for BE or COPD.
- Patients who had a physician claim for COPD or NTMLD at baseline were excluded from the incident BE cohort. Likewise, patients who had a physician claim for BE or NTMLD were excluded from the incident COPD cohort.
- Yearly NTMLD incidence and prevalence were estimated by identifying patients with ≥ 2 medical claims ≥ 30 days apart in the BE and COPD cohorts.
- When calculating incidence, 12 months of prior medical insurance coverage was required for each yearly estimate (for example, to estimate the incidence in 2013, patients who did not have 12 months of insurance coverage in 2012 were excluded).
- The overall rate of NTMLD per 1,000 person-years was estimated from the BE and COPD cohorts using a Poisson regression.

Figure 1: BE and COPD incident cohorts: 2008-2015



BE=bronchiectasis; COPD=chronic obstructive pulmonary disease; NTMLD= nontuberculous mycobacterial lung disease.

RESULTS

Incident BE and COPD Cohorts

- The incident BE and COPD cohorts consisted of 15,430 and 687,993 individuals, respectively (**Table 1**).
- The majority of patients in the BE (64%) and COPD (55%) cohorts were women, with a mean (SD) age of 66 (17.7) years and 62 (19.8) years, respectively.
- Mean Charlson Comorbidity Index scores were numerically higher in the BE cohort compared with the COPD cohort (1.35 vs 0.97).
- Pneumonia was the most frequent comorbid lung disease in both cohorts, occurring in approximately 3.2 times more BE patients than COPD patients (19.3% vs 6.1%).
- Cystic fibrosis was present in only a small percentage of patients in each cohort, with a higher percentage found in the BE cohort compared with the COPD cohort (1.8% vs 0.01%), and aspergillosis was observed in <1% of patients in the BE (0.8%) and COPD (0.03%) cohorts.
- The percentage of patients with immune system diseases was approximately 3 times higher in the BE cohort compared with the COPD cohort (2.8% vs 0.9%).

Table 1: Baseline* characteristics of BE and COPD cohorts

Baseline variables % (n) or mean (SD)	BE n=15,430	COPD n=687,993
Age, mean (SD)	66 (17.7)	62 (19.8)
Female	64.4 (9,936)	55.1 (379,214)
Charlson Comorbidity Index, mean (SD)	1.35 (1.94)	0.97 (1.72)
Aspergillosis	0.8 (128)	0.03 (192)
Asthma	18.9 (2,910)	10.6 (72,647)
Atherosclerosis	5.8 (902)	5.0 (34,266)
CAD	15.1 (2,328)	13.5 (93,016)
CHF	7.8 (1,202)	9.1 (62,787)
Cystic fibrosis	1.8 (273)	0.01 (73)
Depression	7.0 (1,073)	8.7 (59,645)
Diabetes	17.9 (2,759)	21.6 (148,326)
GERD	21.3 (3,289)	13.7 (94,471)
HIV	0.2 (33)	0.3 (1,775)
Hyperlipidemia	49.6 (7,654)	40.4 (277,760)
Hypertension	51.3 (7,914)	45.8 (315,305)
Immune system diseases	2.8 (438)	0.9 (6,151)
Mental disorder	13.6 (2,105)	17.8 (122,385)
Metastatic carcinoma	2.9 (443)	1.4 (9,310)
Moderate or severe liver disease	0.4 (66)	0.4 (2,495)
Myocardial infarction	3.4 (528)	3.5 (23,994)
Obesity	5.5 (854)	9.0 (61,742)
Organ transplant	0.7 (109)	0.2 (1,383)
Pectus excavatum	0.2 (25)	0.04 (275)
Pneumonia	19.3 (2,985)	6.1 (42,127)
Rheumatoid disease	4.6 (3,289)	2.3 (15,985)
Tuberculosis	0.3 (54)	0.04 (285)

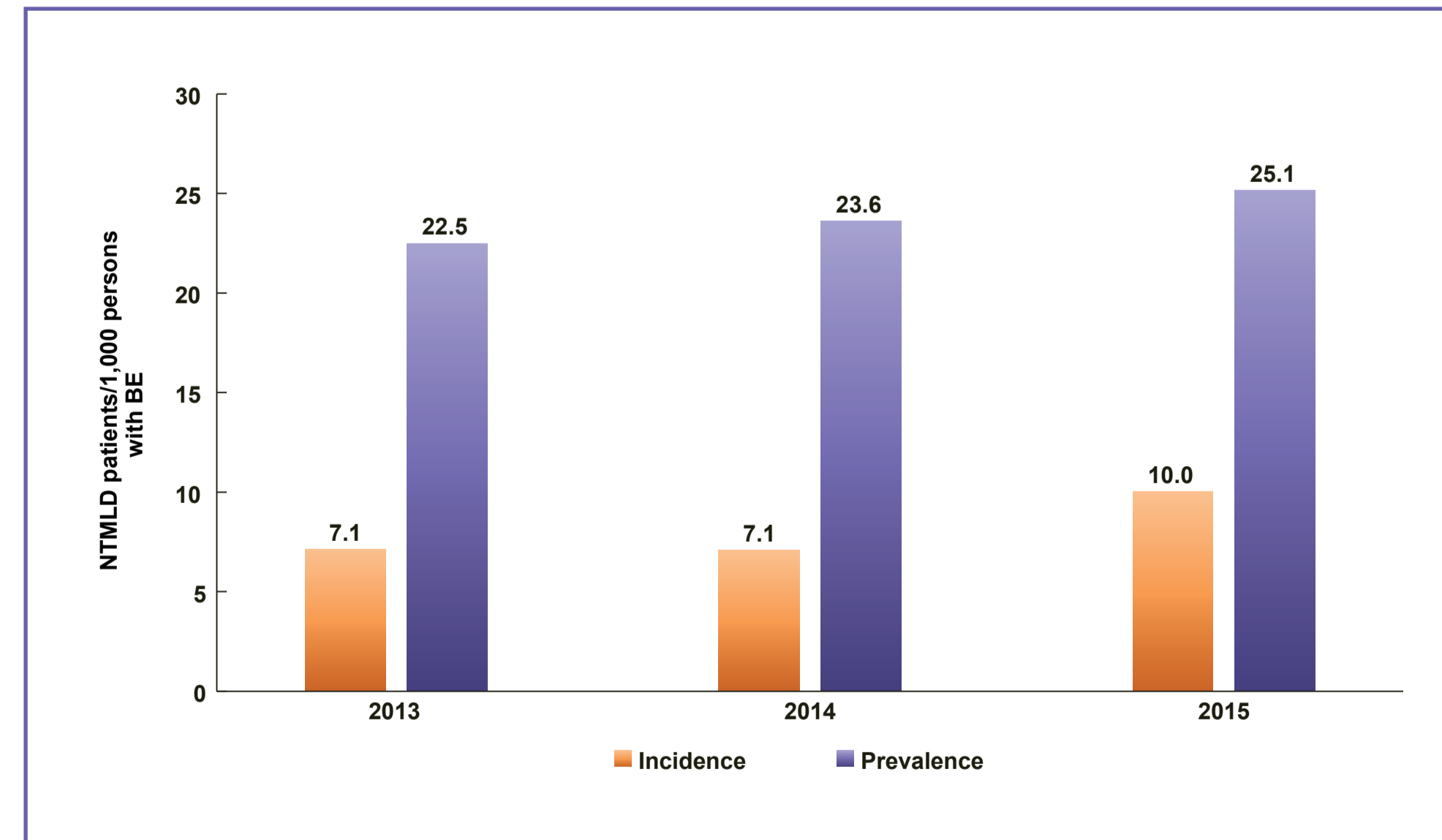
BE=bronchiectasis; CAD=coronary artery disease; CHF=congestive heart failure; COPD=chronic obstructive pulmonary disease; GERD=gastroesophageal reflux disease; HIV=human immunodeficiency virus; SD=standard deviation.

*Baseline is the 12 months before the first BE or COPD diagnosis.

Incidence and Prevalence of NTMLD

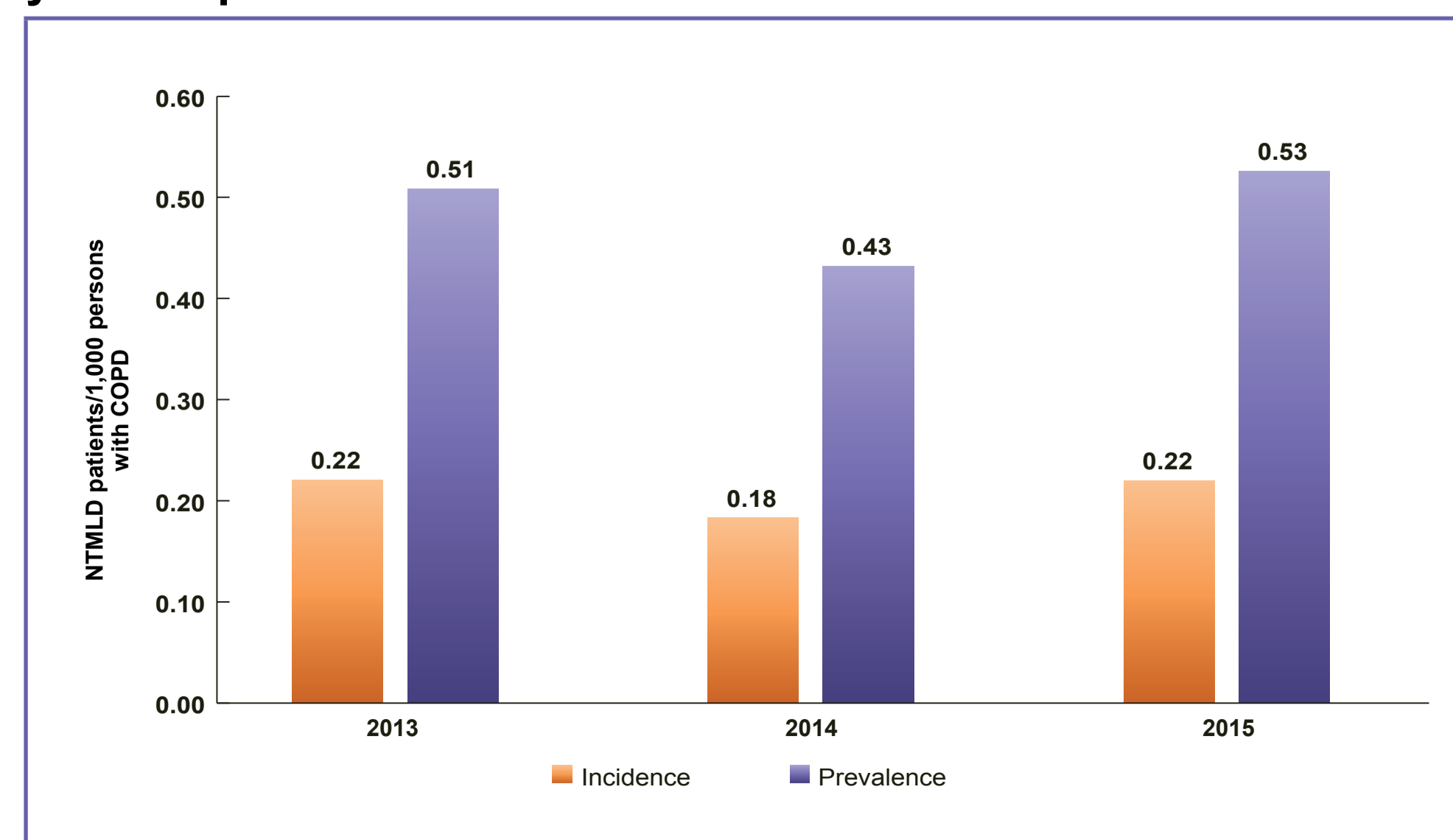
- Patients with BE had a significantly higher risk of NTMLD than patients with COPD (observed rate ratio: 37.8, 95% CI, 32.7-43.7; $P < 0.001$).
- In the BE cohort from 2013-2015, NTMLD incidence increased from 7.1 to 10.0 per 1,000 patients and prevalence increased from 22.5 to 25.1 (**Figure 2**).
- In the COPD cohort, NTMLD incidence and prevalence remained relatively stable from 2013-2015, with an incidence of 0.22 per 1,000 patients and a prevalence of 0.53 per 1,000 patients (**Figure 3**).
- In the BE cohort, age-gender standardized incidence per 1,000 patients in 2015 was higher in women ≥ 65 years of age compared with women < 65 years (12.41 vs 11.84), a pattern which was also observed in the COPD cohort, with standardized incidence of 0.32 and 0.16 in women ≥ 65 years of age and < 65 years, respectively (**Table 2**).
- In the BE cohort, age-gender standardized incidence per 1,000 patients in 2015 was lower in men ≥ 65 years of age compared with men < 65 years (5.62 vs 6.62). In contrast, in the COPD cohort, it was higher (0.17 vs 0.10) in men ≥ 65 years of age compared with men < 65 years (0.17 vs 0.10) (**Table 2**).
- Between 2013 and 2015, the overall rate of NTMLD in the BE cohort was 11.22 per 1,000 person-years and 0.31 per 1,000 person-years in the COPD cohort.

Figure 2: Incidence and prevalence of NTMLD per 1,000 person-years in patients with incident BE



BE=bronchiectasis; NTMLD=nontuberculous mycobacterial lung disease.

Figure 3: Incidence and prevalence of NTMLD per 1,000 person-years in patients with incident COPD



COPD=chronic obstructive pulmonary disease; NTMLD=nontuberculous mycobacterial lung disease.

Table 2: NTMLD incidence and prevalence in incident BE and COPD cohorts*

BE					
Incidence					
Year	Female ≥ 65 y	Male ≥ 65 y	Female < 65 y	Male < 65 y	Overall Incidence
2013	9.94	6.81	4.25	3.04	7.13
2014	10.66	1.75	7.27	3.82	7.08
2015	12.41	5.62	11.84	6.62	10.02
Prevalence					
Year	Female ≥ 65 y	Male ≥ 65 y	Female < 65 y	Male < 65 y	Overall Prevalence
2013	29.81	15.44	23.62	8.37	22.49
2014	30.64	14.42	26.67	10.69	23.61
2015	34.40	14.69	26.99	8.82	25.14
COPD					
Incidence					
Year	Female ≥ 65 y	Male ≥ 65 y	Female < 65 y	Male < 65 y	Overall Incidence
2013	0.35	0.25	0.14	0.07	0.22
2014	0.29	0.19	0.08	0.06	0.18
2015	0.32	0.17	0.16	0.10	0.22
Prevalence					
Year	Female ≥ 65 y	Male ≥ 65 y	Female < 65 y	Male < 65 y	Overall Prevalence
2013	0.87	0.51	0.28	0.23	0.51
2014	0.66	0.43	0.19	0.22	0.43
2015	0.79	0.47	0.31	0.23	0.53

COPD=chronic obstructive pulmonary disease; NTMLD= nontuberculous mycobacterial lung disease. *Number of NTMLD patients per 1,000 persons with BE or COPD.

DISCUSSION

- This nationwide US population-based study provides much needed data on NTMLD incidence and prevalence in incident BE and COPD cohorts.
- In 2015, the prevalence of NTMLD was 2.5% in the BE cohort and 0.05% in the COPD cohort.
- Over the 3-year period from 2013-2015, NTMLD risk in patients with preexisting BE was 38 times that in patients with preexisting COPD.
- There is a wide range of estimates in the literature of rates of NTMLD among patients with preexisting BE; however, most of the studies were based on clinical centers and were not population-based.^{6,7}
 - For example, in patients with BE, the rate of NTMLD has been reported to range from 3% of patients meeting American Thoracic Society criteria for infection in a prospective single-center UK study to 30% of patients meeting criteria for NTM disease in a retrospective single-center US study.^{6,8,9}
 - Also of interest, a meta-analysis of 8 studies of patients with BE (number of patients ranged from 50 to 866) in various countries (Australia, China, Iran, South Korea, Thailand, and the United Kingdom) reported a combined prevalence of NTM infection of 9.3% (95% CI, 5.0%-13.6%); the rate of NTMLD was not reported.⁷
- The incidence and prevalence of NTMLD among patients with preexisting BE and COPD were notably higher than that in the general population.
 - The ratios of NTMLD incidence and prevalence in patients with preexisting COPD compared with the general population were 4.5 and 4.65, respectively.
 - Given the high prevalence of COPD in the general population and the elevated risk of NTMLD among patients with COPD, it is anticipated that the number of patients with NTMLD is large and has been underestimated in the past.
 - The ratios of NTMLD incidence and prevalence in patients with preexisting BE compared with the general population were 211.8 and 214.5, respectively, reflecting an especially pronounced risk of NTMLD in this patient group.

CONCLUSIONS

- NTMLD incidence and prevalence were substantially higher in patients with preexisting BE compared to those with preexisting COPD.
- Following diagnosis with BE, we anticipate that 2% of patients are likely to have NTMLD per year.
- Due to the large number of people with COPD in the general population, the absolute number of patients at risk of NTMLD is also anticipated to be high, representing an important clinical burden in this population.
- Improved awareness of NTMLD risk in patients with BE and COPD can help assure timely diagnosis and appropriate clinical intervention.

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DISCLOSURES

Jennifer Adjemian and Kenneth Olivier are involved in clinical trials sponsored by and have received grant funding from and are consultants to Insmid Incorporated. Quanwu Zhang, Gina Eagle, and Engels Chou are employees of Insmid Incorporated. Xin Li is employed by KMK Consulting, Inc, Morristown, NJ, which provides consulting services to Insmid Incorporated.

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