Incidence and Prevalence of Nontuberculous Mycobacterial Lung Disease in a Large U.S. Managed Care Health Plan, 2008–2015

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Abstract

Rationale: Estimating the annual incidence and prevalence of nontuberculous mycobacterial (NTM) lung disease may assist in improving understanding of the public health and economic impacts of this disease and its treatment.

Objective: To estimate the yearly incidence and prevalence of administrative claims–based NTM lung disease between 2008 and 2015 in a U.S. managed care claims database.

Methods: We used a national managed care claims database (Optum Clinformatics Data Mart) representing a geographically diverse population of approximately 27 million members annually. All medical claims from January 1, 2007, to June 30, 2016, were scanned for diagnosis codes for NTM lung disease (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 031.0 or ICD-10-CM code A31.0). We defined a case of NTM lung disease as having at least two medical claims with a code of 031.0 or A31.0 that were dated at least 30 days apart. Annual incidence and prevalence were estimated for each calendar year from 2008 to 2015.

Results: From 2008 to 2015, the annual incidence of NTM lung disease increased from 3.13 (95% confidence interval [CI], 2.88–3.40) to 4.73 (95% CI, 4.43–5.05) per 100,000 person-years, and the annual prevalence increased from 6.78 (95% CI, 6.45–7.14) to 11.70 (95% CI, 11.26–12.16) per 100,000 persons. The average annual changes in incidence and prevalence were +5.2% (95% CI, 4.0–6.4%; $P < 0.01$) and +7.5% (95% CI, 6.7–8.2%; $P < 0.01$), respectively. For women, the annual incidence increased from 4.16 (95% CI, 3.76–4.60) to 6.69 (95% CI, 6.19–7.22) per 100,000 person-years, and the annual prevalence increased from 9.63 (95% CI, 9.08–10.22) to 16.78 (95% CI, 16.04–17.55) per 100,000 persons. For individuals aged 65 years or older, the annual incidence increased from 12.70 (95% CI, 11.46–14.07) to 18.37 (95% CI, 16.98–19.87) per 100,000 person-years, and the annual prevalence increased from 30.27 (95% CI, 28.41–32.24) to 47.48 (95% CI, 45.37–49.67) per 100,000 persons. The incidence and prevalence of NTM lung disease increased in most U.S. states and overall at the national level.

Conclusions: The incidence and prevalence of NTM lung disease appears to be increasing in the United States, particularly among women and older age groups.

Keywords: nontuberculous mycobacterial infections; incidence; prevalence

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Nontuberculous mycobacterial (NTM) lung disease is an increasingly recognized chronic condition in the United States and is associated with substantial morbidity and mortality (1–6). Increasing incidence has been reported in recent institution- and population-based studies in the United States and abroad (7–13), with increased risk among those older than 50 years of age or with chronic underlying lung diseases such as non–cystic fibrosis bronchiectasis, cystic fibrosis, and emphysema (1, 14–16). The vast majority of NTM lung disease in the United States is caused by *Mycobacterium avium* complex (17). Other species, such as *Mycobacterium abscessus*, *Mycobacterium kansasii*, *Mycobacterium xenopi*, and others, also contribute to this disease burden, particularly outside the United States (18).

Few national estimates of NTM lung disease burden in the United States are available, and estimating the annual incidence and prevalence of NTM lung disease may assist in improving understanding of the public health and economic impacts of this disease and its treatment (5). The most recent U.S.-wide prevalence estimate assessed the time period of 1997–2007 and, based on a Medicare population aged 65 years or older, observed that NTM lung disease increased at an annual rate of 8.2% (10). Beyond regional studies (19), nationwide incidence has not been reported in the United States.

The objective of this study was to estimate the yearly incidence and prevalence of NTM lung disease between 2008 and 2015 using a large U.S. national managed care claims database. Preliminary results of this study were presented as an abstract and poster at the American Thoracic Society 2017 International Conference (20).

Methods

Administrative Claims Database

The Optum Clinformatics Data Mart (CDM) contains eligibility and pharmacy and medical claims data from a large U.S. health plan affiliated with Optum. CDM is a statistically de-identified, Health Insurance Portability and Accountability Act–compliant, closed system of administrative claims that includes patient enrollment, physician, facility, and pharmacy claims; less than one-third of the members have laboratory results.

From 2007 to 2015, the CDM database represented approximately 27 million enrolled members annually, with either medical and pharmacy insurance coverage or medical coverage alone. The individuals covered by this health plan are geographically diverse across the United States, with data for insurance plan members in all 50 states. Although predominantly a commercially insured population, Medicare Advantage (i.e., part C) members have been included with increasing numbers in recent years (~3.5 million in 2015). Table E1 in the online supplement gives the number of beneficiaries by insurance type and study year. Demographic data were summarized and compared with the general population using 2012 and 2015 U.S. Census Bureau data (Tables E2 and E3).

The patient cohort of NTM lung disease was identified from the entire CDM database between January 1, 2007, and June 30, 2016. Optum also provided the numbers of total insured beneficiaries of the health plan as well as breakdowns by age, sex, insurance type (commercial vs. Medicare), and state in yearly time bands.

Claims-based NTM Lung Disease Case Definition

The diagnosis codes for NTM lung disease are 031.0 and A31.0, corresponding to the *International Classification of Diseases, 9th Revision and 10th Revision, Clinical Modification* (ICD-9-CM and ICD-10-CM), respectively. A case of NTM lung disease is defined as an individual who had at least two medical claims with diagnosis code 031.0 or A31.0 that were dated at least 30 days apart between January 1, 2007, and June 30, 2016.

The index date is defined as the date of the first claim with the ICD-9/10-CM diagnosis code for NTM lung disease. Baseline is defined as the period of 12 months preceding the index date.

Incidence and Prevalence Estimation

Annual incidence and prevalence were estimated for each calendar year from 2008 to 2015. Figure E1 shows the flowcharts for prevalence and incidence calculation.

Once all the beneficiaries who met our case definition of NTM lung disease were extracted from CDM between January 1, 2007, and June 30, 2016, the incident cases and prevalent cases were identified from this patient cohort for each calendar year from 2008 to 2015. A case of NTM lung disease is included as an incident case if the beneficiary *1*) had claims with the ICD code 031.0 or A31.0 within that calendar year, *2*) received no claims for the disease in the preceding year, and *3*) had a 24-month enrollment for the calendar year and the preceding year. Similarly, a case of NTM lung disease is included as a prevalent case if the beneficiary *1*) had claims with the ICD code 031.0 or A31.0 within that calendar year and *2*) had a 12-month enrollment for the year. Owing to the chronic nature of NTM lung disease and the fact that patients may relapse or become reinfected after eradication of infection (21), individual beneficiaries could be counted as incident and/or prevalent cases in more than 1 year. When multiple claims with the ICD code 031.0 or A31.0 were received within a calendar year, the beneficiary was counted only once, in line with recommendations of the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines on treatment duration for at least 12 months of receiving two or three antimicrobials (22).

The population at risk for annual incidence estimation was the number of total insured beneficiaries in that calendar year, excluding *1*) the number of beneficiaries without full-year medical insurance coverage for the incident year as well as the preceding year and *2*) the number of beneficiaries with a medical claim for NTM lung disease in the preceding year. The population at risk for annual prevalence estimation was the number of total insured beneficiaries in that calendar year, excluding the number of beneficiaries without full-year medical insurance coverage. Of note, the number of beneficiaries without full-year insurance coverage was estimated by assessing the coverage status of a 5% random sample of the CDM database, under the assumption that the proportion with full-year coverage within the 5% random sample in a given year could be applied to the total beneficiary population in that year.

Incidence of NTM lung disease in each calendar year was calculated by dividing the total number of unique beneficiaries fulfilling the incident case definition by the population at risk for incidence estimation. Prevalence at each calendar year was calculated by dividing the total number of unique beneficiaries fulfilling the prevalent case definition by the population at risk for

prevalence estimation. Both incidence and prevalence were stratified by age, sex, insurance type (commercial vs. Medicare Advantage), and state.

Statistics

Poisson regression models were fitted to the counts of prevalent and incident cases and the at-risk population sizes to estimate the annual incidence and prevalence and their 95% confidence intervals (CIs). Prevalence and incidence stratified by sex, age group, and insurance type were also estimated using the same method.

For the trend analysis in prevalence and incidence over the years, change is assumed to take an exponential function. For any given year t, if the prevalence is Y_t and the annual rate of increase is $b\%$, then the prevalence of the next year is $Y_{t+1} = Y_t(1 + b\%)$. Using a Poisson regression model to fit the annual prevalence at multiple years and letting β be the coefficient of the year variable, the average annual percentage increase is estimated as $\exp(\beta) - 1$. Statistical analyses were conducted using SAS Enterprise Guide (release version 7.15 HF6; SAS Institute).

Results

Beneficiaries

Tables E2 and E3 provide a comparison of demographics of the CDM database with U.S. benchmarks in 2012 and 2015, respectively. From January 1, 2007, to June 30, 2016, a total of 74,984,596 beneficiaries were enrolled in the nationwide health plan affiliated with Optum. Among them, a total of 16,872 insured health plan members had at least one medical claim with the ICD-9/10-CM code for NTM lung disease. Of these beneficiaries, 9,476 met the case definition for NTM lung disease. Among the cases of NTM lung disease, the mean ± standard deviation (SD) number of claims with diagnosis code 031.0 or A31.0 was 31 (±65); the median was 14, and the interquartile range (IQR) was 28. The mean (±SD) number of days between the first and last claims was 639 (±677); the median was 391, and the IQR was 721. Most cases were women ($n = 6{,}530$; 68.9%), and the mean (±SD) age was 67 (±15) years. Most (89.1%) cases were older than 50 years of age (distribution by age, 1–30 yr, 2.8%; 31–40 yr, 2.6%; 41–50 yr, 5.5%; 51–60 yr, 15.3%; 61–70 yr, 26.5%; 71–80 yr, 29.2%; and 81–90 yr, 18.1%). At the time of the first diagnosis, 63.8% of the NTM cases ($n = 9{,}476$) were covered by a commercial plan, and 36.2% were covered by Medicare Advantage. About 15.2% ($n = 1{,}441$) of the cases received the first NTM diagnosis in 2007, followed by 11.9% ($n = 1{,}130$) in 2013, 11.5% ($n = 1{,}092$) in 2015, 11.2% ($n = 1{,}061$) in 2012, and 10.8% ($n = 1{,}019$) in 2014. The regions where these beneficiaries received their first diagnosis varied (Figure 1). States with more than 500 NTM lung disease cases were Florida ($n = 1{,}299$), Texas ($n = 954$), California ($n = 686$), Wisconsin ($n = 608$), New York ($n = 566$), and Georgia ($n = 504$).

Because the baseline period is defined as the 12 months preceding the index date,

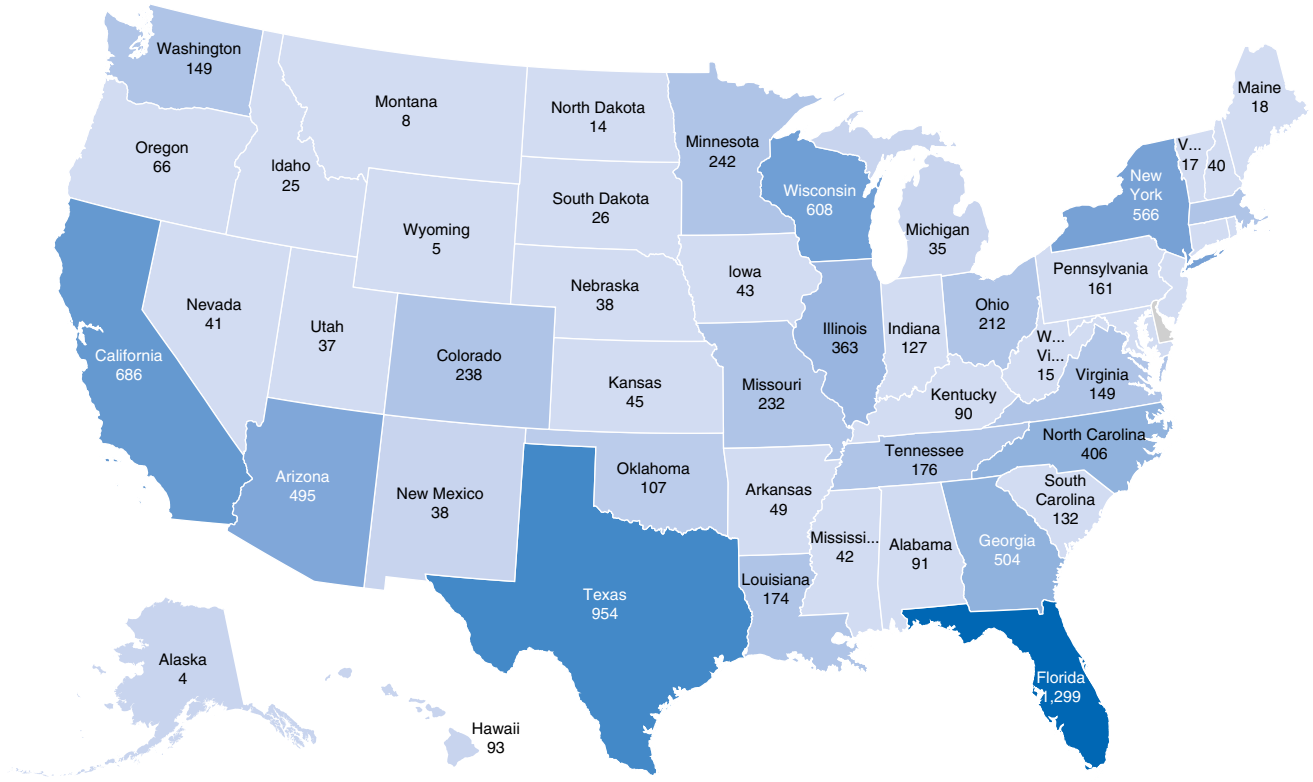

Figure 1. Number of patients by state at the first diagnosis of nontuberculous mycobacterial (NTM) lung disease, January 1, 2007, to June 30, 2016 ($N = 9{,}476$).

evaluation of baseline demographics and characteristics required 12-month continuous insurance enrollment before the index date. Accordingly, demographic and baseline disease characteristics were available for 6,280 cases (Table 1). These cases were predominantly women (68%), had a mean (±SD) age of 69 (±14) years, and had a mean (±SD) Charlson comorbidity index of 2.2 (±2.3). Most of the cases (80.2%) had at least one underlying lung disease, including asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, or prior tuberculosis. Bronchiectasis (37.0%) and COPD (52.6%) were the most common chronic underlying lung diseases observed.

Incidence

The annual incidence of NTM lung disease increased from 3.13 (95% CI, 2.88–3.40) in 2008 to 4.73 (95% CI, 4.43–5.05) in 2015 per 100,000 person-years. The average rate of yearly change for incidence was +5.2% (95% CI, 4.0–6.4; $P < 0.01$). The incidence of NTM lung disease overall and stratified by age, sex, and insurance plan subgroups is shown in Figure 2A. Among people aged younger than 65 years from 2008 to 2015, the incidence of NTM lung disease increased from 1.34 (95% CI, 1.16–1.54) to 1.82 (95% CI, 1.62–2.04) per 100,000 person-years, respectively. The incidence of NTM lung disease in people aged 65 years or older from 2008 to 2015 increased from 12.70 (95% CI, 11.46–14.07) to 18.37 (95% CI, 16.98–19.87) per 100,000 person-years, respectively. In men, the incidence from 2008 to 2015 increased from 2.05 (95% CI, 1.77–2.37) to 2.71 (95% CI, 2.40–3.07) per 100,000 person-years, respectively, compared with an increase in women from 4.16 (95% CI, 3.76–4.60) to 6.69 (95% CI, 6.19–7.22) per 100,000 person-years. The annual incidence in Medicare plan members increased from 2008 to 2015 from 8.89 (95% CI, 7.31–10.82) to 16.38 (95% CI, 14.87–18.05) per 100,000 person-years, respectively. The annual incidence rate in commercial plan members increased from 2008 to 2015 from 2.75 (95% CI, 2.51–3.01) to 2.99 (95% CI, 2.73–3.26) per 100,000 person-years. Table E4A shows the average rate of yearly change of incidence for these subgroups.

Table 1. Baseline demographics and patient characteristics

Baseline Variable	Claims-based NTM Lung Disease (*N = 6,280*)
Age, yr, mean (±SD)	69 (±14.1)
Women, % (*n*)	67.6% (4,246)
Charlson comorbidity index, mean (SD)	2.2 (2.3)
Underlying lung disease	
Aspergillosis, % (*n*)	3.0% (187)
Asthma, % (*n*)	23.2% (1,460)
Bronchiectasis, % (*n*)	37.0% (2,324)
Chronic obstructive pulmonary disease, % (*n*)	52.6% (3,304)
Cystic fibrosis, % (*n*)	1.7% (104)
Pneumonia, % (*n*)	40.2% (2,527)
Tuberculosis, % (*n*)	7.0% (438)
Any of the above lung diseases, % (*n*)	80.2% (5,034)
Atherosclerosis, % (*n*)	8.1% (509)
Arrhythmia, % (*n*)	22.5% (1,415)
Coronary artery disease, % (*n*)	19.4% (1,217)
Cancer, % (*n*)	19.5% (1,227)
Congestive heart failure, % (*n*)	11.6% (727)
Colitis, % (*n*)	4.1% (257)
Crohn disease, % (*n*)	0.8% (49)
Dementia, % (*n*)	0.7% (46)
Depression, % (*n*)	9.4% (590)
Diabetes, % (*n*)	14.4% (905)
Gastroesophageal reflux disease, % (*n*)	26.8% (1,684)
Heart valve disorder, % (*n*)	15.5% (976)
HIV, % (*n*)	1.6% (98)
Hyperlipidemia, % (*n*)	46.4% (2,912)
Hypertension, % (*n*)	50.0% (3,142)
Immune deficiency, % (*n*)	6.2% (392)
Mental disorder, % (*n*)	16.0% (1,002)
Metastatic carcinoma, % (*n*)	3.5% (220)
Moderate or severe liver disease, % (*n*)	0.7% (47)
Multiple sclerosis, % (*n*)	0.4% (22)
Myocardial infarction, % (*n*)	4.7% (297)
Obesity, % (*n*)	3.8% (236)
Organ transplant, % (*n*)	1.4% (88)
Pectus excavatum, % (*n*)	0.2% (12)
Rheumatoid disease, % (*n*)	6.0% (377)
Tobacco use, % (*n*)	10.5% (659)

Definition of abbreviations: HIV = human immunodeficiency virus; NTM = nontuberculous mycobacterial; SD = standard deviation.
Baseline diseases/disorders identified via insurance claims (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM], or ICD-10-CM codes).

Prevalence

The annual prevalence from 2008 to 2015 increased from 6.78 (95% CI, 6.45–7.14) to 11.70 (95% CI, 11.26–12.16) per 100,000 persons, respectively. The average rate of yearly change for prevalence was +7.5% (95% CI, 6.7–8.2; $P < 0.01$). The prevalence of NTM lung disease overall and stratified by age, sex, and insurance plan subgroups is shown in Figure 2B. The respective yearly prevalence estimates for NTM lung disease from 2008 to 2015 in people younger than 65 years of age increased from 2.87 (95% CI, 2.63–3.12) to 4.10 (95% CI, 3.82–4.41) per 100,000 persons compared with an increase in people aged 65 years or older from 30.27 (95% CI, 28.41–32.24) to 47.48 (95% CI, 45.37–49.67) per 100,000 persons. The yearly prevalence estimates from 2008 to 2015 increased in men from 3.79 (95% CI, 3.44–4.18) to 6.45 (95% CI, 5.99–6.94) per 100,000 persons, respectively, and increased in women from 9.63 (95% CI, 9.08–10.22) to 16.78 (95% CI, 16.04–17.55) per 100,000 persons. The annual prevalence estimates in Medicare plan members increased from 2008 to 2015 from 19.47 (95% CI, 17.25–21.97) to 43.11 (95% CI, 40.86–45.49) per 100,000 persons, respectively. The annual prevalence in commercial plan members increased from 2008 to 2015 from 5.95 (95% CI, 5.63–6.30) to 6.77 (95% CI, 6.41–7.15) per 100,000 persons, respectively. Table E4B

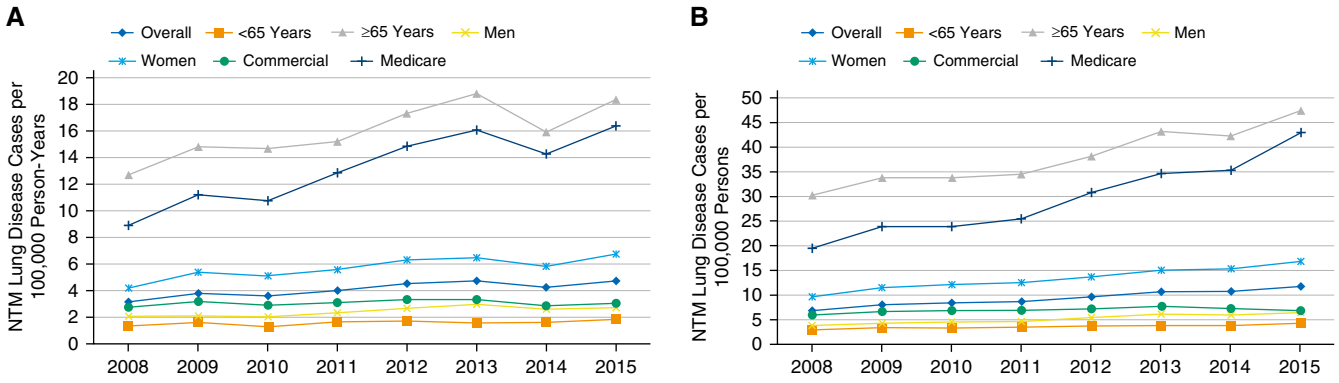

Figure 2. (*A*) Yearly incidence and (*B*) yearly prevalence of nontuberculous mycobacterial (NTM) lung disease (2008–2015) by select subgroups in a U.S. national health insurance plan.

shows the average rate of yearly change of prevalence for these subgroups.

Geographic Variation

As illustrated in Figure 3, it appears that the incidence and prevalence of NTM lung disease from 2008 to 2015 increased in most U.S. states (incidence increased by at least 10% in 29 states, and prevalence increased by at least 10% in 39 states) and overall at the national level. The incidence rates of NTM lung disease in Hawaii and Arizona were consistently in the high range (≥6/100,000 person-years) in 2008 and 2015. The prevalence of NTM lung disease in Hawaii was consistently in the high range (≥17/100,000 person-years) in 2008 and 2015, whereas in Arizona, the prevalence shifted from the 11.51–17.00/100,000 range in 2008 to the ≥17/100,000 range in 2015. Marked increases in both the incidence and prevalence of NTM lung disease were observed in Florida and adjacent states.

Discussion

This study provides epidemiological information on NTM lung disease in the United States after the publication of ATS/IDSA guidelines in 2007, including incidence and prevalence estimated across all states. The annual incidence and prevalence of NTM lung disease significantly increased from 2008 to 2015; the average rates of yearly change were +5.2% and +7.5%, respectively. Women and people aged 65 years or older had consistently higher incidence and prevalence rates than men and people aged less than 65 years, respectively, over this time period.

An increase in the prevalence of NTM lung disease in North America and other regions of the world has been documented in the time period from the mid-1990s to the mid-2000s (23, 24). The 7.5% increase in prevalence observed from 2008 to 2015 in the present analysis is comparable to the 8.2% increase reported from 1997 to 2007 in a large U.S. population-based study based on Medicare part B claims (10). Although the rate of yearly change in prevalence was comparable between these studies, the annual prevalence estimates appeared to differ. In the previous Medicare-based study, the reported annual prevalence (cases/100,000 persons) increased from 20 in 1997 to 47 in 2007 (10). The annual prevalence estimates for NTM lung disease among Medicare Advantage plan members in our study increased from 19.5 per 100,000 persons in 2008 to 43.1 per 100,000 persons in 2015. It is important to note that although our 2008 estimate appears to be lower than the previous study's 2007 estimate, this is likely due to the difference in identification criteria for NTM lung disease. In the previous study, the prevalence estimates were calculated by dividing the total number of unique cases (i.e., individuals assigned at least one NTM lung disease–associated claim) by the total number of beneficiaries (who had at least 1 mo of coverage) during the time period evaluated (10). The present analysis required at least two diagnosis codes at least 30 days apart as well as 12 months of continuous insurance coverage. In addition, the Medicare part B study focused on people aged 65 years or older, whereas our Medicare Advantage subpopulation also included plan members aged younger than 65 years who had disabilities. Nonetheless, we speculate that age is a likely driver of the higher prevalence of NTM lung disease among Medicare Advantage beneficiaries relative to commercially insured beneficiaries in the present study (Figures 2A and 2B).

Another U.S.-based study using a large linked database approach at four integrated healthcare delivery systems reported an increased prevalence of NTM lung disease based on the ATS/IDSA 2007 microbiological criteria (17). In the four healthcare delivery systems combined, the average annual age-adjusted period prevalence for 2004 to 2006 was 5.5 cases per 100,000 persons. This finding appears to be consistent with our overall NTM lung disease prevalence rate for 2008 (6.78 cases per 100,000 persons).

Our study provides a nationwide estimate of incidence for NTM lung disease among beneficiaries in a large insurance plan. A prior population-based study focused on the incidence rate in Oregon (19), using the 2007 microbiological criteria (22), and reported a relatively small increase of 2.2% ($P = 0.21$) in the annual incidence of NTM lung disease between 2007 and 2012 (from 4.8/100,000 person-years to 5.6/100,000 person-years)—figures that are consistent with our yearly incidence rate findings for Oregon. We observed that the incidence of NTM lung disease in Oregon was in the 3.01–4.00/100,000 person-years range in 2008 and in the 4.51–6.00/100,000 person-years range in 2015 (Figure 3A).

There are limitations in this study, including the impact of using ICD codes for the NTM case identification, and drawbacks

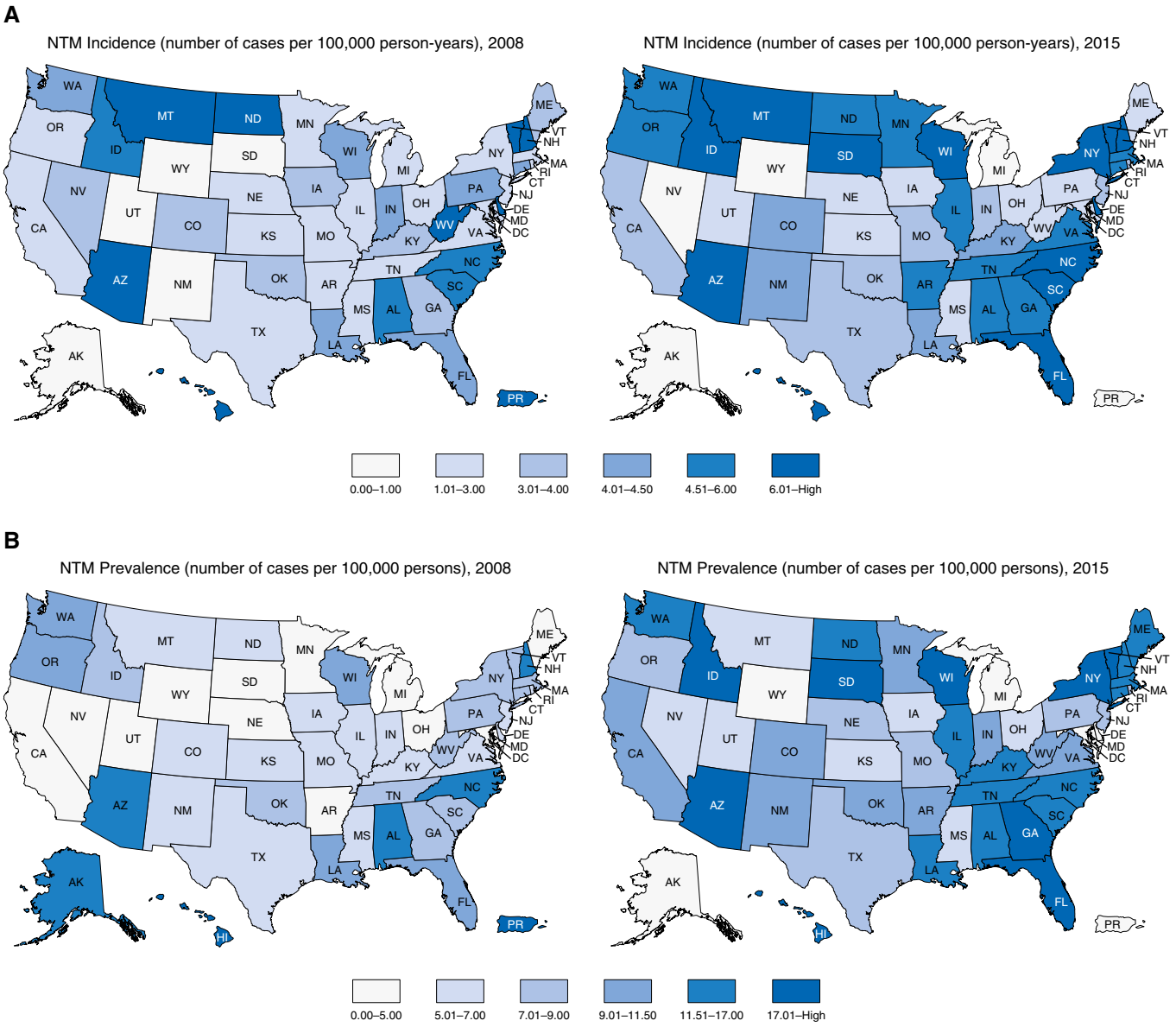

Figure 3. (*A*) Incidence and (*B*) prevalence of nontuberculous mycobacterial (NTM) lung disease in the United States, by state in 2008 and 2015.

that are inherent in claims data–based studies. The ATS/IDSA guidelines published in 2007 indicate that clinical, radiographic, and microbiological criteria are equally important, and all must be met to make a diagnosis of NTM lung disease (22). The claims data we used for this study do not have microbiological or radiographic confirmation of the NTM infection. As a result, case identification based on ICD code may be subject to undercoding as well as overestimation of disease due to miscoding or inappropriate selection of diagnosis codes (5, 25). It was also reported that using ICD-9-CM codes to identify NTM lung disease cases meeting the ATS/IDSA criteria may miss approximately 25–75% of cases (17).

However, a prior publication suggested that claims-based case identification has a high positive predictive value of approximately 82% for NTM lung disease (25). That publication reported a study that constructed case-finding algorithms to find cases of tuberculosis and NTM lung disease at a large health maintenance organization (Kaiser Permanente Northern California) and the Portland Veterans Affairs Medical Center. It was reported that case finding of NTM lung disease based on receiving at least one ICD-9-CM diagnosis code 031.0 detected 9 of 18 (50%; 95% CI, 0.26–0.74) cases in a population with rheumatoid arthritis treated with anti–tumor necrosis factor agents. When chart review was used with ATS/IDSA criteria applied for NTM lung disease, this case-finding algorithm had a high positive predictive value for true disease (82%; 95% CI, 0.48–0.98).

Disease awareness since the publication of the 2007 ATS/IDSA guidelines may have increased diagnostic testing and therefore the number of claims being submitted for testing; however, not all test results will be confirmatory. We believe that the requirement of at least two diagnosis codes

30 days apart reduces the potential of counting claims that were submitted for testing alone as representing cases.

Claims data–based studies have their inherent limitations. For example, real-world ICD coding practices may vary. It is possible that the diagnosis code was chosen to improve reimbursement, leading to a shift in the reported case mix (26, 27). In addition, intrinsic deficiencies in the diagnosis coding system may, to some degree, impair the accurate diagnosis and recording of cases (e.g., incomplete ICD-9-CM or ICD-10-CM menus could lead clinicians to choose inexact codes). It is also possible to have perpetuated coding error through "coding inertia," a tendency to carry the initial code over on subsequent claims. Another consideration is that the representativeness of the Optum CDM database over the United States varies. We noticed a geographic variation in insurance coverage (e.g., less coverage in the Northeast region of the United States) (Table E2) that could affect state-level estimations of incidence and prevalence. The socioeconomic status of the enrolled beneficiaries may also impact NTM lung disease incidence and prevalence; however, we did not have access to socioeconomic data. We excluded individuals who had less than 24 months and less than 12 months of continuous enrollment from the incidence and prevalence calculations, respectively. Nonetheless, we believe that these beneficiaries with full-year enrollment are representative of the entire plan population, because qualification for insurance coverage is not likely related to NTM lung disease or being selected in the 5% random sample.

Medical chart review using the ATS/IDSA criteria can identify NTM lung disease cases more accurately than using claims data alone. However, collecting and analyzing electronic health records nationwide is time-consuming and labor-intensive. We chose administrative claims data for two predominant reasons: *1*) efficiency of extracting data and *2*) access to a nationwide population.

We recognize that factors such as increased clinical awareness, changes in diagnostic evaluation, and issues with real-world coding practice may have contributed to the increases in incidence and prevalence of NTM lung disease observed in this study. Variable changes in frequencies of pulmonary risk factors for NTM lung disease have been observed. Bronchiectasis increased among Medicare beneficiaries between 2000 and 2007 (28). COPD prevalence was reported to have decreased in the United States from 2008–2009 to 2014–2015 (29). A Canadian study modeling the effects of changes in the prevalence of risk factors on the prevalence of NTM lung disease observed that risk factors were generally found to be increasing, but the magnitude of those increases did not completely explain the increases in NTM lung disease prevalence (30). Importantly, the investigators lacked data on the frequency of bronchiectasis. It is very likely that increases in the prevalence of chronic underlying lung diseases that are associated with NTM (e.g., bronchiectasis) might also be driving increases in NTM lung disease. The 2017 British Thoracic Society guidelines also reported that most studies indicate a rise in prevalence over the last four decades (31). Pulmonary NTM is a chronic disease, and the guideline's criterion for treatment success is 12 months of sputum culture negativity while on therapy. Both the chronic nature of the condition and the increase in incidence contributed to the increased prevalence over the years.

The strengths of the present study include the analysis of a large nationwide claims database that is geographically diverse across the United States, coupled with a case definition of NTM lung disease that required two diagnosis codes 30 days apart, resulting in a nationwide real-world population-based estimation of incidence and prevalence of NTM lung disease.

Conclusions

The incidence and prevalence of NTM lung disease appear to be increasing in the United States, particularly among women and the older age groups. ■

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