Incidence and Prevalence of Nontuberculous Mycobacterial Lung Disease in a Large United States 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 a better 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 United States (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 diagnostic codes for NTM lung disease (ICD-9-CM 031.0 or ICD-10-CM A31.0). We defined a case of NTM lung disease as having at least two medical claims with 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% 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 change 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 U.S., particularly among women and older age groups.

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Introduction

Nontuberculous mycobacterial (NTM) lung disease is an increasingly recognized chronic condition in the United States (U.S.) associated with substantial morbidity and mortality (1-6). Increasing incidence has been reported in recent institutional- and population-based studies in the U.S. and abroad (7-13), with increased risk among those older than 50 years 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 U.S. is caused by *Mycobacterium avium* complex (17), although other species such as *Mycobacterium abscessus*, *Mycobacterium kansasii*, *Mycobacterium xenopi*, and others contribute to this disease burden—particularly elsewhere in the world (18).

Few national estimates of NTM lung disease burden in the U.S. are available, and estimating the annual incidence and prevalence of NTM lung disease may assist in a better 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 to 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 U.S.

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.

Methods

Administrative Claims Database

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, HIPAA-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 U.S., with data for insurance plan members in all 50 states. Although predominantly a commercially insured population, Medicare Advantage (ie, Part C) members have been included with increasing numbers in recent years (approximately 3.5 million in 2015). Supplemental Table 1 gives the number of beneficiaries by insurance type and study year. Demographic data were summarized and compared with the general population using year 2012 and 2015 U.S. Census Bureau data (Supplemental Tables 2 and 3).

The patient cohort of NTM lung disease was identified from the entire CDM 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 Nontuberculous Mycobacterial Lung Disease Case Definition

The diagnostic codes for NTM lung disease are 031.0 and A31.0, corresponding to the International Classification of Diseases, 9th revision or 10th revision, clinical modification (ICD-9-CM or ICD-10-CM), respectively. A case of NTM lung disease is defined as an individual who had at least 2 medical claims with 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 diagnostic ICD-9/10-CM 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. Supplemental Figure 1 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 031.0 or A31.0 within that calendar year and 2) had a 12-month enrollment for the year. Due to the chronic nature of NTM lung disease, and the fact that patients may relapse or become re-infected after eradication of infection (27), individual beneficiaries could be counted as incident

and/or prevalent cases in more than 1 year. If multiple claims with 031.0 or A31.0 were received within a calendar year, the beneficiary is counted only once, in line with recommendations from the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines on treatment duration – at least 12 months on 2 or 3 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 CDM, 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 at 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).

Results

Beneficiaries

Supplemental Tables 2 and 3 provide the comparison of demographics of CDM 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 (±SD) number of claims with 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 the last claim was 639 (±677); the median was 391, and the IQR was 721. Most cases were women (n=6,530; 68.9%), who had a mean (±SD) age of 67 (±15) years. Most (89.1%) cases were aged >50 years (distribution by age: 1-30 years, 2.8%; 31-40 years, 2.6%; 41-50 years, 5.5%; 51-60 years, 15.3%; 61-70 years, 26.5%; 71-80 years, 29.2%; and 81-90 years, 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 >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, evaluation of baseline demographics and characteristics required 12-month continuous insurance enrollment prior to the index date. Accordingly, demographic and baseline disease characteristics were available for 6280 cases (Table 1): they were predominantly women (68%), had a mean (±SD) age of 69 (±14) years, and 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. Supplemental Table 4A shows the average rate of yearly change of incidence for these subgroups.

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 65 years and 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. Supplemental Table 4B 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 has 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 epidemiologic information on NTM lung disease in the U.S. following 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 relative to 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 mid-2000s (20, 21). The 7.5% increase in prevalence observed from 2008 to 2015 in the current 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 one month of coverage) during the time period evaluated (10). The current analysis required at least two diagnostic 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 <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 current 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 microbiologic 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

316 disease in Oregon was in the 3.01-4.00/100,000 person-years range in 2008 and in the 4.51-
317 6.00/100,000 person-years range in 2015 (Figure 3A).
318
319 There are limitations in this study, including the impact of using ICD codes for the NTM case
320 identification, and drawbacks that are inherent in claims data-based studies. The ATS/IDSA
321 guidelines published in 2007 indicate that clinical, radiographic, and microbiological criteria are
322 equally important, and all must be met to make a diagnosis of NTM lung disease (22). The
323 claims data we used for this study do not have microbiological or radiographic confirmation of
324 the NTM infection. As a result, case identification based on ICD code may be subject to
325 undercoding as well as overestimation of disease due to miscoding or inappropriate selection of
326 diagnostic codes (5, 23). It was also reported that using ICD-9-CM codes to identify NTM lung
327 disease cases meeting the ATS/IDSA criteria may miss approximately 25% to 75% of cases (17).
328
329 On the other hand, a prior publication has suggested that claims-based case identification has a
330 high positive predictive value of approximately 82% for NTM lung disease (23). This is a study
331 that constructed case-finding algorithms to find cases of tuberculosis and NTM lung disease at a
332 large health maintenance organization (Kaiser Permanente Northern California) and the Portland
333 Veterans Affairs Medical Center. It was reported that case-finding of NTM lung disease based
334 on receiving ≥1 ICD-9-CM 031.0 detected nine out of 18 (50%; 95% CI, 0.26-0.74) cases in a
335 population with rheumatoid arthritis who were treated with anti–tumor necrosis factor agents.
336 When chart review was used with ATS/IDSA criteria applied for NTM lung disease, this case-
337 finding algorithm had a high positive predictive value for true disease (82%; 95% CI, 0.48-0.98).
338

Disease awareness since the publishing 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 diagnostic 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 diagnostic code was chosen to improve reimbursement, leading to a shift in the reported case mix (24, 25). In addition, intrinsic deficiencies in the diagnostic 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 from "coding inertia", a tendency to carry the initial code over on subsequent claims. Another consideration is that the representativeness of Optum CDM over the U.S. varies. We have noticed a geographic variation in insurance coverage (e.g., less coverage in the Northeast region of the U.S., Supplemental Table 2) 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 have excluded individuals who had less than 24 months and 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 into the 5% random sample.

Medical chart review using the ATS/IDSA criteria can identify NTM lung disease cases more accurately than utilizing 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 modelling 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 report a rise in prevalence over the last four decades (26). Pulmonary NTM is a chronic disease—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 current study include the analysis of a large nationwide claims database that is geographically diverse across the U.S., coupled with a case definition of NTM lung disease that required 2 diagnostic codes 30 days apart, resulting in a nationwide real-world population-based estimation of incidence and prevalence of NTM lung disease.

Conclusion

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

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Figure Legends.

Figure 1. Number of patients by state at the First diagnosis of NTM lung disease, January 1, 2007 to June 30, 2016 (n=9,476).

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

Figure 3. Incidence *(A)* and prevalence *(B)* of NTM lung disease in the U.S., by state in 2008 and 2015.

Table 1. Baseline demographics and patient characteristics[a]

Baseline Variable	Claims-Based NTM Lung Disease (N=6280)
Age, mean (±SD), years	69 (±14.1)
Women, % (n)	67.6% (4246)
Charlson Comorbidity Index, mean (SD)	2.2 (2.3)
Underlying lung disease	
Aspergillosis, % (n)	3.0% (187)
Asthma, % (n)	23.2% (1460)
Bronchiectasis, % (n)	37.0% (2324)
Chronic obstructive pulmonary disease, % (n)	52.6% (3304)
Cystic fibrosis, % (n)	1.7% (104)
Pneumonia, % (n)	40.2% (2527)
Tuberculosis, % (n)	7.0% (438)
Any of the above lung disease, % (n)	80.2% (5034)
Atherosclerosis, % (n)	8.1% (509)
Arrhythmia, % (n)	22.5% (1415)
Coronary artery disease, % (n)	19.4% (1217)
Cancer, % (n)	19.5% (1227)
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% (1684)
Heart valve disorder, % (n)	15.5% (976)
HIV, % (n)	1.6% (98)
Hyperlipidemia, % (n)	46.4% (2912)
Hypertension, % (n)	50.0% (3142)
Immune deficiency, % (n)	6.2% (392)
Mental disorder, % (n)	16.0% (1002)
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)

HIV = human immunodeficiency virus.

[a]Baseline diseases/disorders identified via insurance claims (ICD-9-CM or ICD-10-CM codes).

Figure 1.

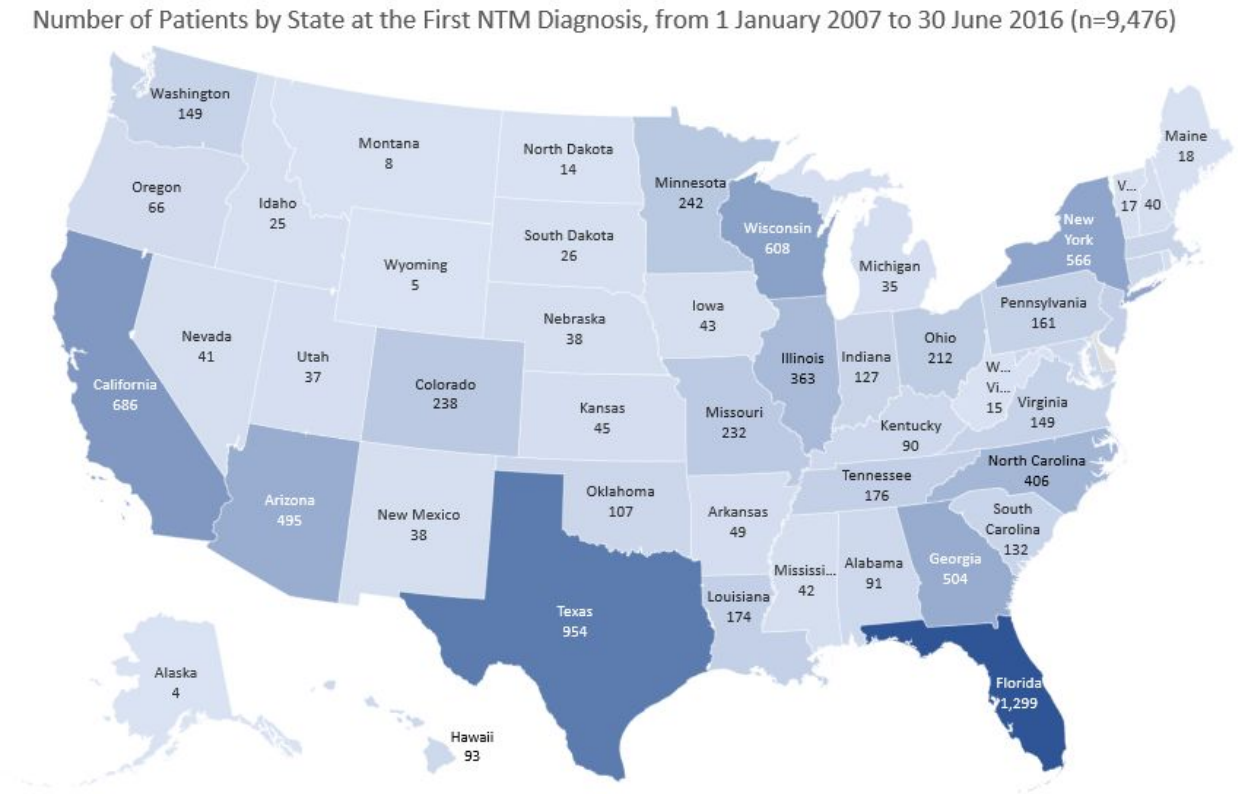
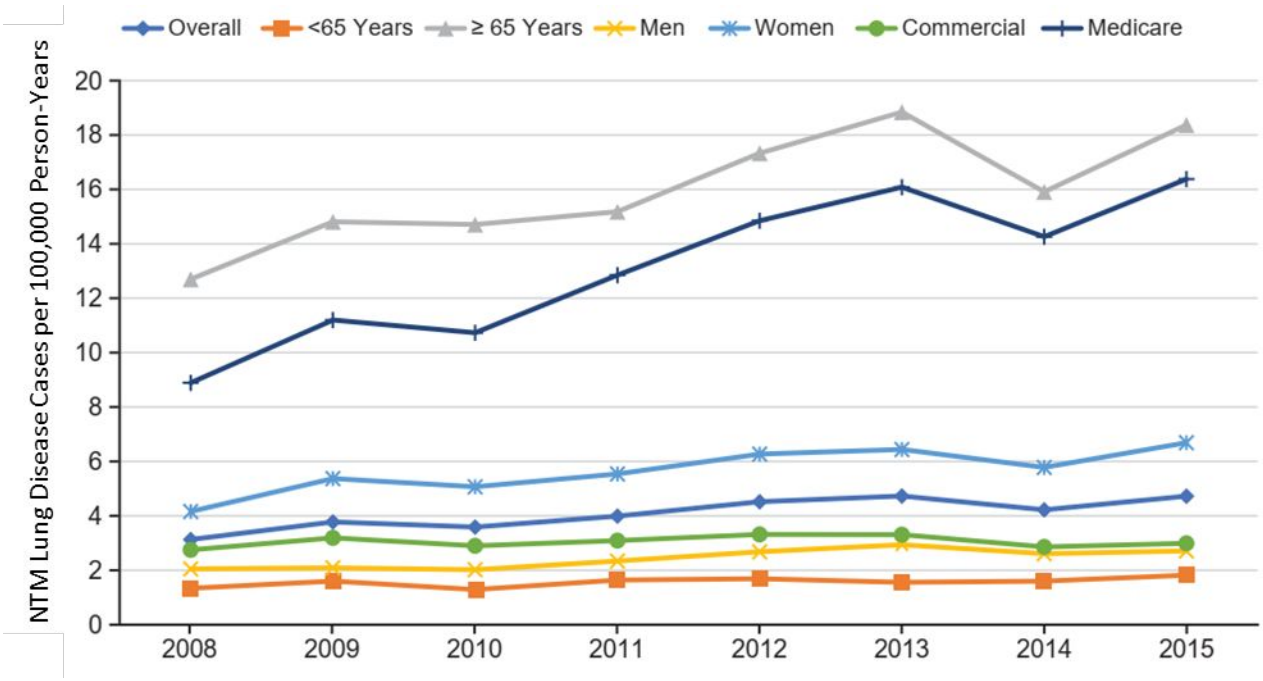

Number of Patients by State at the First NTM Diagnosis, from 1 January 2007 to 30 June 2016 (n=9,476)
Washington 149
Oregon 66
California 686
Idaho 25
Nevada 41
Montana 8
Wyoming 5
Utah 37
Arizona 495
Colorado 238
New Mexico 38
North Dakota 14
South Dakota 26
Nebraska 38
Kansas 45
Oklahoma 107
Texas 954
Minnesota 242
Iowa 43
Missouri 232
Arkansas 49
Louisiana 174
Wisconsin 608
Illinois 363
Michigan 35
Indiana 127
Ohio 212
Kentucky 90
Tennessee 176
Mississi... 42
Alabama 91
Georgia 504
Florida 1,299
South Carolina 132
North Carolina 406
Virginia 149
W... Vi... 15
Pennsylvania 161
New York 566
V... 17
40
Maine 18
Alaska 4
Hawaii 93

Figure 2.

A.


Overall
<65 Years
≥ 65 Years
Men
Women
Commercial
Medicare
NTM Lung Disease Cases per 100,000 Person-Years
0
2
4
6
8
10
12
14
16
18
20
2008
2009
2010
2011
2012
2013
2014
2015

B.

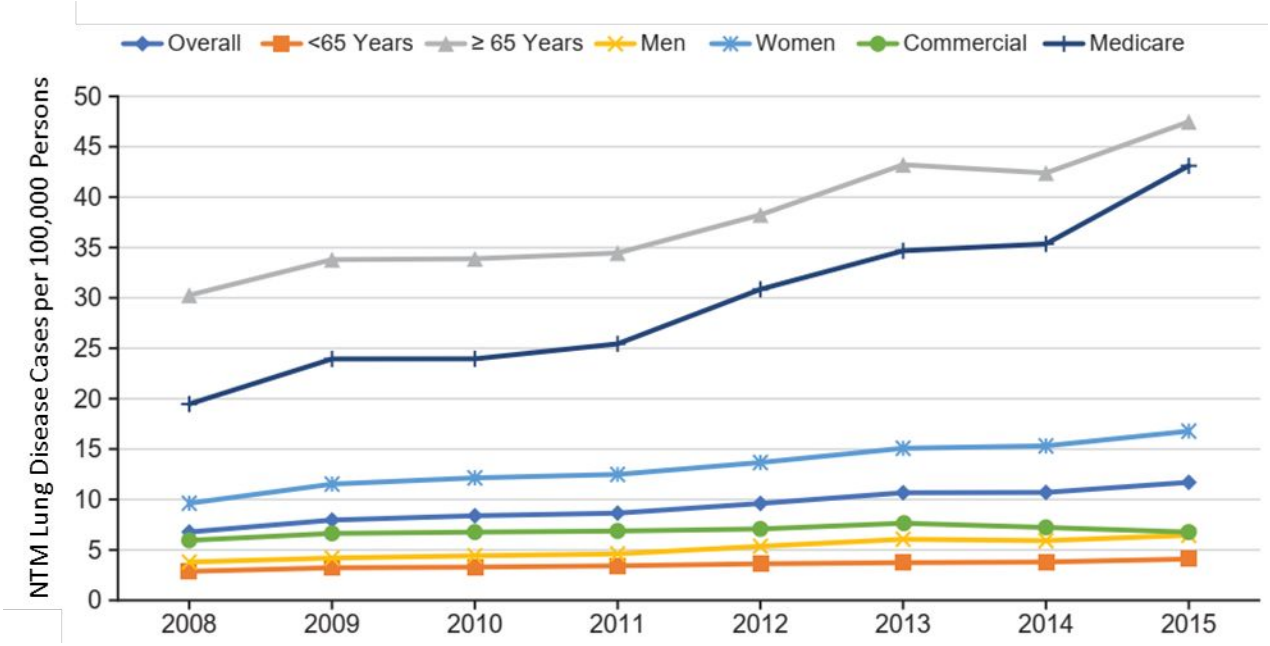
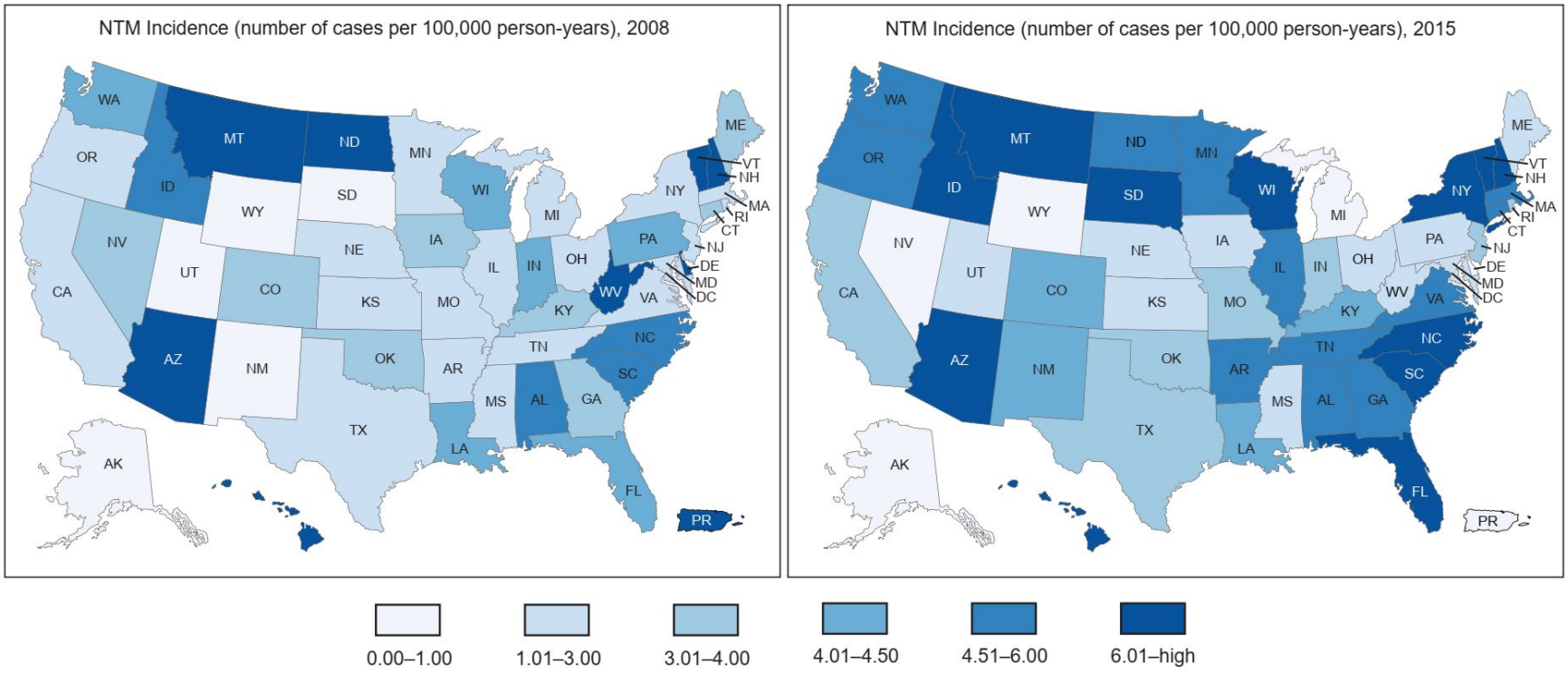
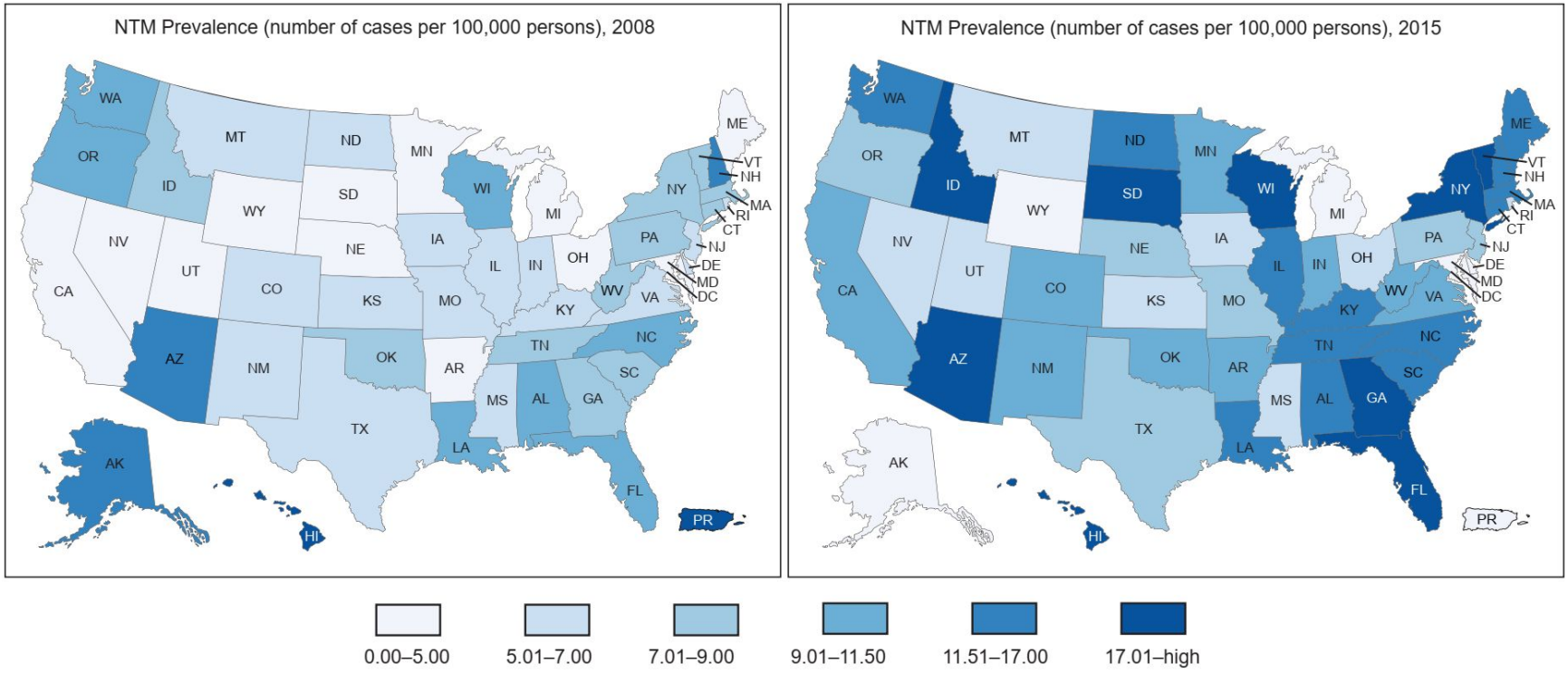

Overall
<65 Years
≥ 65 Years
Men
Women
Commercial
Medicare
NTM Lung Disease Cases per 100,000 Persons
50
45
40
35
30
25
20
15
10
5
0
2008
2009
2010
2011
2012
2013
2014
2015

Figure 3.

A


NTM Incidence (number of cases per 100,000 person-years), 2008
NTM Incidence (number of cases per 100,000 person-years), 2015
WA
OR
CA
ID
NV
MT
WY
UT
AZ
CO
NM
ND
SD
NE
KS
OK
TX
MN
IA
MO
AR
LA
WI
IL
MS
MI
IN
KY
TN
AL
OH
WV
GA
FL
SC
NC
VA
PA
NY
ME
VT
NH
MA
RI
CT
NJ
DE
MD
DC
AK
PR
0.00–1.00
1.01–3.00
3.01–4.00
4.01–4.50
4.51–6.00
6.01–high

B


NTM Prevalence (number of cases per 100,000 persons), 2008
NTM Prevalence (number of cases per 100,000 persons), 2015
WA
OR
CA
ID
NV
MT
WY
UT
AZ
CO
NM
ND
SD
NE
KS
OK
TX
MN
IA
MO
AR
LA
WI
IL
MS
MI
IN
KY
TN
AL
OH
WV
GA
FL
SC
NC
VA
PA
NY
ME
VT
NH
MA
RI
CT
NJ
DE
MD
DC
AK
HI
PR
0.00–5.00
5.01–7.00
7.01–9.00
9.01–11.50
11.51–17.00
17.01–high

Supplemental Tables and Figures.

Supplemental Table 1. Total number of beneficiaries by insurance type and study year

Year	Total Optum® CDM	Optum® CDM Commercial	Optum® CDM Medicare Advantage
2007	27,959,527	26,396,751	1,562,776
2008	27,355,593	25,676,313	1,679,280
2009	26,249,408	24,220,914	2,028,494
2010	26,081,574	23,681,602	2,399,972
2011	27,068,037	24,581,827	2,486,210
2012	28,259,093	25,406,898	2,852,195
2013	29,079,416	25,973,901	3,105,515
2014	27,557,541	24,335,447	3,222,094
2015	27,611,475	24,133,366	3,478,109

CDM = Clinformatics® Data Mart.

Supplemental Table 2. Demographics of Optum® CDM compared with U.S. benchmarks, 2015

Attributes	CDM Commercial	CDM Medicare Advantage	U.S. Population (2015)[a]	U.S. Privately Insured (2015)[a]
Male, %	50	43	49	49
Female, %	50	57	51	51
U.S. Region	**Total Lives**	**Total Lives**	**Total Lives**	**Total Lives**
Northeast, %	10	12	18	21
Midwest, %	24	19	21	25
South, %	42	35	39	29
West, %	24	32	24	25
Age Band	**Total Lives**	**Total Lives**	**Total Lives**	**Total Lives**
00-20 years, %	18	0	34	33
21-39 years, %	32	1	26	26
40-64 years, %	40	9	27	26
65+ years, %	10	91	13	14

[a] Statistical Abstract. U.S. Census.
CDM = Clinformatics® Data Mart.

Supplemental Table 3. Demographics of Optum® CDM compared with U.S. benchmarks, 2012

Ethnicity	CDM Lives (commercial and Medicare Advantage) Total Lives	U.S. Population (2012)[a] Total Lives	U.S. Privately Insured (2012)[a] Total Lives
White, %	73	63	71
African American, %	4	13	10
Hispanic, %	9	17	11
Asian, %	4	6	6
Other/unknown, %	9	1	2
Median household income		**2010[b]**	
	$62,500	$44,600	NA
Median net worth			
	$175,000	$77,300	NA

[a] U.S. Census Bureau.
[b] Federal Reserve – Survey of Consumer Finance.
CDM = Clinformatics® Data Mart; NA = not available.

Supplemental Table 4. Average rate of yearly change of incidence and prevalence

A

Incidence	Average Rate of Yearly Change (%)	95% CI (%)	*P* Value
Overall	5.2	4.0-6.4	<.01
≥65 Years	4.5	3.1-5.9	<.01
<65 Years	3.3	1.3-5.4	<.01
Women	5.3	3.9-6.7	<.01
Men	5.2	3.1-7.4	<.01
Medicare	7.6	5.4-9.8	<.01
Commercial	0.6	-0.7-2.0	0.37

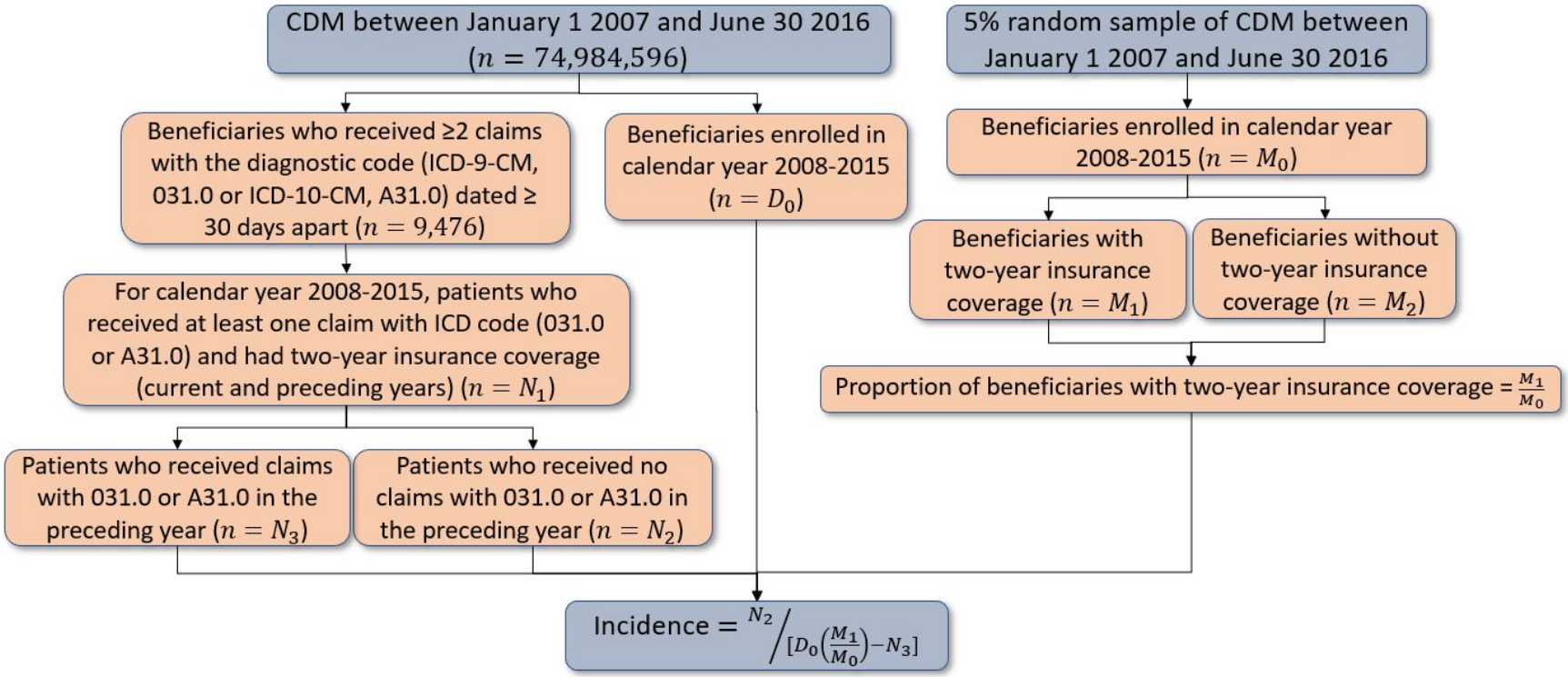
B

Prevalence	Average Rate of Yearly Change (%)	95% CI (%)	*P* Value
Overall	7.5	6.7-8.2	<.01
≥65 Years	6.4	5.5-7.3	<.01
<65 Years	4.6	3.3-5.8	<.01
Women	7.4	6.5-8.2	<.01
Men	8.0	6.7-9.5	<.01
Medicare	11.3	10.0-12.7	<.01
Commercial	2.1	1.3-2.9	<.01

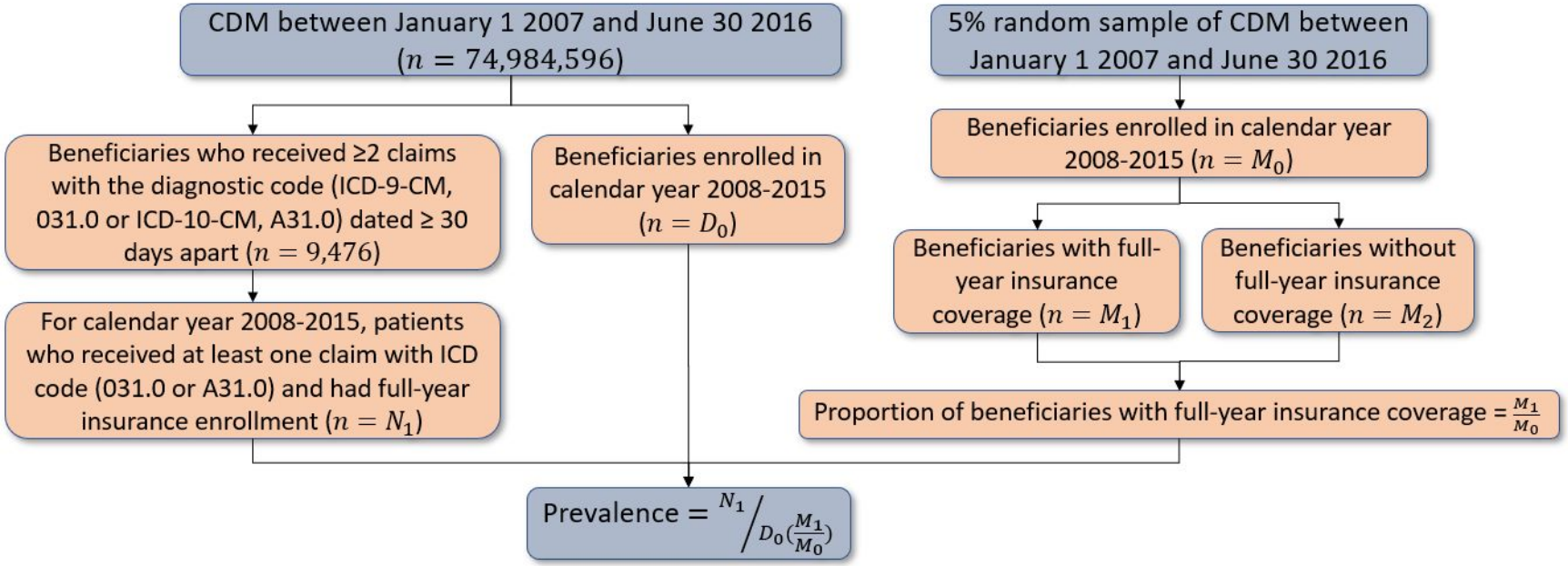
Supplement Figure 1. Flowchart used to calculate claims-based yearly incidence *(A)* and prevalence *(B)*. ICD-9-CM = International Classification of Diseases, 9th revision, clinical modification; ICD-10-CM = International Classification of Diseases, 10th revision, clinical modification.

Supplemental Figure 1.

A.



B.


CDM between January 1 2007 and June 30 2016 ($n = 74{,}984{,}596$)
Beneficiaries who received ≥2 claims with the diagnostic code (ICD-9-CM, 031.0 or ICD-10-CM, A31.0) dated ≥ 30 days apart ($n = 9{,}476$)
For calendar year 2008-2015, patients who received at least one claim with ICD code (031.0 or A31.0) and had full-year insurance enrollment ($n = N_1$)
Beneficiaries enrolled in calendar year 2008-2015 ($n = D_0$)
5% random sample of CDM between January 1 2007 and June 30 2016
Beneficiaries enrolled in calendar year 2008-2015 ($n = M_0$)
Beneficiaries with full-year insurance coverage ($n = M_1$)
Beneficiaries without full-year insurance coverage ($n = M_2$)
Proportion of beneficiaries with full-year insurance coverage = $\frac{M_1}{M_0}$
Prevalence = $N_1 / D_0(\frac{M_1}{M_0})$