


Trends and Sociodemographic Characteristics of Nontuberculous Mycobacterial Infections in South Korea: A Nationwide NHIS-Based Study (2010–2022)

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Jeong Mi Seo¹ , Sungchan Kang², Taeyoon Lim³, So-mi Shin¹, Jake Whang¹, Jinsoo Ko¹ and Gyeong In Lee⁴ 

¹Research & Development Center, The Korean Institute of Tuberculosis, Cheongju, ²Graduate School of Public Health, Seoul National University, Seoul, ³Yonsei University College of Medicine, Seoul, ⁴The Korean Institute of Tuberculosis, Cheongju, Republic of Korea

Abstract

Background: In South Korea, nontuberculous mycobacteria (NTM) is not a notifiable disease, while the absence of a national surveillance system hampers accurate assessment of its incidence. Therefore, this study utilized National Health Insurance Service (NHIS) claims data to investigate nationwide trends in NTM occurrence over the past decade.

Methods: We used NHIS claims (2010–2022) to assemble a cohort with International Classification of Diseases, 10th Revision A31 (A31.0, A31.1, A31.8, A31.9). For incidence, cases diagnosed in 2010–2011 were excluded. Incidence was estimated under three definitions: ≥ 2 outpatient visits or ≥ 1 inpatient admission with A31 during the study period; same as A, but with ≤ 180 days between visits; meeting B plus ≥ 1 antibiotic prescription within 180 days (treatment initiation). Age-standardized prevalence and incidence were calculated using the 2010 Korean population.

Results: A total of 178,287 newly diagnosed NTM cases were identified from 2012 to 2022 (mean age 51.4 years; 66.8 % female). The age-standardized prevalence increased from 15.5 to 69.8 per 100,000 in 2010 to 2022. Incidence peaked in 2017 (38.9/100,000), then declined to 26.9 in 2022. Age-specific incidence of NTM infection showed distinct sex-related patterns. Among men, incidence was consistently concentrated in older adults, particularly those ≥ 80 years, throughout 2012–2022. In contrast, women experienced a marked epidemiologic shift beginning in 2017, with incidence in their 20s and 30s surpassing older age groups. Medical Aid beneficiaries consistently showed higher incidence rates. By region, Daejeon and Chungnam showed the greatest increase in incidence rates in 2022, compared to 2012.

Conclusion: NTM infection is increasing in Korea, with distinct epidemiologic patterns by sex, age, and socioeconomic status. The rising burden, especially among young women and the socioeconomically disadvantaged, warrants targeted public health strategies.

Keywords: Nontuberculous Mycobacteria; Epidemiology; Prevalence; Incidence; National Health Programs; Republic of Korea

Address for correspondence Gyeong In Lee

The Korean Institute of Tuberculosis, Korean National Tuberculosis Association, 168-5 Osongsaengmyeong 4-ro, Osong-eup, Heungdeok-gu, Cheongju 28158, Republic of Korea

Phone 82-43-249-4900

Fax 80-43-249-4972

E-mail gyeonginlee@hanmail.net

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Introduction

Nontuberculous mycobacteria (NTM) are environmental opportunistic pathogens that are widely present in soil, water, and household plumbing systems¹. These organisms can cause chronic pulmonary infections in immunocompromised individuals, or those with pre-existing lung conditions². NTM pulmonary disease (NTM-PD) is typically diagnosed through a combination of clinical symptoms, radiographic abnormalities, and repeated isolation of the organism³. The disease is notoriously difficult to treat, requiring prolonged antibiotic regimens with high failure rates, and is increasingly recognized as a public health concern⁴. Globally, the prevalence of NTM-PD has doubled in recent decades in countries such as the United States and Germany^{5,6}. In South Korea, studies suggest an over 30-fold increase since 2003⁷. In East Asian countries, such as Japan, Taiwan, and South Korea, the incidence of NTM-PD is particularly prominent among distinct subpopulations, including females, the elderly, and never-smokers, underscoring the need for deeper understanding of its epidemiologic characteristics and underlying mechanisms⁸⁻¹⁰.

In South Korea, the incidence of NTM-PD has been steadily rising, prompting a surge in epidemiologic studies using national health insurance claims data and clinical research in tertiary care settings¹¹⁻¹⁸. However, unlike tuberculosis, NTM is not a notifiable infectious disease; therefore, increases in isolate counts or diagnosis code-based incidence do not necessarily reflect real-world disease occurrence. Therefore, because epidemiologic studies of NTM often employ author-specific diagnostic definitions, the prevalence and incidence estimates for the same year can differ to some extent (Supplementary Table S1). Park et al.¹⁹ cautioned that reliance solely on diagnostic codes may overestimate disease burden, underscoring the need for clinically validated case definitions that incorporate laboratory testing. Also, prior investigations were mostly cross-sectional or restricted to specific demographic groups, while nationwide trend analyses stratified by sociodemographic characteristics remain rare.

While NTM-PD shows a disproportionately high prevalence among women—particularly those in their 20s to 50s—the underlying pathophysiology remains unclear^{13,14,19-21}. Beyond biological factors, such as aging, chronic lung disease, and immunosuppression, socioeconomic determinants—including income level, geographic region, and access to healthcare—may contribute to infection risk^{11,21,22}. Nevertheless, quantitative assessments of the impact of these determinants' on

incidence are limited; in particular, few studies have evaluated temporal dynamics by household income level.

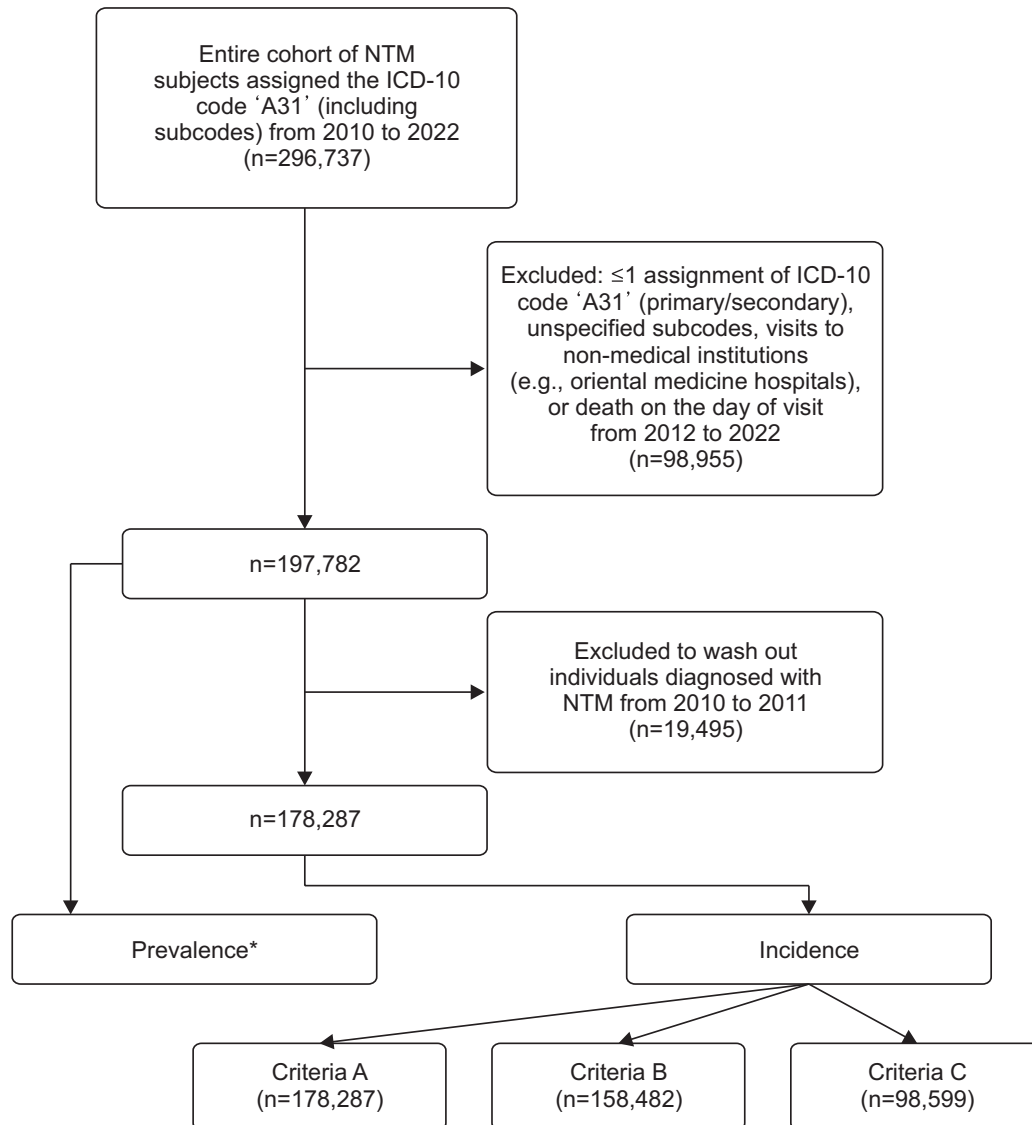
Therefore, this study analyzed 10 years of nationwide claims data from the National Health Insurance Service (NHIS) for the period 2012–2022 to examine temporal trends in the incidence and prevalence of NTM-PD in South Korea. By stratifying incidence rates according to various sociodemographic factors—including sex, age group, insurance type (employment-based policyholders, local subscribers, and Medical Aid beneficiaries), insurance premium quintile, and geographic region—we aimed to characterize spatiotemporal patterns and heterogeneity in disease burden. To our knowledge, this is the first nationally representative, longitudinal trend analysis to comprehensively capture such variation. These findings provide a foundation to identify high-risk populations and inform region- and population-specific public health strategies for NTM prevention and control.

Materials and Methods

1. Data source and study population

We utilized the NHIS database to conduct a nationwide investigation of individuals diagnosed with NTM infection in South Korea. A retrospective cohort of 296,737 individuals was established by identifying all residents who maintained health insurance eligibility between January 1, 2010, and December 31, 2022, and were diagnosed with A31 (including all subcodes) based on the International Classification of Diseases, 10th Revision (ICD-10). To ensure accurate estimation of incidence, 19,495 individuals diagnosed in 2010 or 2011 were excluded during the washout period. In addition, 98,955 individuals were excluded due to one or fewer assignments of ICD-10 code A31 as a primary or secondary diagnosis, unclear A31 subcode information, missing values for key demographic variables (including sex, age, region of residence, or insurance type), visits to non-medical institutions (e.g., traditional medicine clinics), or death on the date of diagnosis. A total of 178,287 individuals were included in the final analysis (Figure 1). This study was exempted from review by the Institutional Review Board (IRB) of the Korean National Tuberculosis Association (KNTA), in accordance with its exemption criteria (2023-KNTA-IRB-04). The requirement for informed consent was waived by the IRB owing to the retrospective design and use of de-identified data.

Figure 1. Flowchart of study. Prevalence was defined as the number of patients with a nontuberculous mycobacteria (NTM) diagnosis in each year; therefore, duplicate counts across multiple years may occur (251×372 mm; 150×150 DPI). ICD-10: International Classification of Diseases, 10th Revision.



2. Diagnosis of NTM infection

The prevalence of NTM infection was calculated as the number of patients with an NTM diagnosis in each calendar year among the total cohort of 197,782 individuals (Figure 1). Accordingly, patients with diagnoses persisting for more than 1 year may have been counted more than once across years. However, duplicate cases within the same year were removed prior to calculation. Age-standardized prevalence rates were derived using the 2010 Korean population as the standard population.

The incidence of NTM infection was defined as newly diagnosed cases each year from 2012 to 2022. The cases were identified based on the date of the initial

diagnosis; therefore, no duplicate cases occurred throughout the study period. Similar to prevalence, age-standardized incidence rates were calculated using the 2010 Korean population as the standard population. To address potential overestimation based on diagnostic codes and to assess the proportion of patients who initiated treatment, incidence was further stratified using three definitions:

- (1) Criteria A: two or more outpatient visits or one or more inpatient admissions with a principal or additional diagnosis coded as A31 over the entire study period;
- (2) Criteria B: same as Criteria A, but restricted to visits within 180 days;
- (3) Criteria C: meets Criteria B and received at least

one antibiotic prescription within 180 days of diagnosis (treatment initiation).

A total of 18 antibiotics, including macrolide-class agents, were used in the analysis, Supplementary Table S2 providing the complete list.

3. Variables

The variables analyzed included sex, age, region of residence, year of diagnosis (based on the first visit), insurance type (e.g., employment-based policyholders, local subscribers, Medical Aid), and insurance premium quintile. The NHIS database includes an insurance premium variable that stratifies the population into

20 equal-sized quantiles based on average monthly contributions. As insurance premiums are calculated based on household income, lower premium quantiles generally indicate lower income levels. For this study, Medical Aid recipients (who do not pay premiums) were designated as quantile 0. The remaining 20 quantiles for National Health Insurance (employment-based and self-employed) subscribers, were grouped into five broader income categories: quantiles 1–4, 5–8, 9–12, 13–16, and 17–20.

4. Statistical analysis

For continuous variables, such as age, annual means

Table 1. Baseline characteristics of subjects with nontuberculous mycobacteria infection

Characteristic	Total	Male	Female	p-value
Number	178,287 (100.0)	59,128 (33.2)	119,159 (66.8)	
Mean age, yr	51.4±21.4	56.2±23.1	49.0±20.1	<0.001
Age group, yr				
0–9	8,352 (4.7)	4,389 (7.4)	3,963 (3.3)	<0.001
10–19	4,024 (2.3)	1,673 (2.8)	2,351 (2.0)	
20–29	19,278 (10.8)	2,554 (4.3)	16,724 (14.0)	
30–39	22,623 (12.7)	4,632 (7.8)	17,991 (15.1)	
40–49	22,487 (12.6)	5,179 (8.8)	17,308 (14.5)	
50–59	29,535 (16.6)	7,953 (13.5)	21,582 (18.1)	
60–69	30,346 (17.0)	11,942 (20.2)	18,404 (15.4)	
70–79	27,268 (15.3)	13,801 (23.3)	13,467 (11.3)	
≥80	14,374 (8.1)	7,005 (11.8)	7,369 (6.2)	
Insurance type				
Employment-based policyholders	120,626 (67.7)	40,040 (67.7)	80,586 (67.6)	<0.001
Local subscribers	49,813 (27.9)	16,024 (27.1)	33,789 (28.4)	
Medical Aid	7,848 (4.4)	3,064 (5.2)	4,784 (4.0)	
Year				
2012	7,505 (4.2)	3,098 (5.2)	4,407 (3.7)	<0.001
2013	9,805 (5.5)	3,991 (6.7)	5,814 (4.9)	
2014	10,544 (5.9)	4,287 (7.3)	6,257 (5.3)	
2015	15,392 (8.6)	5,845 (9.9)	9,547 (8.0)	
2016	21,214 (11.9)	7,269 (12.3)	13,945 (11.7)	
2017	21,525 (12.1)	6,520 (11.0)	15,005 (12.6)	
2018	19,292 (10.8)	6,064 (10.3)	13,228 (11.1)	
2019	20,799 (11.7)	6,326 (10.7)	14,473 (12.1)	
2020	18,025 (10.1)	5,267 (8.9)	12,758 (10.7)	
2021	18,128 (10.2)	5,578 (9.4)	12,550 (10.5)	
2022	16,058 (9.0)	4,883 (8.3)	11,175 (9.4)	

Values are presented as number (%) or mean±standard deviation. Demographic distribution by age, sex, and type of health insurance coverage among a total of 178,287 patients.

were compared using the nonparametric Kruskal–Wallis test. For categorical variables—including sex, region of residence, comorbidities, insurance type, and insurance premium quintile—annual frequency distributions were assessed using the chi-square test. All statistical analyses were performed using SAS Enterprise Guide version 8.4 (SAS Institute, Cary, NC, USA).

Results

1. Baseline characteristics of participants

From January 2012 to December 2022, a total of 178,287 individuals were newly diagnosed with NTM infection, with a mean age of 51.4 years. Of these, 59,128 (33.2%) were male and 119,159 (66.8%) were female, indicating that the proportion of women was more than twice that of men. Among males, 55.4% were aged 60 years or older, whereas among females, 61.8% were between 20 and 59 years of age, reflecting

Figure 2. Age-standard (A) prevalence and (B) incidence rates of nontuberculous mycobacteria (NTM) disease in South Korea, 2010 to 2022. Annual age-standardized prevalence and incidence rates of NTM infection in South Korea from 2010 to 2022. Prevalence includes all individuals with ≥ 2 outpatient visits or ≥ 1 inpatient visit with International Classification of Diseases, 10th Revision (ICD-10) code A31 within a given year. Incidence was defined using the same criteria, with newly diagnosed cases only. Standardization was performed using the 2010 Korean mid-year population as reference (343×443 mm; 150×150 DPI).

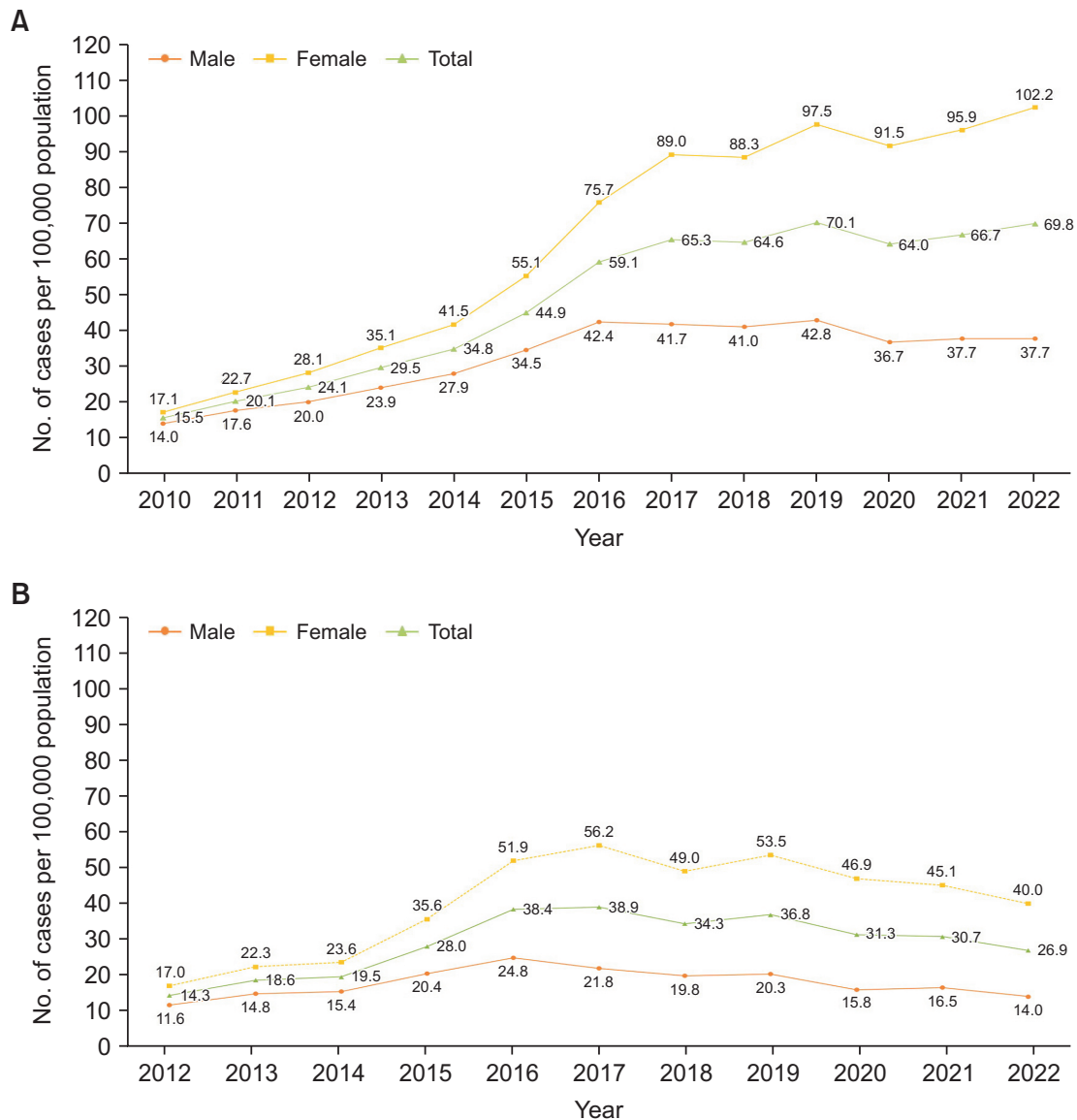
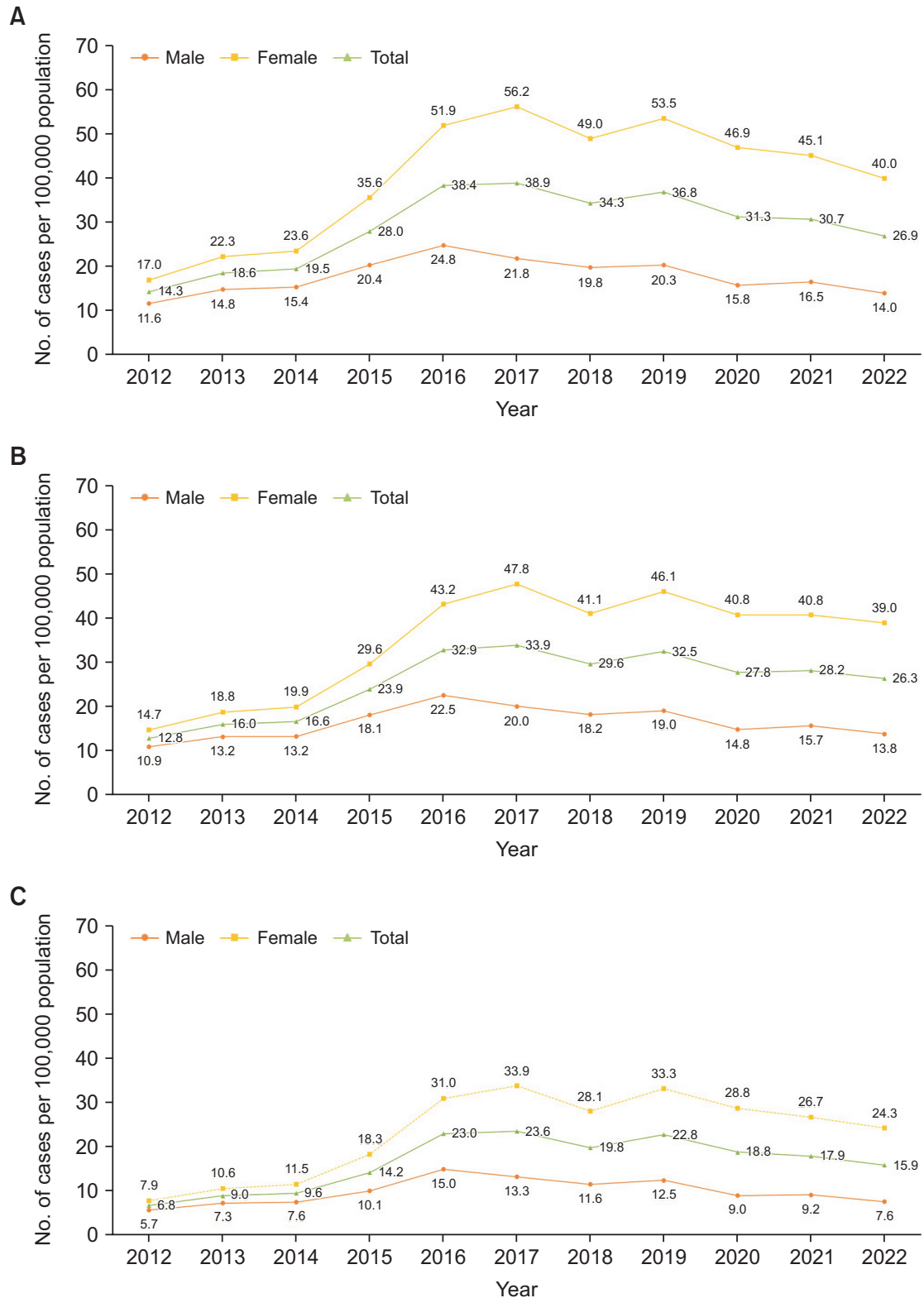


Figure 3. Age-standard incidence rate according to nontuberculous mycobacteria (NTM) diagnostic definition. Annual age-standardized incidence rates of NTM infection calculated using three diagnostic definitions: (A) Criteria A (≥ 2 outpatient visits or ≥ 1 inpatient visit at any time), (B) Criteria B (same as A, but within 180 days), and (C) Criteria C (meeting criterion B with ≥ 1 NTM-related antibiotic prescription). Criteria C resulted in significantly lower incidence estimates than A or B, especially highlighting differences in diagnostic stringency and potential overestimation with broader definitions (338 \times 455 mm;150 \times 150 DPI).

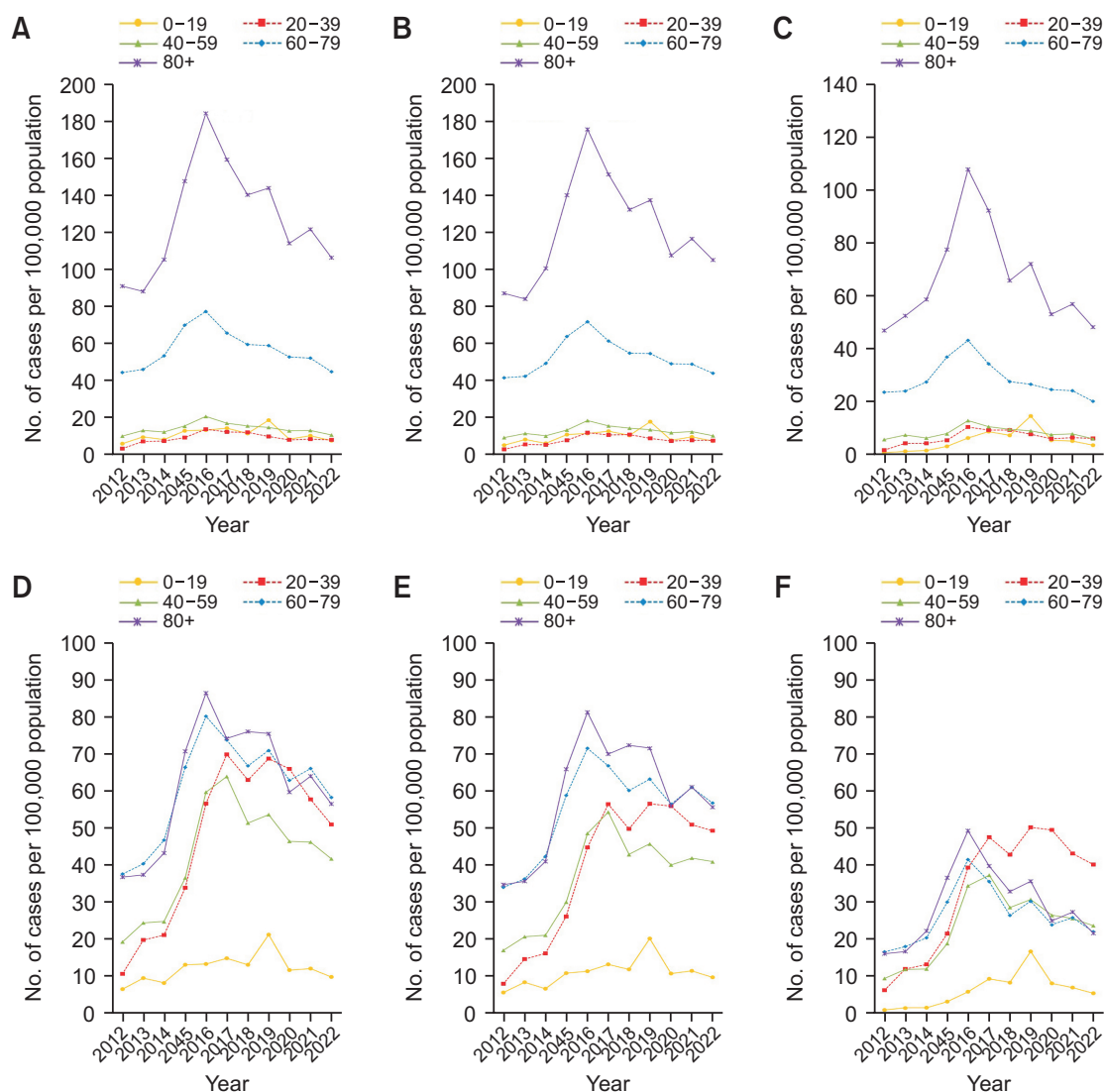


a younger age distribution in women. Notably, female cases were evenly distributed across age groups: 20s (14.0%), 30s (15.1%), 40s (14.5%), and 50s (18.1%), suggesting a tendency for earlier diagnosis in women. Regarding insurance type, 67.7% were enrolled through employment-based policyholders, 27.9% through local subscribers, and 4.4% were Medical Aid beneficiaries. The annual number of newly diagnosed cases increased from 7,505 in 2012, peaked at 21,525 in 2017, then gradually declined to 16,058 in 2022 (Table 1).

2. Prevalence rates by year

Prevalence rates of NTM infection increased significantly in both men and women over the study period. The crude prevalence in men rose from 14.0 to 57.7 per 100,000 in 2010 to 2022, representing a 4.1-fold increase, while in women, it rose from 17.1 to 124.3 per 100,000 during the same period—a 7.3-fold increase (Supplementary Table S3). Age-standardized prevalence also increased 2.7-fold in men—and approximately 6-fold in women—compared to 2010 levels (Figure 2A, Supplementary Table S3). Notably, female prevalence accelerated sharply after 2016, whereas the increase among men was more gradual.

Figure 4. Age-specific incidence rates by nontuberculous mycobacteria (NTM) diagnostic definitions. Age-specific incidence rates of NTM infection for (A, B, C) men and (D, E, F) women, shown by diagnostic definition. In men, the highest incidence was consistently observed in those aged ≥ 80 years. In women, a marked shift was observed with incidence sharply increasing among those aged 20–30 years after 2017, particularly under Criteria C, indicating a rise in actual treatment initiation among younger female patients (338 \times 454 mm; 150 \times 150 DPI).



These findings suggest that NTM infection trends likely reflect a rise in disease burden over time, with clear sex- and age-specific epidemiologic differences—particularly in the disproportionately high prevalence and earlier onset in women.

3. Incidence rates by year and case definition

In men, the crude incidence increased from 12.3 per 100,000 in 2012 to a peak of 28.5 in 2016, then declined to 19.1 in 2022. Among women, it rose from 17.5 in 2012 to a peak of 58.5 in 2017, followed by a decrease to 43.5 in 2022 (Supplementary Table S4). Age-standardized incidence reached its peak in 2016 for men and in 2017 for women, subsequently declining in both groups. However, the overall magnitude of increase over the decade was more pronounced in women (Figure 2B, Supplementary Table S4).

While age-standardized incidence trends were broadly similar across all three criteria—showing a rise followed by a decline—the absolute rates varied substantially, depending on the case definition. Incidence estimates under Criteria C were on average 1.7 to 2.1 times lower than those based on Criteria A, illustrating how case definitions can dramatically influence the estimated scale of NTM infection (Figure 3). Nevertheless, the consistent overall upward trend across all definitions likely represents an increase in clinical disease

burden over time.

4. Crude incidence rates by sex and age

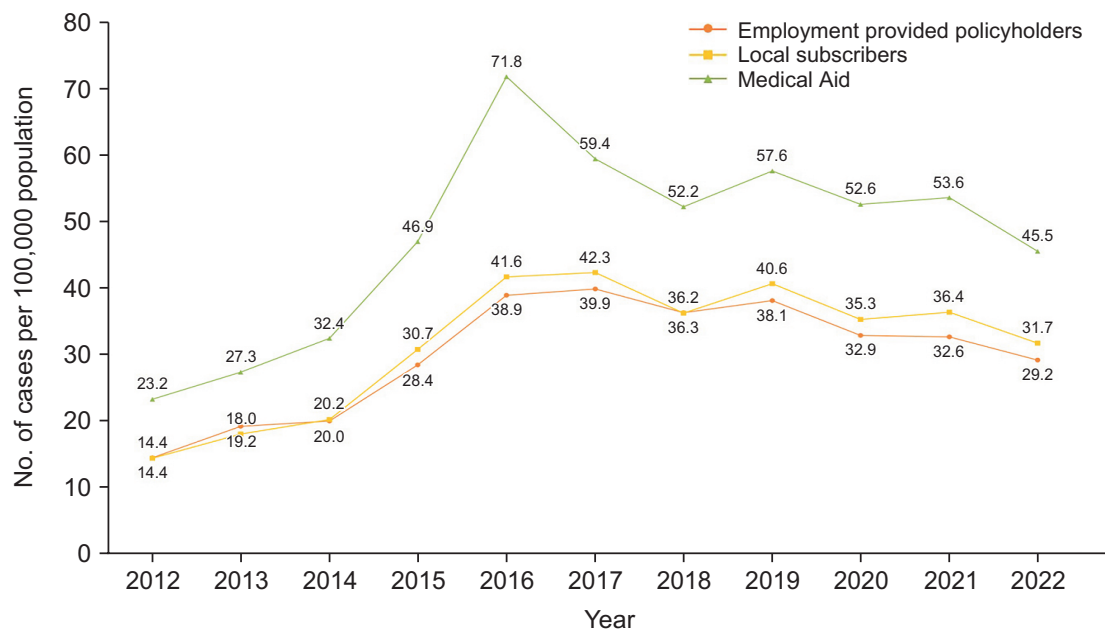
Age-specific incidence patterns of NTM infection differed markedly by sex, and were consistently observed across all diagnostic criteria (Criteria A, B, and C), and study years (Figure 4).

Among men, the highest incidence was consistently observed in the ≥ 80 age group throughout the study period (2012–2022), followed by those aged 60–69. For example, in 2016, the crude incidence in men aged ≥ 80 reached 184.2 per 100,000 under Criteria A—more than double the rate among women of the same age group (86.3 per 100,000). This finding reaffirms that NTM infection in men is predominantly concentrated in older age groups.

In contrast, women initially showed a similar age distribution skewed toward older adults, until a dramatic shift occurred beginning in 2017. Incidence rates among women in their 20s and 30s sharply increased, surpassing those of women in their 40s and 50s, and this pattern persisted through 2022. Rather than a transient fluctuation, this trend appears to represent a sustained epidemiologic transition.

For children under the age of 10, incidence remained low in both sexes throughout the study period, except for a modest temporary increase observed in 2019.

Figure 5. Crude incidence rate of nontuberculous mycobacteria (NTM) infection by type of insurance coverage. Crude incidence rates of NTM infection by health insurance coverage type (employment-based policyholders, local subscribers, Medical Aid). Medical Aid recipients consistently showed the highest incidence throughout the study period, reflecting higher disease burden among economically disadvantaged and medically vulnerable populations (338×243 mm; 150×150 DPI).



5. Crude incidence rates by socioeconomic status (insurance type and insurance premium quintile)

When examining crude incidence rates of NTM infection by insurance type, both employment-based policyholders and local subscribers had identical rates of 14.4 per 100,000 in 2012. By 2022, these rates had increased modestly to 29.2 and 31.7 per 100,000, respectively, maintaining similar levels between the two groups.

In contrast, Medical Aid recipients—who are presumed to represent the lowest income group—showed a markedly higher incidence, rising from 23.2 to 45.5 per 100,000 in 2012 to 2022, a steeper increase than that observed in other insurance types (Figure 5, Supplementary Table S5). Across all three insurance types, women consistently exhibited higher incidence rates than men (Supplemental Figure S1).

Analysis of NTM incidence across these categories revealed that Medical Aid recipients showed the highest incidence rates (Figure 6), suggesting that economically disadvantaged populations are disproportionately affected by NTM infection.

6. Crude incidence rates by region

Incidence rates of NTM infection increased significantly from 2012 to 2022 across most regions in South Korea (Table 2, Figure 7). Notably, Daegu, Daejeon, Chun-

nam, and Jeju experienced more than a three-fold increase during this period, with Chungnam recording the highest rate in 2022 at 55.7 per 100,000.

However, regional trends in incidence extended beyond a simple upward trajectory, displaying heterogeneous temporal and sex-specific patterns (Figure 8). In Seoul and Gyeonggi Province, incidence rates rose steadily after 2014; however, while Seoul has shown a recent decline, Gyeonggi has maintained elevated rates since 2017. Daejeon and Sejong experienced sharp spikes in 2016 and 2019, respectively, with Daejeon exhibiting the most pronounced sex disparity in incidence across the entire study period.

In Chungnam, a rapid increase was observed among women beginning in 2019, and Busan experienced a steep rise between 2016 and 2017, also predominantly among women. Daegu and Incheon showed steady increases with minimal sex differences, while Gyeongbuk demonstrated a nonlinear pattern—an initial surge in 2013, followed by a transient decline and subsequent rebound. Jeju displayed the highest level of volatility, with alternating surges and drops after 2020.

In contrast, regions such as Gwangju, Ulsan, Gangwon, Chungbuk, Jeonbuk, Jeonnam, and Gyeongnam exhibited relatively modest and stable increases, without abrupt changes in specific years. These findings suggest that the observed regional variability in magni-

Figure 6. Crude incidence rate of nontuberculous mycobacteria (NTM) infection by insurance premium quintile. Crude incidence rates across five health insurance premium quintiles. The 0th quintile represents Medical Aid recipients. A clear inverse relationship was observed between income level and NTM incidence, suggesting socioeconomic disparities in NTM burden (338×256 mm; 150×150 DPI).

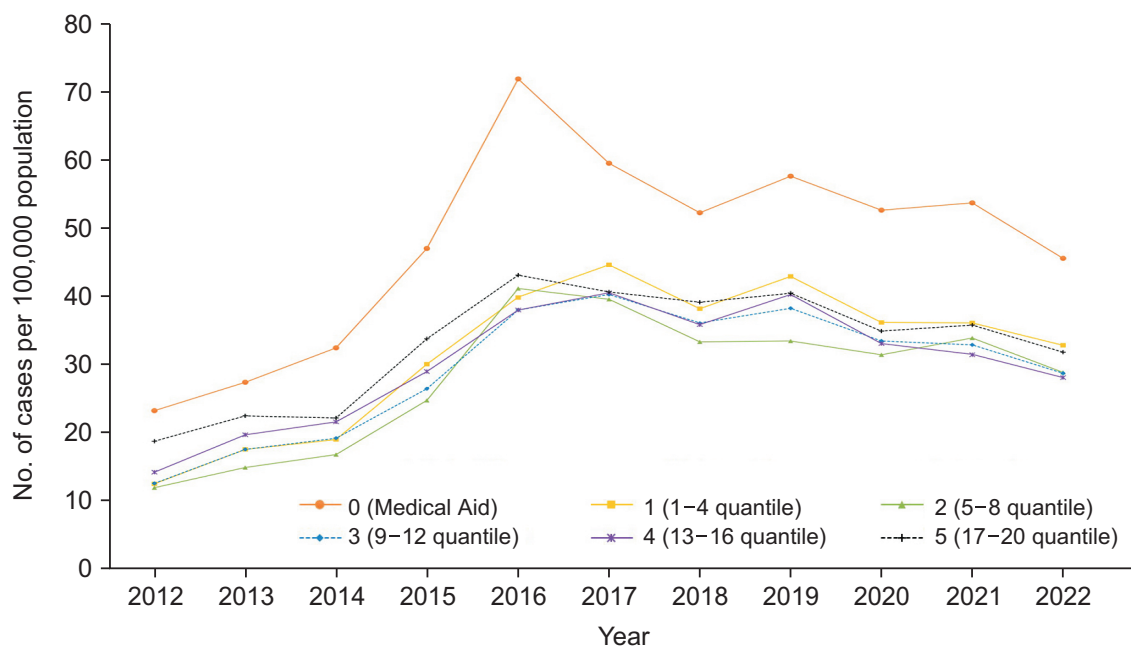


Table 2. Crude incidence rate of nontuberculous mycobacteria infection by region

District	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Seoul	17.2	20.0	20.7	45.1	56.0	53.1	45.4	40.5	35.7	33.4	29.3
Busan	12.8	12.8	11.6	16.7	57.0	46.5	26.0	23.7	19.3	17.5	15.9
Daegu	9.5	13.2	13.8	16.3	23.7	37.6	39.5	58.9	41.7	44.2	35.0
Incheon	11.1	13.7	15.4	17.4	29.6	39.5	23.9	28.8	28.5	25.0	19.9
Gwangju	13.4	15.2	13.2	18.2	19.1	22.6	20.0	20.1	21.3	26.3	24.9
Daejeon	12.8	18.1	31.3	62.3	94.5	63.2	51.6	102.7	47.4	57.3	45.5
Ulsan	5.9	9.0	7.5	10.8	16.3	18.2	16.4	22.4	18.0	17.2	15.8
Sejong	0.0	13.7	15.2	38.9	60.2	38.4	48.0	72.0	33.4	25.3	18.8
Gyeonggi-do	18.4	18.7	17.2	28.5	38.6	42.0	37.6	37.7	36.7	39.1	37.9
Gangwon-do	11.9	14.2	19.3	34.6	30.5	27.8	28.4	30.0	26.4	23.5	25.4
Chungcheongbuk-do	11.0	10.3	14.7	19.3	25.6	23.1	22.1	22.8	19.4	25.1	19.7
Chungcheongnam-do	11.7	14.3	25.8	29.5	49.5	63.1	85.2	101.3	83.7	76.1	55.7
Jeollabuk-do	20.8	14.9	22.1	28.0	39.6	41.5	37.7	35.0	28.7	40.0	40.1
Jeollanam-do	15.6	15.4	18.8	24.4	22.9	25.1	29.2	29.0	28.1	30.6	29.8
Gyeongsangbuk-do	19.8	75.9	76.3	53.1	61.1	62.0	57.4	59.0	44.2	43.1	39.7
Gyeongsangnam-do	8.4	11.6	13.2	15.8	18.6	18.4	19.2	20.5	20.9	21.0	17.8
Jeju-do (island)	9.9	20.0	18.6	22.9	17.4	21.4	21.2	36.0	87.8	60.4	35.3

Crude incidence rate was calculated as cases per 100,000 people.

Figure 7. Crude incidence rate of nontuberculous mycobacteria (NTM) infection by region between 2012 and 2022. Crude incidence rates of NTM infection by region in 2012 and 2022. Most regions exhibited more than a three-fold increase in incidence, with particularly steep rises in Daejeon, Chungnam, and Jeju. These results suggest regional variation in NTM epidemiology over time (338×256 mm; 150×150 DPI).

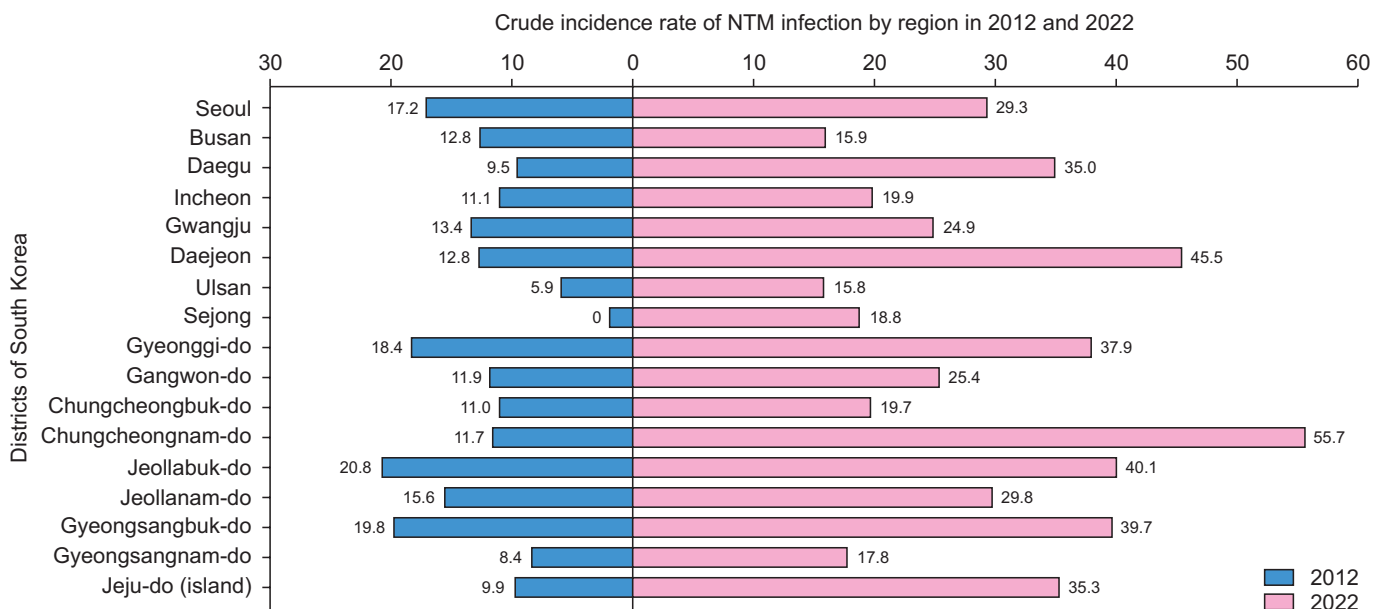
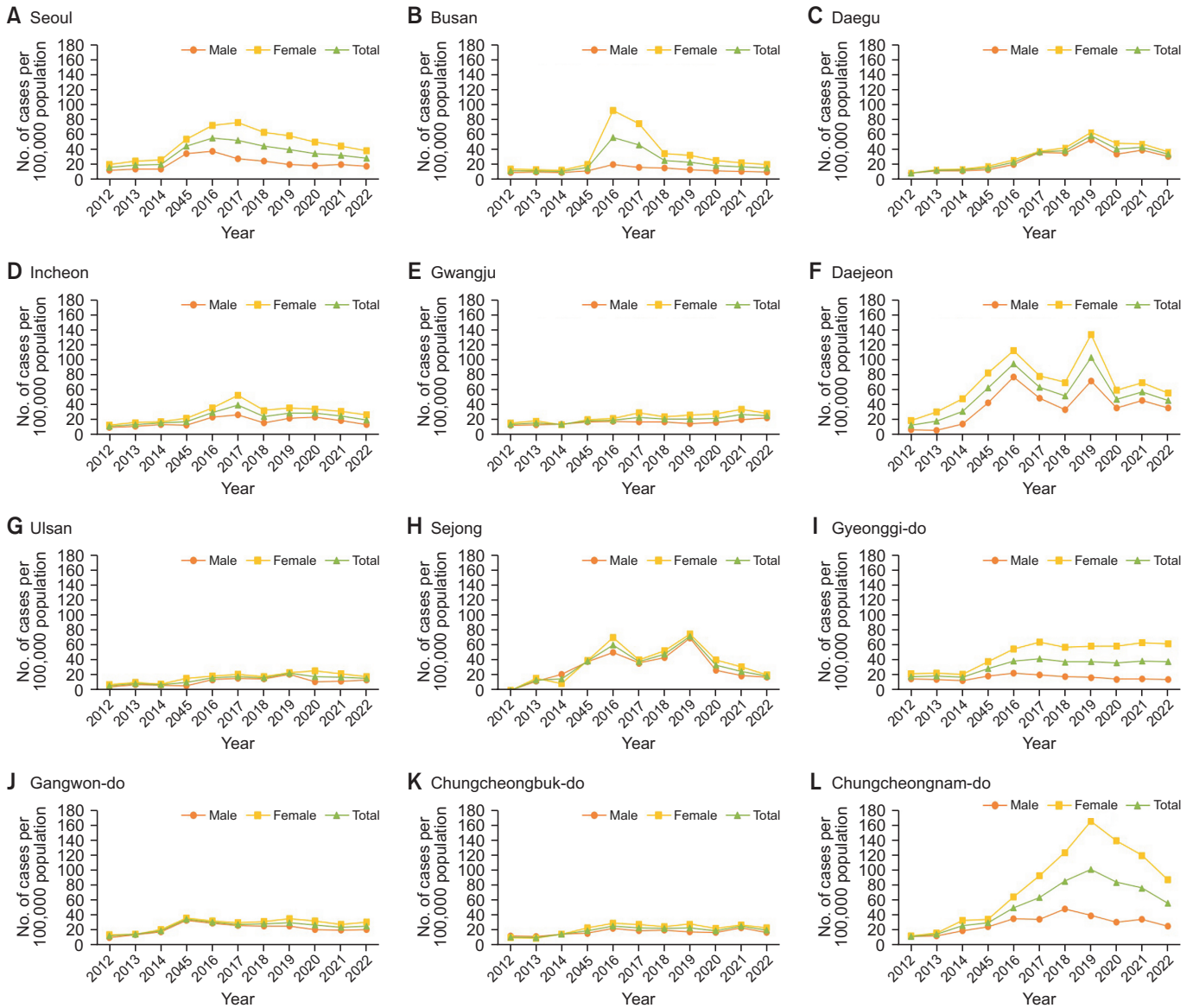


Figure 8. Crude incidence rate of nontuberculous mycobacteria (NTM) infection by region in South Korea. (A-Q) Yearly trends in crude incidence rates of NTM infection from 2012 to 2022, stratified by sex across 17 administrative regions. Distinct regional patterns were observed, including sharp increases in both male and female incidence in Daejeon (2016 and 2019) and Jeju (2020). Some regions such as Seoul showed a recent plateau or decline, while others like Gyeonggi maintained high rates post-2017. Chungcheongnam-do was the region with the largest difference in incidence rates between men and women. These trends may reflect local health policy interventions, screening programs, or diagnostic behavior shifts (338×376 mm; 150×150 DPI).



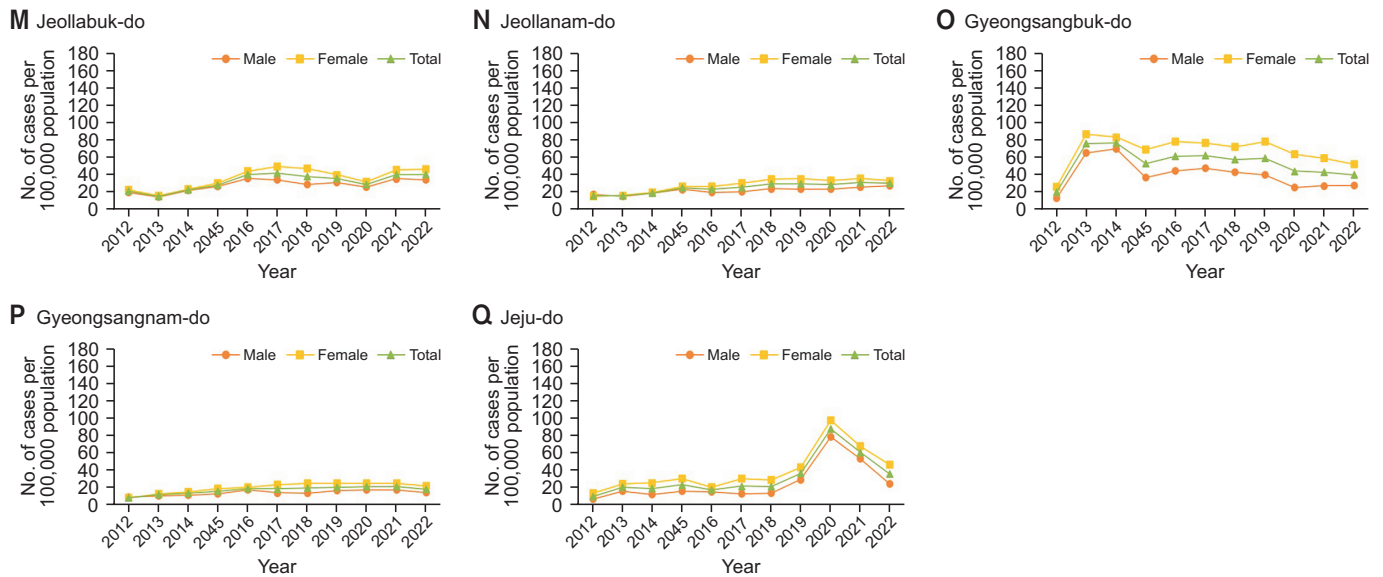
tude, timing, and sex distribution of incidence cannot be attributed solely to background prevalence, but may reflect region-specific factors.

Discussion

This study quantitatively analyzed annual trend changes and sociodemographic patterns of NTM infection in South Korea using complete population-level claims

data from the NHIS between 2012 and 2022. The age-standardized prevalence increased approximately 4.5-fold, from 15.5 to 69.8 per 100,000 in 2010 to 2022 (Supplementary Table S3). Incidence peaked at 39.0 per 100,000 in 2017, rising from 14.3 in 2012, before declining to 26.9 in 2022 (Supplementary Table S4). Given that NTM infection is a chronic condition characterized by frequent recurrence and reinfection^{3,23,24}, the observed rise in prevalence likely reflects expanded

Figure 8. Continued.



diagnostic activity, as well as an underlying increase in the number of patients requiring clinical treatment.

Analysis of age- and sex-specific incidence revealed distinct structural differences. Among men, the highest incidence was consistently observed throughout the study period in those aged ≥ 80 years, with rates progressively declining in younger age groups. In contrast, beginning in 2017, women exhibited a sharp increase in incidence among those in their 20s and 30s, effectively reversing the previously observed pattern centered on older age groups. This trend persisted even under the most conservative diagnostic definition (Criteria C). Notably, even when restricting the analysis to patients who initiated treatment (as defined under Criteria C), women in their 20s and 30s exhibited the highest incidence across all age groups, suggesting an underlying increase in clinically significant disease burden.

Most infectious diseases are influenced by host susceptibility, which is shaped both by immune status, age, and nutritional state, and by sex. In the context of NTM infection, the nodular bronchiectatic form has traditionally been observed more frequently in postmenopausal women, suggesting a possible protective role of female sex hormones—a phenomenon often referred to as ‘Lady Windermere syndrome’²⁵. However, the sharp increase in incidence among women in their 20s and 30s observed in this study cannot be fully explained by existing theories, indicating that alternative pathophysiologic mechanisms or sociobehavioral factors may be contributing to this emerging trend.

Indeed, recent studies in South Korea have reported a higher incidence of NTM infection among women who received hormone replacement therapy²⁶. Immunological research has also suggested that the expression patterns of pro-inflammatory and anti-inflammatory cytokines may differ depending on estrogen levels²⁷. Although the precise mechanisms remain unclear, it is plausible that specific immunoregulatory environments or hormonal rhythms in premenopausal women may influence susceptibility to infection. These findings underscore the need for future immuno-epidemiologic studies to elucidate the underlying pathways.

Socioeconomic factors were also found to have a significant impact on the incidence of NTM infection. Medical Aid recipients exhibited the highest incidence rates, aligning with previous findings that individuals in this group may have increased vulnerability to infection due to their age structure and nutritional status^{28,29}. Analysis by insurance premium quintile—used as a proxy for income level—also revealed an inverse relationship, with lower-income groups showing higher incidence. These findings suggest that NTM infection is closely linked to socioeconomic vulnerability.

Regional analysis revealed increased incidence in most areas, but with heterogeneous patterns in terms of timing, sex differences, and magnitude of change. For example, Daejeon, Chungnam, and Jeju experienced sharp spikes in incidence primarily among women during specific years, coinciding with intensified tuberculosis screening initiatives targeting high-risk groups³⁰. These include the 2016 amendment of the

Tuberculosis Prevention Act³¹, the implementation of mandatory tuberculosis certification for visa issuance to foreign nationals from high-risk countries³², and the launch of mobile screening programs for older adults in 2019³³. Such interventions likely contributed to increased testing volume and diagnostic yield. These findings illustrate that beyond environmental factors, policy-level interventions and shifts in clinical practice can have substantial impacts on reported NTM incidence.

These findings suggest that NTM infection is a complex disease that emerges at the intersection of multiple factors—including pathophysiology, diagnostic systems, social structures, and policy interventions. Future research should aim to establish a more sophisticated disease surveillance framework by incorporating sex- and age-specific susceptibility analyses, integrating standardized diagnostic definitions with laboratory data, and addressing regional disparities in diagnostic accessibility.

This study holds significant value, as it analyzed the spatiotemporal patterns of NTM infection across the entire South Korean population, and provided quantitative evidence to address ongoing debates. By comprehensively examining the emergence of NTM among women in their 20s and 30s, the concentration of cases among socioeconomically vulnerable groups, and the temporal alignment between policy interventions and diagnostic rate changes, this study offers practical foundational data to inform future public health strategies focused on high-risk populations and early intervention policies. So far as we are aware, this is the first study to conduct a multilayered analysis of regional NTM incidence trends over the past decade in Korea.

Nevertheless, this study has several limitations. First, the NHIS claims database does not include clinical information, such as chest imaging findings or microbiological culture results, which are required by the diagnostic criteria of the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA). As such, diagnoses based solely on ICD-10 codes may not fully correspond to clinically confirmed NTM cases. In addition, due to the study design, which excluded individuals with fewer than two outpatient visits, some true cases—such as patients who received only a single diagnosis and were under follow-up—may have been omitted from the analysis. Second, this study compared incidence estimates based on Criteria A and B. While both showed similar trends for most of the study period, a discrepancy emerged during the last 3 years (2020–2022), with a decline observed only under Criteria A. This difference likely stems from

the definitions themselves: Criteria A is based on ‘≥2 outpatient visits during the entire study period,’ whereas Criteria B requires ‘≥2 outpatient visits within 180 days.’ For newly diagnosed individuals at the end of the observation period, a second visit may not have occurred yet, or may not have been captured at the time of analysis, leading to an artificial decline in incidence under Criteria A. This phenomenon can be interpreted as a temporary underestimation due to the observation window limitation. In addition, because NTM infection was defined solely based on diagnostic codes without incorporating acid-fast bacilli smear or mycobacterial culture results, the analysis may not fully capture patients who met clinical diagnostic criteria. Third, in the analyses stratified by insurance type, premium quintile, and geographic region, age-standardized incidence rates could not be calculated due to the unavailability of age-disaggregated mid-year population statistics from the national census at the corresponding subgroup levels. This limitation may restrict the interpretability of findings across these stratified variables.

In summary, the incidence of NTM infection in Korea was higher among women than men, increased with age, and was particularly elevated among Medical Aid recipients. Notably, unlike in men, the incidence among younger women has been rising, highlighting the need for careful investigation and ongoing surveillance to determine whether this reflects a true increase in clinical cases, or a potential overestimation related to diagnostic practices. Furthermore, given the heterogeneous temporal patterns of incidence increases across administrative regions, ongoing monitoring of region-specific environmental conditions, climatic changes, demographic shifts, and NTM species distribution will be essential.

Authors' Contributions

Conceptualization: Whang J, Ko J, Lee GI. Methodology: Seo JM, Whang J, Lee GI. Formal analysis: Whang J. Data curation: Kang S, Lim T, Shin S. Funding acquisition: Lee GI. Writing - original draft preparation: Seo JM, Whang J. Writing - review and editing: all authors. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Material

Supplementary material can be found in the journal homepage (<http://www.e-trd.org>).

Supplementary Table S1. Summary of study characteristics and NTM case definitions in included epidemiological studies from South Korea.

Supplementary Table S2. Types of antibiotics considered in the analysis.

Supplementary Table S3. Crude and age-standardized prevalence rates of nontuberculous mycobacteria infection from 2010 to 2022.

Supplementary Table S4. Crude and age-standardized incidence rates of nontuberculous mycobacteria infection from 2010 to 2022.

Supplementary Table S5. Crude incidence rates of nontuberculous mycobacteria infection by insurance type.

Supplementary Figure S1. Sex-specific incidence rates by type of health insurance coverage from 2012 to 2022.

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