BMC Infectious Diseases

RESEARCH

Open Access

Smoking history is not independently associated with broad-spectrum antibiotic use in two nationally representative cohorts of adult men in South Korea

Da Seul Park[1†], Shin Hye Yoo[2,3†], Minkyeong Lee[4], Jiyeon Bae[4], Seung Soon Lee[5], Jeong-Han Kim[4,8*†], Jin-Ah Sim[1,6,7,9*†] and Hee Jung Choi[4]

Abstract

Background Smoking is linked to an increased risk of infectious diseases, underscoring the importance of smoking prevention and cessation in improving public health. However, using smoking history as a surrogate marker of infection severity may have unintended consequences, potentially prompting clinicians to prescribe broad-spectrum antibiotics more readily for patients with a history of smoking. This study evaluated whether smoking history was independently associated with the increased prescription of broad-spectrum antibiotics to adult men in the general population of South Korea.

Methods We analyzed data from two nationally representative cohorts of Korean adult men enrolled in the National Health Insurance Service (NHIS): the National Sample Cohort (NSC) and the Health Screening Cohort (HEALS). Smoking status was classified using data from self-reported questionnaires collected from 2009 to 2013. Participants were followed from 2013 to 2021 to assess broad-spectrum antibiotic use. The primary outcome was the receipt of at least one prescription of antipseudomonal penicillins, antipseudomonal cephalosporins, carbapenems, or glycopeptides for at least 3 consecutive days. We used a composite outcome to assess the use of antibiotics targeting resistant Gram-negative organisms. After accounting for confounders, the association between smoking status and antibiotic use was evaluated using multivariable regression models.

Results The NHIS–NSC cohort included 50,134 adult men (17,300 never-smokers and 32,834 smokers), and the NHIS–HEALS cohort included 42,979 adult men (20,145 never-smokers and 22,834 smokers). In both cohorts, the rate of prescription of broad-spectrum antibiotics was low. For the composite outcome, the adjusted incidence rate ratios (IRR) for smokers compared to never-smokers were 1.55 (95% confidence interval [CI] = 0.67–3.52) in NHIS–NSC and

[†]Da Seul Park and Shin Hye Yoo contributed equally as first authors.

[†]Jeong-Han Kim and Jin-Ah Sim contributed equally to this work.

*Correspondence:
Jeong-Han Kim
wjdgks0525@gmail.com
Jin-Ah Sim
jin-ah.sim@hallym.ac.kr

Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

0.59 (95% CI = 0.24–1.46) in NHIS–HEALS. Smoking history was not significantly associated with the use of different antibiotic subclasses in these cohorts. For glycopeptides, the adjusted IRRs were 1.07 (95% CI = 0.23–5.10) in NHIS–NSC and 3.47 (95% CI = 0.70–17.13) in NHIS–HEALS, and neither association was statistically significant.

Conclusion In these two cohorts, the prescription rates of broad-spectrum antibiotics were low, and we did not observe evidence of an independent association between smoking history and their use. These findings suggest that smoking history alone should not be regarded as sufficient justification for prescribing broad-spectrum agents and emphasize the importance of basing prescribing decisions on comprehensive clinical assessment.

Keywords Smoking, Infection, Broad-spectrum antibiotics

Introduction

Cigarette smoking is a significant threat to public health, contributing to a substantial burden of preventable diseases and premature deaths worldwide [1, 2]. Smoking is being increasingly recognized as a risk factor for infectious diseases, particularly respiratory infections, with increased rates of infection even among healthy adult populations [3, 4]. Beyond its association with infection risk, several studies have examined the relationship between smoking habits and the prescription of antibiotics, and some smoking patterns suggest a dose–response relationship [5, 6]. However, whether smoking history increases the clinical need for broad-spectrum antibiotics in the general adult population is unknown.

The overuse of broad-spectrum antibiotics remains a global concern, contributing to antimicrobial resistance and increased healthcare costs [7]. While broad-spectrum antibiotics are often prescribed based on clinical indications such as suspected infections with resistant microorganisms, antibiotic use may also be influenced by non-clinical factors, including diagnostic uncertainty, perceived patient risk, institutional norms, and clinician behavior [8–10]. In this context, the growing emphasis on smoking as a risk factor for infectious diseases and sepsis, while appropriate and important from a public health perspective, may carry unintended consequences by influencing antibiotic prescribing patterns in ways that are not always clinically justified [11–13]. Smoking history may lead clinicians to overestimate infection severity in patients with infectious diseases [14], or may also prompt healthcare providers to overemphasize the significance of fever or elevated inflammatory markers in patients hospitalized for non-infectious conditions, potentially resulting in the unnecessary use of broad-spectrum agents in patients without clear infectious indications [5].

These concerns underscore the need to investigate whether smoking status independently predicts exposure to broad-spectrum antibiotics, particularly those targeting extended-spectrum β-lactamase (ESBL) producing *Enterobacterales*, *Pseudomonas aeruginosa*, or methicillin-resistant *Staphylococcus aureus* (MRSA), in populations for whom the effect of comorbid conditions is minimal. In this study, we examined this association using two nationally representative cohorts of South Korean adults. In South Korea, the prevalence of smoking is markedly higher among men than women, with 2021 national survey data indicating rates of 31.3% and 6.9%, respectively [15], and the epidemiology of certain infections, such as urinary tract infections, differs substantially by sex [16]. These pronounced sex-based differences in smoking behavior and infection risk informed our decision to restrict the study population to men, allowing a more accurate assessment of the association between smoking and broad-spectrum antibiotic use.

Methods

Study population

This nationwide, population-based retrospective cohort study analyzed data from the National Health Insurance Service (NHIS) of South Korea. Operated under a government-managed single-payer model, the NHIS provides compulsory health insurance coverage to nearly 100% of the Korean population. Its database comprehensively captures data—demographic characteristics, diagnostic codes based on the International Classification of Diseases, 10th Revision, prescription records, and mortality data—for reimbursed healthcare services. In South Korea, antibiotics are strictly prescription-based, and all antibiotic use is systematically recorded in the national claims database.

We used two nationally representative cohorts of Korean adult men enrolled in the NHIS: the National Sample Cohort (NSC) and the Health Screening Cohort (HEALS). The NHIS–NSC was constructed using a 2.2% stratified random sample of the eligible Korean population aged 18 years or older and is designed to represent approximately 5% of the national population over time [17]. The NHIS–HEALS comprises a 10% sample of adults aged 40–79 years who underwent national health screening examinations, representing individuals engaged in routine preventive care [18]. Both cohorts contain longitudinal data on sociodemographic characteristics, medical procedures, prescriptions, and health screening results. The design differences show distinct

distributions of age, comorbidities, healthcare-seeking behaviors, and baseline antibiotic use.

Therefore, we selected these two cohorts because both include validated information on smoking status, derived from standardized health screening questionnaires, enabling consistent exposure assessment across two distinct but complementary populations. Given their distinct sampling frames and age structures, we analyzed each cohort separately to minimize heterogeneity and to assess reproducibility across cohorts. Although some individuals may be represented in both cohorts, we treated these groups as independent populations and conducted all analyses separately within each cohort.

Outcome

The primary outcome was the incidence of broad-spectrum antibiotic prescriptions from 2013 to 2021. Broad-spectrum antibiotics were defined based on the World Health Organization classification and established clinical guidelines [19] and included four major classes: antipseudomonal penicillins, antipseudomonal cephalosporins, carbapenems, and glycopeptides (Supplementary Table 1). To address the limitation that detailed microbiological data and clinical indications were not available in this retrospective claims-based study, and to minimize the influence of transient use, only prescriptions lasting three or more consecutive days were considered as the outcome measure.

To account for the sequential use of multiple antibiotic classes with overlapping Gram-negative coverage, a composite outcome was defined as any instance in which antipseudomonal penicillins, cephalosporins, or carbapenems were prescribed continuously for at least 3 days, including escalation or de-escalation among these classes during the same treatment episode. Glycopeptides were analyzed separately, given their distinct spectrum of activity targeting gram-positive organisms.

Eligibility criteria

Smoking status was determined using self-reported questionnaires from national health screenings, with 2009 serving as the primary reference point for exposure classification. Because follow-up for antibiotic use began in 2013, smoking status was defined to reflect consistent exposure at the index time point. Participants who reported being smokers in 2009 were classified as smokers. Never-smokers were defined as individuals who reported never having smoked in 2009 and reaffirmed this status in 2013, increasing confidence that they remained non-smokers throughout follow-up. Accordingly, individuals who initiated smoking or quit smoking between 2009 and 2013 were excluded, as their exposure status could not be assumed to remain stable during the interval. Participants with inconsistent or missing responses across the two time points were also excluded.

Data collection

Baseline characteristics included age, sex, socioeconomic status (measured by insurance premium quantiles), health behavior (alcohol consumption and physical activity frequency), body mass index (BMI), and residential area (urban or rural). Age was categorized into five groups: 18–39 years, 40–59 years, 60–79 years, and ≥ 80 years. Alcohol consumption was classified into three categories: none, 1–4 days per week, and 5–7 days per week. Physical activity was classified into three categories: none, 1–4 days per week, and 5–7 days per week. BMI (in kg/m^2) was categorized as < 25 (normal weight), 25–30 (overweight), and ≥ 30 (obesity).

Statistical analysis

Continuous variables were expressed as means and standard deviations, and categorical variables were presented as numbers and percentages. Group comparisons were conducted using the Wilcoxon rank-sum test for continuous variables and the chi-square test for categorical variables. Incidence rates of antibiotic use were calculated as the number of qualifying prescription events per 1,000 person-years, and incidence rate ratios (IRRs) comparing smokers and never-smokers were estimated using Poisson regression models with robust standard errors. Multivariable analyses were performed using three models: an unadjusted model (Model 1); a model adjusted for age and income status (Model 2); and a fully adjusted model (Model 3), which additionally included all other covariates with a P-value < 0.010 in univariate analyses to minimize residual confounding. All models were fit and reported separately for NHIS-NSC and NHIS-HEALS, allowing us to evaluate consistency across cohorts. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 50,134 adult men from the NHIS–NSC cohort (17,300 never-smokers and 32,834 smokers) and 42,979 from the NHIS–HEALS cohort (20,145 never-smokers and 22,834 smokers) were included in the analysis (Fig. 1; Table 1). In the NHIS–NSC cohort, although the absolute differences between groups were modest, never-smokers were significantly older, reported lower alcohol consumption, and were more likely to belong to higher income brackets compared to smokers (Table 1). The NHIS–HEALS cohort showed similar patterns of group differences. However, due to the inherent inclusion of individuals aged 40 years and older, this cohort had a

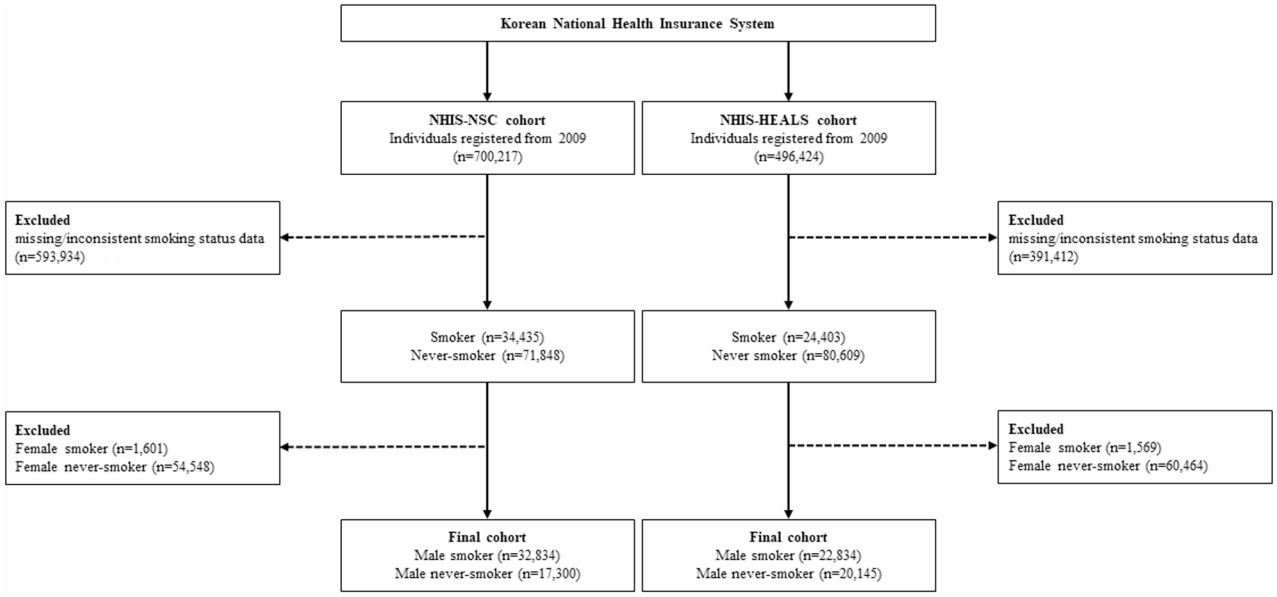


Fig. 1 Flow chart of the study population

Table 1 Baseline characteristics

	National Sample Cohort (NHIS-NSC)			Health Screening Cohort (NHIS-HEALS)		
	Never-smoker (*n* = 17,300)	**Smoker (*n* = 32,834)**	***p*-value**	**Never-smoker (*n* = 20,145)**	**Smoker (*n* = 22,834)**	***p*-value**
Age, mean (standard deviation)	50.4 (14.2)	46.4 (11.6)	< 0.001	61.9 (9.0)	58.5 (7.1)	< 0.001
18–39 years	4,772 (27.6)	10,608 (32.3)		Excluded	Excluded	
40–59 years	7,756 (44.8)	17,496 (53.3)		10,166 (50.5)	15,330 (67.1)	
60–79 years	4,442 (25.7)	4,564 (13.9)		9,084 (45.1)	7,198 (31.5)	
≥ 80 years	330 (1.9)	166 (0.5)		895 (4.4)	306 (1.4)	
Insurance premium quantiles			< 0.001			< 0.001
1 (lowest)	712 (4.1)	1,353 (4.1)		1,095 (5.4)	1,387 (6.1)	
2–3	1,542 (8.9)	2,719 (8.3)		2,342 (11.6)	2,541 (11.1)	
4–5	2,094 (12.1)	4,572 (13.9)		2,503 (12.5)	3,017 (13.2)	
6–7	3,722 (21.5)	8,729 (26.6)		3,455 (17.2)	4,427 (19.4)	
8–9	5,868 (31.9)	10,911 (33.2)		5,682 (28.6)	6,798 (29.8)	
10 (highest)	3,362 (19.5)	4,550 (13.9)		4,978 (24.7)	4,664 (20.4)	
Alcohol consumption (days per week)			< 0.001			< 0.001
None	7,927 (45.8)	8,197 (25.0)		10,728 (53.3)	6,781 (29.7)	
1–4	8,791 (50.8)	22,434 (68.3)		8,108 (40.2)	12,652 (55.4)	
5–7	582 (3.4)	2,203 (6.7)		1,309 (6.5)	3,401 (14.9)	
Exercise (days per week)			< 0.001			< 0.001
None	6,341 (36.7)	12,476 (38.0)		22 (0.1)	24 (0.1)	
1–4	6,800 (39.3)	13,827 (42.1)		4,653 (23.1)	6,015 (26.3)	
5–7	4,159 (24.0)	6,531 (19.9)		15,470 (76.8)	16,795 (73.6)	
Body mass index (kg/m^2)			< 0.001			< 0.001
< 25	10,751 (62.1)	19,936 (60.7)		13,262 (65.8)	15,476 (67.8)	
25–30	5,876 (34.0)	11,322 (34.5)		6,411 (31.8)	6,897 (30.2)	
≥ 30	673 (3.9)	1,576 (4.8)		472 (2.4)	461 (2.0)	
Residential area			0.828			< 0.001
Urban	7,487 (43.3)	14,243 (43.4)		8,677 (43.1)	10,426 (45.7)	
Rural	9,813 (56.7)	18,591 (56.6)		11,468 (56.9)	12,408 (54.3)	

higher overall mean age than the NHIS–NSC cohort. Additionally, compared to the NHIS–NSC cohort, individuals in the NHIS–HEALS cohort tended to have higher household income levels, reported greater physical activity, and had slightly lower BMI, indicating a generally healthier profile.

Broad-spectrum antibiotic use in the NHIS–NSC cohort

The overall incidence of broad-spectrum antibiotic use for at least 3 consecutive days was low across all antibiotic classes (Table 2). For the composite outcome, the incidence rate was 0.069 per 1,000 person-years in never-smokers and 0.040 per 1,000 person-years in smokers. In Model 3, smoking was not significantly associated with increased antibiotic use (adjusted IRR = 1.55, 95% CI = 0.67–3.52; $p = 0.310$). The analysis by individual antibiotic classes showed no significant differences between smokers and never-smokers in three model. For glycopeptides, the incidence rate was 0.017 per 1,000 person-years in never-smokers and 0.012 in smokers. The adjusted IRR for glycopeptide use in smokers compared to never-smokers was 1.07 (95% CI = 0.23–5.10; $p = 0.871$), indicating no significant association.

Broad-spectrum antibiotic use in the NHIS-HEALS cohort

In the NHIS–HEALS cohort, the rate of use of broad-spectrum antibiotics for at least 3 consecutive days was low across antibiotic classes (Table 3). For the composite outcome, the rate of use was 0.010 per 1,000 person-years in never-smokers and 0.060 in smokers. In the fully adjusted model, smoking was not significantly associated with the composite outcome (adjusted IRR = 0.59, 95% CI = 0.24–1.46; $p = 0.204$). No significant differences were observed between smokers and never-smokers in this cohort across antibiotic classes, including antipseudomonal penicillins, cephalosporins, and carbapenems. For glycopeptides, the rate of use was 0.010 per 1,000 person-years in never-smokers and 0.009 in smokers. Although the unadjusted suggested an elevated risk, this association was no longer statistically significant in model 3 (adjusted IRR = 3.47, 95% CI = 0.70–17.13; $p = 0.128$).

Discussion

Our findings showed that smoking status was not consistently associated with increased use of broad-spectrum antibiotics targeting ESBL-producing *Enterobacterales*, *P.aeruginosa*, or MRSA in two large-scale, nationally representative cohorts of Korean adult men. Although smokers may require more aggressive antimicrobial therapy due to perceived infection risk or severity, our

Table 2 Comparison of outcomes between smokers and non-smokers in the NHIS National sample cohort

	Event (*n*)	Incidence rate per 1,000 person-years	Model 1[a]		Model 2[b]		Model 3[c]	
			IRR (95% CI)	*p*-value	Adjusted IRR (95% CI)	*p*-value	Adjusted IRR (95% CI)	*p*-value
Composite outcome (penicillin + cephalosporin + carbapenem)								
Never-smoker	12	0.069	1 (reference)		1 (reference)		1 (reference)	
Smoker	13	0.040	0.58 (0.26–1.27)	0.173	1.42 (0.64–3.18)	0.392	1.55 (0.67–3.518)	0.310
Anti-pseudomonal penicillin								
Never-smoker	1	0.006	1 (reference)		1 (reference)		1 (reference)	
Smoker	4	0.012	2.00 (0.22–17.89)	0.535	0.32 (0.04–2.91)	0.311	0.29 (0.03–2.65)	0.868
Anti-pseudomonal cephalosporin								
Never-smoker	6	0.035	1 (reference)		1 (reference)		1 (reference)	
Smoker	4	0.012	0.34 (0.10–1.21)	0.097	2.99 (0.83–10.77)	0.094	3.18 (0.86–11.74)	0.913
Carbapenems								
Never-smoker	5	0.029	1 (reference)		1 (reference)		1 (reference)	
Smoker	5	0.015	0.52 (0.15–1.79)	0.297	1.29 (0.36–4.64)	0.700	1.58 (0.42–5.98)	0.926
Glycopeptides								
Never-smoker	3	0.017	1 (reference)		1 (reference)		1 (reference)	
Smoker	4	0.012	0.71 (0.16–3.15)	0.648	1.42 (0.31–5.53)	0.656	1.07 (0.23–5.10)	0.871

Data were expressed as numbers or IRRs with 95% CIs. NHIS, National Health Insurance Service; IRR, incidence rate ratio; CI, confidence interval

[a]Model 1 unadjusted

[b]Model 2 adjusted for age and income status

[c]Model 3 adjusted for age, income status, and all other covariates with a *p*-value < 0.010 in univariate analyses

Table 3 Comparison of outcomes between smokers and non-smokers in the NHIS health screening cohort

	Event (*n*)	Incidence rate per 1,000 person-years	Model 1[a]		Model 2[b]		Model 3[c]	
			IRR (95% CI)	*p*-value	Adjusted IRR (95% CI)	*p*-value	Adjusted IRR (95% CI)	*p*-value
Composite outcome (penicillin + cephalosporin + carbapenem)								
Never-smoker	8	0.010	1 (reference)		1 (reference)		1 (reference)	
Smoker	14	0.060	6.00 (2.52–14.30)	< 0.001	0.61 (0.25–1.48)	0.068	0.59 (0.24–1.46)	0.204
Anti-pseudomonal penicillin								
Never-smoker	0	0	1 (reference)		1 (reference)		1 (reference)	
Smoker	2	0.009	N/A		N/A		N/A	N/A
Anti-pseudomonal cephalosporin								
Never-smoker	6	0.007	1 (reference)		1 (reference)		1 (reference)	
Smoker	6	0.026	3.71 (1.20–11.52)	0.023	1.19 (0.38–3.77)	0.768	1.13 (0.34–3.71)	0.786
Carbapenems								
Never-smoker	2	0.002	1 (reference)		1 (reference)		1 (reference)	
Smoker	6	0.026	13.00 (2.62–64.41)	0.002	0.44 (0.11–1.83)	0.067	0.51 (0.12–2.19)	0.156
Glycopeptides								
Never-smoker	8	0.010	1 (reference)		1 (reference)		1 (reference)	
Smoker	2	0.009	0.90 (0.19–4.24)	0.894	3.68 (0.76–17.82)	0.028	3.47 (0.70–17.13)	0.128

Data were expressed as numbers or IRRs with 95% CIs. NHIS, National Health Insurance Service; IRR, incidence rate ratio; CI, confidence interval

[a]Model 1 unadjusted

[b]Model 2 adjusted for age and income status

[c]Model 3 adjusted for age, income status, and all other covariates with a *p*-value < 0.010 in univariate analyses

findings do not support this assumption. Therefore, smoking history alone should not be used as a surrogate marker of infection severity or as a primary rationale for prescribing broad-spectrum agents. Instead, antibiotic prescribing decisions should be guided by objective clinical indicators and individualized patient assessments.

Smoking exerts direct pathophysiologic effects on the respiratory tract and has been consistently associated with an increased incidence and severity of respiratory infections, including bronchitis, pneumonia, influenza, and COVID-19 [20–23] as well as an increased risk of developing severe respiratory manifestations, such as acute respiratory distress syndrome [24, 25]. However, the severity of pneumonia does not necessarily justify the use of broad-spectrum antibiotic therapy, particularly in patients with a low risk of colonization by resistant pathogens such as *P.aeruginosa* or MRSA [26]. Evidence linking smoking to non-respiratory or systemic infections remains relatively limited [4], and it is unclear whether findings from respiratory conditions can be extrapolated to other types of infection. Furthermore, the effect of smoking on the severity of systemic infections is unclear and warrants further investigation.

Our findings should not be interpreted as diminishing the well-established public health harms of smoking. On the contrary, the link between smoking and an increased risk of infections reinforces the importance of smoking cessation as a critical public health priority. However, well-intentioned descriptive norms in public health messaging can sometimes yield unintended consequences, leading to behavioral outcomes that diverge from their original purpose [27]. Antibiotic prescribing is influenced by multiple clinical and behavioral factors beyond clinical indications alone [9]. From the prescriber's perspective, decisions may be shaped by diagnostic uncertainty, perceived patient risk, institutional norms, and cognitive biases [28]. From the patient's perspective, individuals with a history of smoking may expect or request more aggressive treatment—including antibiotics—based on their perceived vulnerability [29]. In this context, using smoking history as a surrogate marker of infection severity may contribute to the overuse of broad-spectrum agents and undermine antimicrobial stewardship efforts. Our findings highlight the need for an evidence-based understanding of the relationship between smoking and antibiotic use. Such insights may also inform behaviorally-oriented interventions, such as those grounded in the Health Belief Model, by clarifying how perceived risk influences clinician and patient behaviors in infection management [30].

A key strength of this study lies in its use of two complementary, nationally representative cohorts. In epidemiologic research, ensuring that the study population reflects the broader target population is essential for

generating findings that inform clinical care and public health policy. The NHIS–NSC was constructed through stratified random sampling to represent the entire Korean population, thereby enhancing the generalizability of our findings across diverse demographic and clinical backgrounds [17]. In contrast, the NHIS–HEALS cohort consists of individuals who participated in routine health screening programs and are generally healthier, with fewer serious medical conditions. This cohort represents a relatively "healthy" population in which the association between smoking and antibiotic exposure can be examined with minimal confounding from underlying disease burden [18]. By leveraging both cohorts separately, we evaluated whether associations replicate across complementary populations. Analyzing NHIS-NSC and NHIS-HEALS separately balances population-level representativeness with internal validity, supporting the robustness of our findings and their applicability to antimicrobial stewardship and health communication efforts in various real-world contexts.

This study has limitations. First, although both cohorts were constructed using systematic sampling methods, the study population may not fully reflect the broader Korean adult population. The overall incidence of broad-spectrum antibiotic use was low in both cohorts, which may have limited the statistical power to detect significant differences between the groups. The reversal of the crude IRR after adjustment also suggests underlying confounding—largely attributable to age-related differences in healthcare utilization—although residual confounding cannot be fully excluded. Second, to capture clinically meaningful antibiotic use, we limited our analysis to prescriptions of broad-spectrum antibiotics with a duration of 3 days or more. While this approach aimed to reduce misclassification, the determination of clinical appropriateness was based on retrospective data and may not accurately reflect the original clinical context. Third, we could not distinguish former from current smokers, and our requirement for consistent smoking status between 2009 and 2013 led to the exclusion of individuals who quit or initiated smoking during this period. This reduced exposure misclassification but limited our ability to assess patterns of antibiotic use across changing smoking behaviors. Fourth, the study did not capture information on smoking intensity or duration (e.g., pack-years), precluding the evaluation of dose–response relationships between smoking exposure and broad-spectrum antibiotic use. We also were unable to adjust for comorbid conditions, which may influence healthcare utilization and antibiotic prescribing; thus, residual confounding cannot be ruled out. Fifth, the study population consisted exclusively of Korean adult men, which may limit the generalizability of the findings to Korean adult women and to populations in countries with different healthcare systems, social norms, or cultural attitudes toward antibiotic use. Finally, we did not exclude individuals with prior broad-spectrum antibiotic use, and differences in past exposure may influence subsequent prescribing patterns.

In this large-scale population-based study of general adult men in South Korea, broad-spectrum antibiotic use was infrequent, and we did not observe evidence of an association between smoking status and increased use. These findings support the need for prescribing decisions guided by objective clinical indicators rather than smoking history alone and may inform future approaches in antimicrobial stewardship and health communication.

Abbreviations

BMI	Body mass index
ESBL	Extended-spectrum β-lactamase
IRR	Incidence rate ratio
MRSA	Methicillin-resistant *Staphylococcus aureus*
NHIS	National Health Insurance Service
NSC	National Sample Cohort
HEALS	Health Screening Cohort

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-12363-7.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Conceptualization and methodology: SHY, JHK, JAS. Data curation: DSP, SHY, JHK, and JAS. Data analysis: DSP, SHY, JHK, and JAS. Original draft preparation: DSP, SHY, JHK, and JAS. Review and editing: MKL, JYB, SSL, and HJC. All authors have read and approved the final manuscript.

Funding

This research was supported by the Glocal University Project from the Ministry of Education and the National Research Foundation of Korea (GLOCAL-202504350001). No other disclosures were reported.

Data availability

The data used in this study are not publicly available due to restrictions under the Korean NHIS data protection policies. However, deidentified individual-level NHIS data are available to researchers who meet the criteria for access to confidential data under a Data Use Agreement.

Declarations

Ethical approval

This study was approved by the Institutional Review Board of Seoul National University Hospital (Approval Number: H2209-001-1353), which waived the need for written informed consent because of the retrospective nature of the study. All personal identifiers were anonymized for confidentiality before data processing. This study complied with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details
[1]Department of Artificial Intelligence Convergence, Hallym University, Chuncheon, South Korea
[2]Center for Palliative Care and Clinical Ethics, Seoul National University Hospital, Seoul, South Korea
[3]Department of Human Systems Medicine, Seoul National University College of Medicine, Seoul, South Korea
[4]Division of Infectious Diseases, Department of Internal Medicine, Ewha Womans University College of Medicine, Mokdong Hospital, Seoul, South Korea
[5]Division of Infectious Diseases, Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, South Korea
[6]Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong-si, Gyeonggi, South Korea
[7]Department of Population and Quantitative Health Science, UMass Chan Medical School, Worcester, MA, USA
[8]Division of Infectious Diseases, Department of Internal Medicine, Ewha Womans University College of Medicine, Mokdong Hospital, 1071, Anyangcheon-ro, Yangcheon-gu, Seoul, Seoul, South Korea
[9]Department of Artificial Intelligence Convergence, Hallym University, 1 Hallymdaehak-gil, Chuncheon-si 24252, Gangwon-do, South Korea

Received: 26 August 2025 / Accepted: 11 December 2025
Published online: 18 December 2025

References

1. Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, et al. 50-year trends in smoking-related mortality in the united States. N Engl J Med. 2013;368(4):351–64.
2. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. The health consequences of smoking: 50 years of Progress. A report of the surgeon general. Atlanta, GA: Centers for Disease Control and Prevention; 2014.
3. Jiang C, Chen Q, Xie M. Smoking increases the risk of infectious diseases: A narrative review. Tob Induc Dis. 2020;18:60.
4. Kjerulff B, Kaspersen KA, Dinh KM, Boldsen J, Mikkelsen S, Erikstrup LT, et al. Smoking is associated with infection risk in healthy blood donors. Clin Microbiol Infect. 2023;29(4):506–14.
5. Blix HS, Hjellvik V, Litleskare I, Ronning M, Tverdal A. Cigarette smoking and risk of subsequent use of antibacterials: a follow-up of 365,117 men and women. J Antimicrob Chemother. 2011;66(9):2159–67.
6. Steinberg MB, Akincigil A, Kim EJ, Shallis R, Delnevo CD. Tobacco smoking as a risk factor for increased antibiotic prescription. Am J Prev Med. 2016;50(6):692–8.
7. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance-the need for global solutions. Lancet Infect Dis. 2013;13(12):1057–98.
8. Broom J, Broom A, Kirby E. The drivers of antimicrobial use across institutions, stakeholders and economic settings: a paradigm shift is required for effective optimization. J Antimicrob Chemother. 2019;74(9):2803–9.
9. Warreman EB, Lambregts MMC, Wouters RHP, Visser LG, Staats H, van Dijk E, et al. Determinants of in-hospital antibiotic prescription behaviour: a systematic review and formation of a comprehensive framework. Clin Microbiol Infect. 2019;25(5):538–45.
10. Teixeira Rodrigues A, Roque F, Falcao A, Figueiras A, Herdeiro MT. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. Int J Antimicrob Agents. 2013;41(3):203–12.
11. Oliver K, Lorenc T, Tinkler J, Bonell C. Understanding the unintended consequences of public health policies: the views of policymakers and evaluators. BMC Public Health. 2019;19(1):1057.
12. Adekanmbi V, Jones H, Farewell D, Francis NA. Antibiotic use and deprivation: an analysis of Welsh primary care antibiotic prescribing data by socioeconomic status. J Antimicrob Chemother. 2020;75(8):2363–71.
13. Palin V, Molter A, Belmonte M, Ashcroft DM, White A, Welfare W, et al. Antibiotic prescribing for common infections in UK general practice: variability and drivers. J Antimicrob Chemother. 2019;74(8):2440–50.
14. Musher DM. Pseudomonas pneumonia in smokers. Clin Infect Dis. 2001;33(3):415.
15. Kwon KN, Lee K, Chung W. The economic cost of direct smoking in South Korea. Prev Med Rep. 2024;46:102865.
16. Medina M, Castillo-Pino E. An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol. 2019;11:1756287219832172.
17. Lee J, Lee JS, Park SH, Shin SA, Kim K. Cohort profile: the National health insurance Service-National sample cohort (NHIS-NSC), South Korea. Int J Epidemiol. 2017;46(2):e15.
18. Seong SC, Kim YY, Park SK, Khang YH, Kim HC, Park JH, et al. Cohort profile: the National health insurance Service-National health screening cohort (NHIS-HEALS) in Korea. BMJ Open. 2017;7(9):e016640.
19. Sharland M, Zanichelli V, Ombajo LA, Bazira J, Cappello B, Chitatanga R, et al. The WHO essential medicines list aware book: from a list to a quality improvement system. Clin Microbiol Infect. 2022;28(12):1533–5.
20. Hylkema MN, Sterk PJ, de Boer WI, Postma DS. Tobacco use in relation to COPD and asthma. Eur Respir J. 2007;29(3):438–45.
21. Nuorti JP, Butler JC, Farley MM, Harrison LH, McGeer A, Kolczak MS, et al. Cigarette smoking and invasive Pneumococcal disease. Active bacterial core surveillance team. N Engl J Med. 2000;342(10):681–9.
22. Feldman C, Anderson R. Cigarette smoking and mechanisms of susceptibility to infections of the respiratory tract and other organ systems. J Infect. 2013;67(3):169–84.
23. van Zyl-Smit RN, Richards G, Leone FT. Tobacco smoking and COVID-19 infection. Lancet Respir Med. 2020;8(7):664–5.
24. McGeoch LJ, Ross S, Massa MS, Lewington S, Clarke R. Cigarette smoking and risk of severe infectious respiratory diseases in UK adults: 12-year follow-up of UK biobank. J Public Health (Oxf). 2023;45(4):e621–9.
25. Zhang L, Xu J, Li Y, Meng F, Wang W. Smoking on the risk of acute respiratory distress syndrome: a systematic review and meta-analysis. Crit Care. 2024;28(1):122.
26. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with Community-acquired Pneumonia. An official clinical practice guideline of the American thoracic society and infectious diseases society of America. Am J Respir Crit Care Med. 2019;200(7):e45–67.
27. Robert B, Cialdini LJ, Demaine, Brad J, Sagarin DW, Barrett. Kelton Rhoads, Patricia L. Winter. Managing social norms for persuasive impact. Social Influence. 2006;1(1):3–15.
28. Richards AR, Linder JA. Behavioral economics and ambulatory antibiotic stewardship: A narrative review. Clin Ther. 2021;43(10):1654–67.
29. Linder JA, Singer DE. Desire for antibiotics and antibiotic prescribing for adults with upper respiratory tract infections. J Gen Intern Med. 2003;18(10):795–801.
30. Wang X, Liu C, Zheng S, Zhang X, Lin R, Duan L, et al. The public's irrational use of antibiotics for upper respiratory tract infections: a cross-sectional study based on the health belief model. Sci Rep. 2025;15(1):17220.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.