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Trends in Sedative-Hypnotic Prescription Among Insomnia Patients: A Nationwide Cohort Study From 2010 to 2022 in Korea

Jiyoon Shin,[1,2*] **So Yon Jun**,[3*] **Donghyun Won**,[3,4] **Minah Kim**,[1] **Su Young Lee**,[5] **Mincheol Seo**,[1,6] **Aesun Shin**,[3,4] **and Yu Jin Lee**[1]

[1]Department of Psychiatry and Center for Sleep and Chronobiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea
[2]Department of Psychiatry, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea
[3]Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea
[4]Integrated Major in Innovative Medical Science, Seoul National University Graduate School, Seoul, Korea
[5]Department of Psychiatry, Yonsei Forest Mental Health Clinic, Seoul, Korea
[6]Department of Psychiatry, Veteran Health Service Medical Center, Seoul, Korea

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Address for Correspondence:
Aesun Shin, MD, PhD
Department of Preventive Medicine, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Korea.
Email: shinaesun@snu.ac.kr

Yu Jin Lee, MD, PhD
Department of Psychiatry and Center for Sleep and Chronobiology, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Korea.
Email: ewpsyche@snu.ac.kr

*Jiyoon Shin and So Yon Jun contributed equally to this work.

ORCID iDs
Jiyoon Shin
https://orcid.org/0000-0003-0510-993X
So Yon Jun
https://orcid.org/0009-0002-4310-3459
Donghyun Won
https://orcid.org/0009-0008-1832-4210

ABSTRACT

Background: Global insomnia prevalence increased during the coronavirus disease 2019 (COVID-19) pandemic, driving higher demand for sedative-hypnotics. The objective of this study was to compare sedative-hypnotic prescription patterns in South Korea from 2010 to 2022 and assess the potential impact of the COVID-19 pandemic.
Methods: This population-based cohort study from January 1, 2010, to December 31, 2022, used the Korean National Health Insurance's Health Insurance Sharing Service database of 8,136,437 (60.4% female) unique insomnia patients aged 18 and older. Prescriptions for sedative-hypnotic groups (benzodiazepines, non-benzodiazepines, antidepressants, and antipsychotics), number of patients prescribed sedative-hypnotics, and predicted and observed prescription rates by sex, age, and sedative-hypnotic group were analyzed.
Results: The number of prescriptions per 1,000 population increased across all sedative-hypnotic groups before and during the pandemic. Women and the elderly had higher prescriptions for all sedative-hypnotic groups compared to men and other age groups. Antidepressant prescriptions saw the highest percentage increase (men 38.6%; women 37.1%) in 1st half of 2020 compared to 2019, followed by antipsychotics (men 28.9%; women 25.7%). Antidepressant prescriptions showed the largest increase relative to predicted levels across all age groups from 2020 to 2021, while non-benzodiazepines exhibited the smallest increase (men 5.6%; women 4.5%). In the 18–29 age group, prescriptions for all sedative-hypnotic groups exceeded predicted numbers in 2021.
Conclusion: This study found that sedative-hypnotic prescriptions steadily increased from 2010 to 2022, with the trend becoming more pronounced during the COVID-19 pandemic, when prescription rates tended to exceed predicted levels in Korea. Monitoring the use of sedative-hypnotics for insomnia in women, the elderly, and young adults is essential for potential adverse effects and associated mental problems.

Keywords: Insomnia; Sedative-Hypnotics; Prescription; COVID-19 Pandemic; Benzodiazepines; Non-Benzodiazepines; Korea

Minah Kim
https://orcid.org/0009-0006-9278-0279
Su Young Lee
https://orcid.org/0000-0003-3125-3409
Mincheol Seo
https://orcid.org/0000-0002-8889-9473
Aesun Shin
https://orcid.org/0000-0002-6426-1969
Yu Jin Lee
https://orcid.org/0000-0001-5195-2579

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Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contributions

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INTRODUCTION

Insomnia symptoms affect approximately one-third to one-half of the population at some point in their lifetime.[1] The global prevalence of insomnia was significantly impacted by the coronavirus disease 2019 (COVID-19) outbreak, which began in December 2019 and persisted until May 2023. In South Korea, the prevalence of insomnia symptoms was reported at 32.9% during the pandemic.[2] In China, it reached 39.1%, remaining high at 41.8% even after the pandemic stabilized.[3] A global systemic review reported an increase in insomnia symptoms during the pandemic, with 52.6% experiencing subthreshold insomnia and 16.7% experiencing clinically significant insomnia.[4] While previous studies have generally reported a higher prevalence of insomnia in women.[5,6] the impact of sex on insomnia during the pandemic remains unclear.[4,7] A national sleep survey found the highest prevalence of insomnia during the pandemic among men aged 20–29 and women aged 30–39,[2] which contrasts with previous findings indicating that older adults typically exhibit higher prevalence rates.[8]

Benzodiazepines and non-benzodiazepines are commonly used to treat insomnia,[9] along with low-dose antidepressants and antipsychotics. While sedative-hypnotic use has been decreasing in many countries over the past decade,[10,11] at the onset of the COVID-19 pandemic, several western countries experienced an increase in sedative-hypnotic prescriptions, with variations in prescription patterns by sex and age.[12-14] In the United States, women had higher rates of benzodiazepine prescriptions, and both sexes saw increases in non-benzodiazepines and antidepressant prescriptions.[12,14] Antidepressant prescriptions also rose across all age groups in Denmark, Norway,[12] and France[13] with the increase being more pronounced in youth. However, antidepressant prescriptions were reported to decrease during the pandemic in Portugal[15] and England.[16] Few studies have compared the expected prescription rates, based on pre-pandemic longitudinal data, with the actual prescription rates during the pandemic.

Short-term use of sedative-hypnotics can be effective for treating insomnia, but long-term use increases the risk of abuse, dependence, and withdrawal symptoms.[17] Long-term use is also associated with a higher likelihood of falls in older adults,[18] higher mortality rates,[19,20] greater incidence of cancer[19,21] and dementia,[22] and an increased risk of suicidality.[23] Given these potential adverse effects, monitoring prescription trends of sedative-hypnotics is important. Previous studies on South Korean prescription trends from 2007–2011[24] and 2011–2015[25] reported increases over time, but research on subsequent periods is lacking.

This study aimed to investigate prescription trends for sedative-hypnotics in adult patients diagnosed with insomnia in South Korea from 2010 to 2022. Given prior reports that women and younger adults are more vulnerable to pandemic-related insomnia symptoms,[2] it also sought to examine changes in prescription patterns during the COVID-19 pandemic by sex and age. Additionally, we aimed to compare observed and predicted prescription rates during the pandemic. We hypothesized that sedative-hypnotic prescriptions increased both before and during the pandemic, with prescriptions during the pandemic exceeding predictions and varying by sex and age.

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METHODS

Data collection

We used data from the Korean National Health Insurance's Health Insurance Sharing Service (NHISS) database. The Korean National Health Insurance covers approximately 97–98% of the total population, and the NHISS database includes data from inpatient and outpatient clinics as well as local community healthcare centers.

We used a customized dataset of insomnia patients aged 18 and older from the NHISS database, covering the period from January 1, 2010, to December 31, 2022, to evaluate changes in sedative-hypnotic prescriptions before and during the COVID-19 pandemic. Insomnia patients were identified using diagnostic codes F51.0 (nonorganic insomnia) or G47.0 (insomnia) according to the Korean Standard Classification of Diseases, 8th Revision, based on the International Classification of Diseases, Tenth Revision. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Sedative-hypnotics classification

Four sedative-hypnotic groups were included in our analysis: 1) benzodiazepines, 2) non-benzodiazepines (zolpidem, eszopiclone), 3) antidepressants (mirtazapine, low-dose formulations of doxepin, amitriptyline, imipramine, nortriptyline, trazodone), and 4) antipsychotics (low-dose formulations of quetiapine, chlorpromazine, levomepromazine). For antidepressants and antipsychotics, low-dose formulations were specifically defined based on commercially available dosage. Individual prescriptions were classified into each sedative-hypnotic group by substance name according to their World Health Organization Anatomical Therapeutic Chemical (ATC) classification codes. Benzodiazepines were further categorized by their half-life as 'short-acting' (< 3 hours), 'intermediate-acting' (3–20 hours), and 'long-acting' (> 20 hours). A list of ATC codes, benzodiazepine categorization, and low-dosage formulations is provided in the **Supplementary Table 1**.

Statistical analysis

Data on the total number of prescriptions for each sedative-hypnotic group and individual drug were used to assess prescription frequency and time trends from 2010 to 2022. The number of prescriptions issued over each 6-month half-year period (January–June or July–December) was divided by the mid-year population to calculate prescriptions per 1,000 population. Mid-year population numbers were obtained from the Korean Statistical Information Service. The number of patients prescribed sedative-hypnotics was also analyzed.

We conducted a subgroup analysis by sex, age group (18–29, 30–39, 40–49, 50–59, 60–69, ≥ 70), and sedative-hypnotic group for each half-year period during the COVID-19 pandemic (2020–2021) and the year preceding the pandemic (2019). Data from 2022 were excluded, as social-distancing rules in South Korea were relaxed by early 2022 and fully lifted by April 4, 2022. Percentage increases in prescriptions for each half-year period in 2020 and 2021 were compared to the corresponding periods in 2019. Multi-drug prescriptions were also analyzed, and the six most common drug combinations were identified for each half-year period.

A linear regression model was used to predict the expected number of monthly prescriptions per 1,000 population for each sedative-hypnotic group during 2020 and 2021, based on the data from 2010 to 2019. The model included year as a continuous variable to model linear

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change in prescriptions over time and month as a categorical variable to assess seasonal patterns. Further subgroup analysis was conducted by sex and age group. The expected prescription rates were compared to the observed, with 95% confidence limits (CLs) calculated for each monthly prediction. All calculations were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics statement

The study was approved by the Institutional Review Board (IRB) for Human Subjects of Seoul National University Hospital (IRB No. 2306-121-1440). Informed consent was waived because of the retrospective nature of public data from NHIS.

RESULTS

Demographics

From 2010 to 2022, 8,136,437 (60.4% female) patients with unique identifier codes were analyzed, including 3,610,941 (60.8% female) unique patients during the pandemic period (2019 to 2021). The yearly data analyzed included: 2,074,139 patients in 2010 (mean ± standard deviation age 60.7 ± 25.2; 63.4% female), 2,853,489 in 2011 (mean age 61.2 ± 25.4; 62.4% female), 3,131,832 in 2012 (mean age 61.4 ± 25.5; 62.2% female), 3,255,417 in 2013 (mean age 61.1 ± 25.3; 61.8% female), 3,408,023 in 2014 (mean age 61.4 ± 25.5; 61.6% female), 3,594,187 in 2015 (mean age 61.5 ± 25.6; 61.0% female), 3,928,248 in 2016 (mean age 61.6 ± 25.6; 60.7% female), 4,052,058 in 2017 (mean age 61.6 ± 25.6; 60.7% female), 4,304,070 in 2018 (mean age 61.9 ± 25.8; 60.6% female), 4,567,687 in 2019 (mean age 61.9 ± 25.8; 60.3% female), 4,827,125 in 2020 (mean age 62.1 ± 25.8; 60.5% female), 5,124,972 in 2021 (mean age 62.2 ± 25.9; 60.8% female), and 5,377,481 in 2022 (mean age 62.4 ± 26.0; 60.7% female).

Sedative-hypnotic prescriptions in South Korea 2010–2022

Zolpidem was the single most frequently prescribed sedative-hypnotics drug for both sexes from 2010 to 2022, followed by alprazolam and trazodone. Prescriptions for all drugs, excluding chlorpromazine and chlordiazepoxide, were higher in women than in men (**Supplementary Table 2**).

Among sedative-hypnotic groups, non-benzodiazepines were the most prescribed, followed by intermediate-acting benzodiazepines, antidepressants, long-acting benzodiazepines, short-acting benzodiazepines, and antipsychotics in both sexes (**Table 1**).

Table 1. The number of prescriptions for sedative-hypnotics groups according to sex, National Health Insurance Sharing Service, 2010–2022

Rank	Total		Men		Women	
	Sedative-hypnotic group	No. of prescriptions	Sedative-hypnotic group	No. of prescriptions	Sedative-hypnotic group	No. of prescriptions
1	Non-BDZ hypnotics	113,133,194	Non-BDZ hypnotics	44,058,433	Non-BDZ hypnotics	69,074,761
2	Intermediate-acting BDZ	78,423,469	Intermediate-acting BDZ	29,583,002	Intermediate-acting BDZ	48,840,467
3	Antidepressant	65,812,270	Antidepressant	25,505,009	Antidepressant	40,307,261
4	Long-acting BDZ	61,807,424	Long-acting BDZ	24,922,293	Long-acting BDZ	36,885,131
5	Short-acting BDZ	21,117,252	Short-acting BDZ	7,942,663	Short-acting BDZ	13,174,589
6	Antipsychotic	15,689,096	Antipsychotic	6,865,219	Antipsychotic	8,823,877

BDZ = benzodiazepine.

Fig. 1. Number of prescriptions prescribed sedative-hypnotics during half-yearly, National Health Insurance Sharing Service, 2010–2022.
BDZ = benzodiazepine.

From 2010 to 2022, the number of prescriptions per 1,000 population showed an increasing trend across all sedative-hypnotics groups (**Fig. 1**). The number of patients prescribed a sedative-hypnotic also showed an upward trend over the years (**Supplementary Fig. 1**). In every year, women were prescribed sedative-hypnotics more frequently than men.

Prescription trends during the COVID-19 pandemic

Analysis of prescriptions during the pandemic (2019–2021) revealed an increasing trend in the number of prescriptions per 1,000 population across all age groups for both sexes (**Supplementary Figs. 2**-7). During the pandemic, benzodiazepines and non-benzodiazepines were prescribed more frequently to older age groups. For each half-year period, short-acting

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benzodiazepine prescriptions were 8 times higher in men and 4 times higher in women aged ≥ 70 compared to those aged ≤ 30. Non-benzodiazepine prescriptions increased the most in men aged 70 and older, doubling from the 60–69 age group.

Women had more prescriptions for all sedative-hypnotics groups than men in the ≤ 50 age groups. Men and women had a similar number of prescriptions for short-acting benzodiazepines and antidepressants in the ≥ 70 age group, and antipsychotics in the ≥ 50 age groups.

Commonly prescribed multi-drug combinations involved one benzodiazepine paired with another type of sedative-hypnotic group (**Supplementary Fig. 8**). The most common combination from 2019 and 2021 was intermediate-acting benzodiazepines with non-benzodiazepines.

During the pandemic, sedative-hypnotic prescriptions showed an overall increasing trend (**Table 2**). Antidepressant prescriptions had the highest percentage increase, increasing by 38.6% for men and 37.1% for women in the 1st half of 2020. Prescriptions for antidepressants continued to rise throughout 2021 in both sexes. Antipsychotic prescriptions showed the second-highest percentage increase. Non-benzodiazepine hypnotic prescriptions showed the lowest percentage increase in both sexes from 2019 to 2021.

The number of patients prescribed sedative-hypnotics also increased during the pandemic. The number of patients prescribed antipsychotics showed the highest percentage increase (23.5% in total; 26.1% in women; 20.2% in men) among all sedative-hypnotic groups from the 2nd half of 2019 to the 2nd half of 2021 (**Supplementary Table 3**). Intermediate-acting benzodiazepines had the second-highest increase in the number of prescribed patients (20.8%) from 2019 to 2021. The increase in the number of patients prescribed antidepressants was also higher in women (15.3%) than men (11.9%) during this period.

Table 2. Number of prescriptions prescribed sedative-hypnotics during the coronavirus disease 2019 pandemic half-yearly, National Health Insurance Sharing Service, 2019–2021

Sedative-hypnotic group	Sex	2019 1°H	2019 2°H	2020 1°H	Percentage change from 2019 1°H to 2020 1°H (%)	2020 2°H	Percentage change from 2019 2°H to 2020 2°H (%)	2021 1°H	Percentage change from 2019 1°H to 2021 1°H (%)	2021 2°H	Percentage change from 2019 2°H to 2021 2°H (%)
Short-acting BDZ	Total	910,578	960,743	1,004,127	10.27	1,036,057	7.84	1,062,499	16.68	1,059,822	10.31
	Male	345,499	365,406	379,952	9.97	388,730	6.38	396,625	14.80	394,619	7.99
	Female	565,079	595,337	624,175	10.46	647,327	8.73	665,874	17.84	665,203	11.74
Intermediate-acting BDZ	Total	3,723,480	4,008,060	4,158,269	11.68	4,427,763	10.47	4,658,696	25.12	4,829,632	20.50
	Male	1,428,544	1,552,036	1,595,473	11.69	1,688,321	8.78	1,746,452	22.25	1,790,165	15.34
	Female	2,294,936	2,456,024	2,562,796	11.67	2,739,442	11.54	2,912,244	26.90	3,039,467	23.76
Long-acting BDZ	Total	2,683,084	2,864,709	3,225,076	20.20	3,478,943	21.44	3,511,248	30.87	3,481,056	21.52
	Male	1,094,630	1,191,277	1,321,344	20.71	1,418,451	19.07	1,412,814	29.07	1,391,833	16.84
	Female	1,588,454	1,673,432	1,903,732	19.85	2,060,492	23.13	2,098,434	32.11	2,089,223	24.85
Non-BDZ hypnotics	Total	5,126,414	5,251,342	5,379,940	4.95	5,467,305	4.11	5,547,698	8.22	5,601,316	6.66
	Male	2,047,206	2,114,650	2,162,160	5.62	2,204,869	4.27	2,217,303	8.31	2,235,791	5.73
	Female	3,079,208	3,136,692	3,217,780	4.50	3,262,436	4.01	3,330,395	8.16	3,365,525	7.30
Antidepressant	Total	2,773,218	2,913,887	3,817,487	37.66	4,382,903	50.41	4,550,182	64.08	4,636,066	59.10
	Male	1,088,781	1,156,845	1,508,687	38.57	1,728,226	49.39	1,768,595	62.44	1,788,415	54.59
	Female	1,684,437	1,757,042	2,308,800	37.07	2,654,677	51.09	2,781,587	65.13	2,847,651	62.07
Antipsychotic	Total	794,349	903,191	1,009,515	27.09	1,093,173	21.03	1,110,197	39.76	1,118,598	23.85
	Male	346,735	400,540	446,811	28.86	480,648	20.00	479,594	38.32	472,484	17.96
	Female	447,614	502,651	562,704	25.71	612,525	21.86	630,603	40.88	646,114	28.54

BDZ = benzodiazepine, H = half-year.

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Predicted and observed monthly prescriptions

For short-acting benzodiazepines, observed prescriptions per 1,000 populations were higher than predicted for women in both 2020 and 2021 (**Fig. 2**). Prescription rates in men exceeded

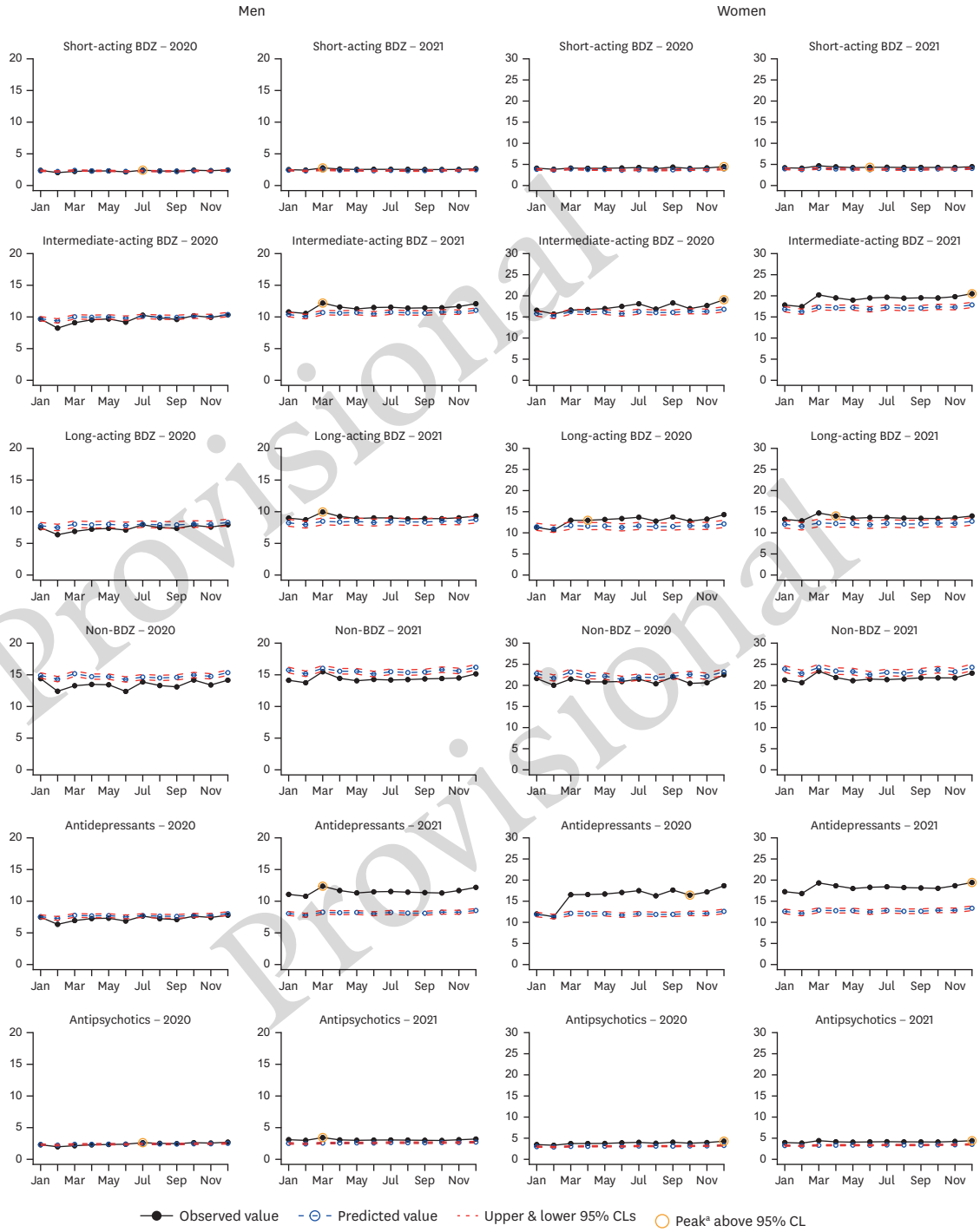

Fig. 2. Observed versus predicted number of monthly sedative-hypnotic prescriptions per 1,000 population to male and female patients, 2020–2021.
BDZ[b] = benzodiazepine, CL = confidence limit.
[a]Peaks that are significantly ($P < 0.05$) above the 95% CL are marked.
[b]Short-acting benzodiazepines include triazolam, etizolam, mexazolam. Intermediate-acting benzodiazepines include, alprazolam, bromazepam, clotiazepam, lorazepam, and clonazepam. Long-acting benzodiazepines include flunitrazepam, flurazepam, clobazam, clorazepate dipotassium, chlordiazepoxide, ethyl loflazepate.

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predicted levels from February 2021 (5.29%, $P = 0.008$) onward. The 18–29 age group exhibited significantly higher increases than predicted levels from May 2020 onward (**Fig. 3**).

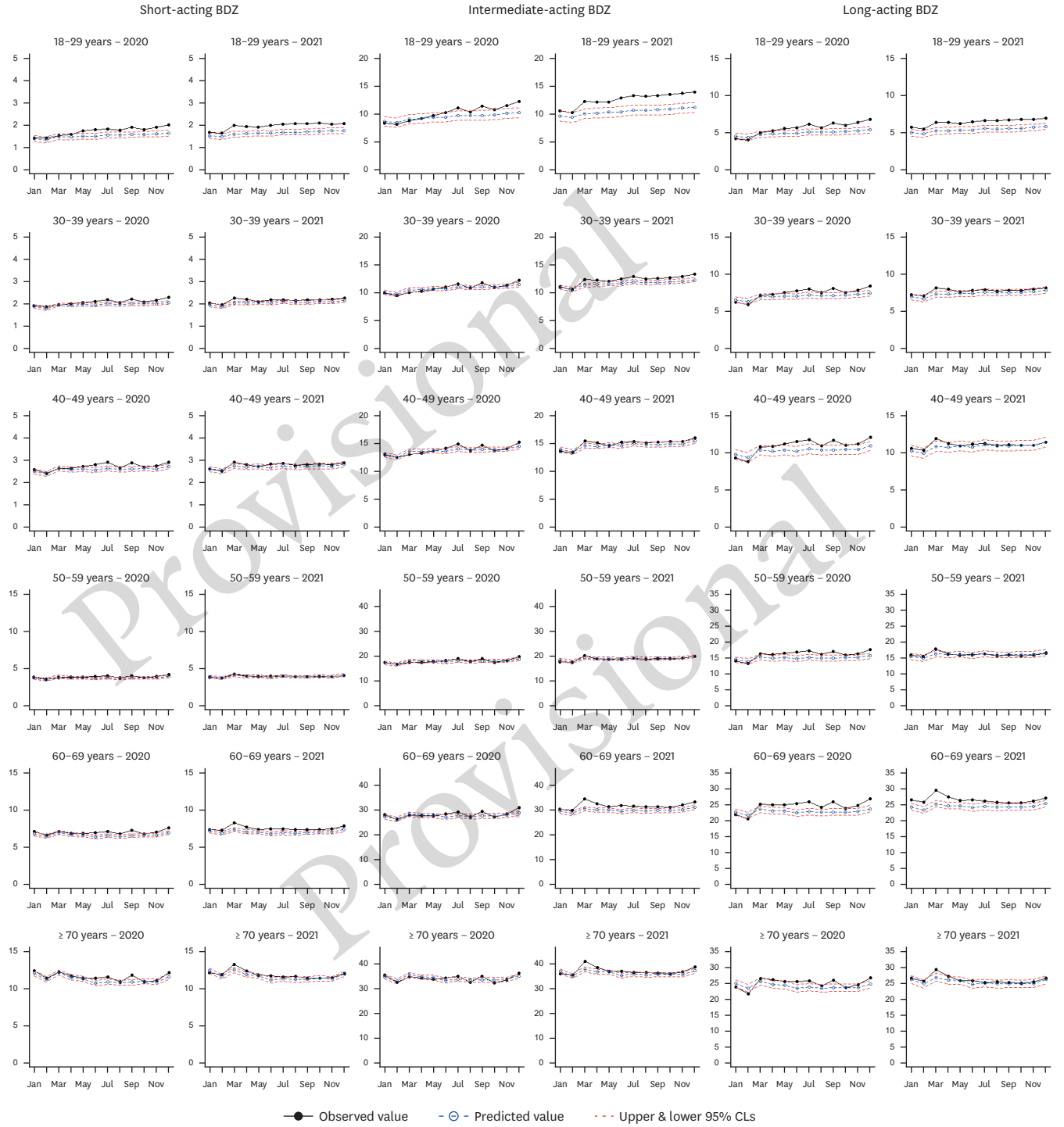

Fig. 3. Observed versus predicted number of monthly sedative-hypnotics prescriptions per 1,000 population by sedative-hypnotics group and stratified by age-group, 2020–2021.
BDZ[a] = benzodiazepine, CL = confidence limit.
[a]Short-acting benzodiazepines include triazolam, etizolam, mexazolam. Intermediate-acting benzodiazepines include, alprazolam, bromazepam, clotiazepam, lorazepam, and clonazepam. Long-acting benzodiazepines include flunitrazepam, flurazepam, clobazam, clorazepate dipotassium, chlordiazepoxide, ethyl loflazepate.

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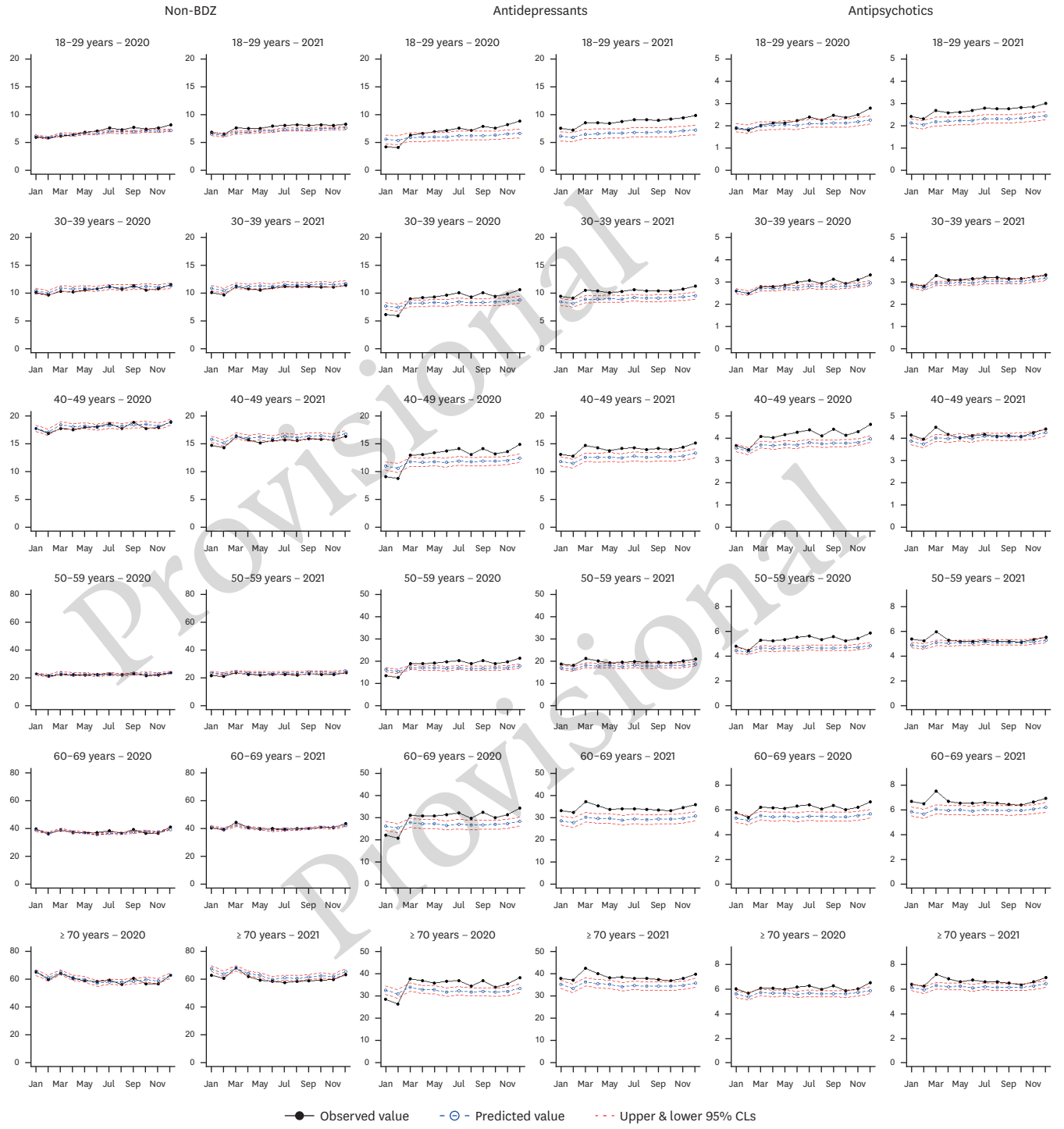

Fig. 3. (Continued) Observed versus predicted number of monthly sedative-hypnotics prescriptions per 1,000 population by sedative-hypnotics group and stratified by age-group, 2020–2021.
BDZ[a] = benzodiazepine, CL = confidence limit.
[a]Short-acting benzodiazepines include triazolam, etizolam, mexazolam. Intermediate-acting benzodiazepines include, alprazolam, bromazepam, clotiazepam, lorazepam, and clonazepam. Long-acting benzodiazepines include flunitrazepam, flurazepam, clobazam, clorazepate dipotassium, chlordiazepoxide, ethyl loflazepate.

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The observed prescription rates for intermediate-acting benzodiazepines in 2020 were lower than or within the 95% CL prediction range for men. In 2021, the rates were higher than predicted (**Fig. 2**). For women, prescriptions became significantly higher than predicted starting in May 2020 (4.6%, $P = 0.001$) and remained above predicted levels throughout 2021. In 2020, the highest increase was observed in the 18–29 age group and continued to exceed predictions throughout 2021. All age groups showed the largest monthly increases in prescriptions from February to March 2021 (**Fig. 3**).

Long-acting benzodiazepine prescriptions for men rose above predicted levels from January to April and in June 2021 (**Fig. 2**). For women, prescriptions were higher than predicted starting in March 2020 (9.42%, $P = 0.010$). Prescriptions for all age groups began increasing after March 2020, with most age groups showing prescriptions above predicted values during the 2nd half of 2020 (**Fig. 3**). In 2021, the 18–29 and 60–69 age groups had higher-than-predicted prescription rates throughout the year, with a significant peak occurring for all other age groups in March.

Non-benzodiazepine prescriptions were generally below predicted levels for both sexes in 2020 and 2021 (**Fig. 2**). Significant peaks in prescriptions were observed for men in March 2021 for all sedative-hypnotics groups except non-benzodiazepines. The 18–29 age group had higher-than-predicted prescriptions from the 2nd half of 2020 onward, while prescriptions in all other age groups remained lower than or within the predicted range (**Fig. 3**).

Antidepressant prescriptions for women showed the largest increase from February (−0.24%, $P = 0.004$) to March 2020 (26.67%, $P = 0.025$), continuing to rise throughout 2021 (**Fig. 2**). For men, prescriptions remained lower than predicted in 2020 but significantly exceeded predicted levels in 2021. All age groups showed the largest monthly increase in prescriptions from February to March 2020, with ≥ 30 age groups showing prescriptions significantly above predicted levels. Prescriptions for all age groups remained above the upper 95% CL throughout 2021, with the highest prescription rates occurring in March for ≥ 50 age groups (**Fig. 3**).

Antipsychotic prescriptions for men became higher than predicted starting in July 2020 (7.12%, $P = 0.001$) and remained high throughout 2021 (**Fig. 2**). For women, prescription rates were significantly higher than predicted from March 2020 onward. Prescriptions were higher than predicted for the 18–29 and 30–39 age groups in the 2nd half of 2020. All other age groups had higher than predicted prescription rates starting from March to December 2020 (**Fig. 3**). In 2021, all age groups showed the largest monthly increase in prescriptions from February to March. Prescription rates generally exceeded predicted levels throughout 2021 for the 18–29, 60–69, and ≥ 70 groups.

DISCUSSION

This population-based cohort study investigated the prescription trends for sedative-hypnotics in adult South Korean patients diagnosed with insomnia from 2010 to 2022 including COVID-19 pandemic period. Both the number of sedative-hypnotic prescriptions and the number of patients prescribed these medications showed a consistent increase during the study period. In 2021, prescriptions for all sedative-hypnotic groups, except non-benzodiazepines, exceeded the predicted amounts for both sexes. Notably, antidepressant

prescriptions increased more than predicted across age groups from 1st half of 2020, and this trend persisted through 2021.

The increase in sedative-hypnotic prescriptions in South Korea during the pandemic onset aligns with findings from other countries.[12-14,26-28] However, South Korea's continuous rise in sedative-hypnotics use before and during the COVID-19 pandemic appears unique. Studies in Finland,[29] France,[27] Scotland,[30] and Northern Ireland[31] observed decreases in sedative-hypnotic prescriptions during the pre-pandemic period from 2000 to 2010. During the pandemic, Poland,[32] Brazil,[33] Canada,[34] and Sweden[35] reported no changes. While hypnotic and anxiolytic prescriptions increased in Portugal[15] and England,[16] antidepressant prescriptions decreased. In populations[31,36] that saw an increase in prescriptions during the early waves of the pandemic, prescriptions later dropped to pre-pandemic levels.

The continued rise in sedative-hypnotics use likely reflects pandemic-specific social circumstances. South Korea implemented social distancing before COVID-19 was declared a pandemic. By February 29th, 2020, the public was advised to stay home, and by March, large-scale gatherings were banned and public spaces closed.[37] In December 2020, gatherings of more than four individuals were prohibited, and businesses were ordered to close by 9 p.m. We observed that most sedative-hypnotic prescriptions peaked in March 2021, three months after restrictive social distancing measures were implemented. These restrictive measures persisted into 2021 and were only eased in November 2021, which might have exacerbated insomnia symptoms.

Several factors may be associated with increased sedative-hypnotic prescription in South Korea during the COVID-19 pandemic. First, the rise in prescriptions may reflect high healthcare accessibility and hospital utilization in South Korea, including access to COVID-19-dedicated hospitals and emergency centers.[38] Second, pandemic-related disruptions—such as lockdowns and social distancing restrictions—likely altered sleep schedules, leading to circadian rhythm misalignment and sleep disturbances.[39] During the pandemic, individuals with early or late chronotypes reported sleeping longer, and individuals generally tended to sleep and wake up later.[39,40] Third, the rise in mental disorders during the pandemic, including insomnia-associated conditions such as depression, anxiety, post-traumatic stress disorder, and substance abuse, likely drove increases in sedative-hypnotic prescriptions.[41,42]

During the pandemic, South Korean women were prescribed more sedative-hypnotics than men across all drug groups, suggesting that the pandemic exacerbated sex disparities in mental health. This disparity may be due to the higher prevalence of insomnia among women,[2] with female sex identified as an aggravating factor for insomnia during the pandemic.[2,43] Overall, women were more likely to experience mental health issues as they faced greater physical, mental, and social challenges during the pandemic.[14,44] However, given that men are generally less likely to seek mental health treatment,[45] sex-based differences in treatment-seeking behaviors should be considered when interpreting prescription trends.

In 2021, antidepressants were prescribed significantly more than predicted for both sexes across all age groups, compared to other sedative-hypnotic groups. This increase may indicate a rise in insomnia cases accompanied by depression and anxiety, consistent with previous studies reporting increased mental health issues during the pandemic.[41,46,47]

Additionally, intermediate- and long-acting benzodiazepines and antipsychotics were also prescribed more than predicted for both sexes. In contrast, prescriptions for non-benzodiazepines remained within predicted ranges. Given that antidepressants, antipsychotics, and benzodiazepines are used to treat mood disorders and anxiety,[48,49] our findings may suggest an increase in insomnia accompanied by mood disorders and anxiety during the pandemic.

Zolpidem was the most frequently prescribed sedative-hypnotic agent during 2010–2022, consistent with previous studies on sedative-hypnotic use.[25,50] This prescription pattern may reflect diagnostic coding practices in South Korea, where ICD-10 codes such as F51.0 (nonorganic insomnia) and G47.0 (insomnia) are routinely used for reimbursement. Unlike benzodiazepines, which are often prescribed under diagnostic codes for anxiety disorders or mood disorders, and antidepressants or antipsychotics, which are reimbursable under mood disorder diagnoses, zolpidem is typically prescribed with a primary diagnosis of insomnia. Our use of insomnia-related codes (e.g., F51.0 or G47.0) as the basis for identifying prescriptions may have contributed to the high estimated use of zolpidem. Additionally, zolpidem is subject to a 28-day prescription limit under South Korea's national pharmaceutical regulations. This restriction may further contribute to the overrepresentation of zolpidem in insurance claims data relative to other sedative-hypnotics with longer prescription durations.

The 18–29 age group showed marked differences between observed and predicted prescriptions for all sedative-hypnotic groups. Younger adults were significantly impacted by lockdowns and experienced more mental health issues.[51-56] The shift to remote learning significantly reduced social interaction and physical activity, while lockdowns exacerbated employment difficulties.[2,57,58] These factors likely contributed to increased mental health issues, including insomnia, among young adults.[54] Additionally, we found that sedative-hypnotic prescription rates increased with age, consistent with previous findings of higher sleep disorder prevalence among older adults.[25,59] Elderly COVID-19 patients also frequently experienced delirium,[60] driving a high demand for sedative-hypnotics such as low-dose antipsychotics. Given the limited effectiveness of sedative-hypnotics,[61] their potential adverse effects in older patients,[17-23,62] and their frequent implication in suicide attempts among the elderly,[63] careful prescription monitoring is essential for older adults. Pharmacovigilance and clinical monitoring—including routine screening for insomnia and co-occurring psychiatric symptoms—are warranted to ensure safe and appropriate sedative-hypnotic prescribing practices in both the elderly and younger adults.

This study has several limitations. First, we used insurance diagnostic codes to identify patients with insomnia, which may not always reflect actual clinical diagnoses. As a result, prescriptions for insomnia patients diagnosed solely with depression or anxiety disorders might have been overlooked. However, since non-benzodiazepine prescriptions require an insomnia diagnosis, the data for these prescriptions are likely accurate. Second, we may have underestimated total number of insomnia-associated prescriptions, as certain medications used in clinical practice (e.g., olanzapine, escitalopram, paroxetine) were excluded from our analysis. These medications were excluded to reduce potential confounding effects, as they are not primarily used to treat insomnia. Third, we lacked precise data on prescription dosage, duration, and intervals. Fourth, differences in prescription periods across sedative-hypnotic groups, such as zolpidem's 28-day prescription limit, may have led to an overestimation of non-benzodiazepine prescriptions. Fifth, melatonin—a widely used

hypnotic—was not included in our analysis. Melatonin is not reimbursed under the Korean National Health Insurance system and is not recorded in insurance claims databases, making its prescription patterns difficult to assess in ICD-based analyses. The 28-day zolpidem prescription limit and the exclusion of melatonin should be considered when interpreting the distribution of sedative-hypnotic prescriptions in our study. Finally, we could not fully assess prescription trends during the entire pandemic and post-pandemic period.

Future studies should examine post-pandemic trends in sedative-hypnotic prescriptions and their associations with mental health outcomes, particularly in populations disproportionately affected by the pandemic. Growing evidence suggests that sleep disturbances, depression, and anxiety may persist following COVID-19 infection, which is often associated with various neurologic sequelae.[64] Additionally, COVID-19 patients experiencing insomnia and anxiety have reported significantly reduced quality of life.[65] These findings underscore the need to investigate how both COVID-19 infections and the pandemic period have impacted sedative-hypnotic prescribing and co-occurring psychiatric symptom trajectories. Such investigations could offer critical insights into the long-term impact of the pandemic on sleep disturbances, sedative-hypnotic prescribing behavior, and chronic psychiatric morbidity in vulnerable populations.

This study's extended study period, covering both pre-pandemic and pandemic years, provides a comprehensive analysis of prescription patterns. We observed a continuous increase in sedative-hypnotic prescriptions, with a marked rise during the COVID-19 pandemic in South Korea, particularly among women and the elderly. In 2021, prescription rates exceeded predictions for both sexes, with significant increases in all sedative-hypnotics groups among young adults. This rise suggests that COVID-19 pandemic may have exacerbated insomnia and insomnia-associated mental disorders. These findings underscore the need for monitoring sedative-hypnotic use in South Korean adults to prevent overprescribing and the potential adverse effects of these medications.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
ATC codes of sedative-hypnotics

Supplementary Table 2
Number of prescriptions for sedative-hypnotic drugs commonly used for patients with insomnia in 2010–2022, by sex

Supplementary Table 3
Number of patients prescribed sedative-hypnotics during the coronavirus disease 2019 pandemic half-yearly, 2019–2021

Supplementary Fig. 1
Number of patients prescribed sedative-hypnotics half-yearly, 2010–2022, by sex.

Supplementary Fig. 2
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 1st half of 2019 (January–June), by sex and age group.

Supplementary Fig. 3
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 2nd half of 2019 (July–December), by sex and age group.

Supplementary Fig. 4
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 1st half of 2020 (January–June), by sex and age group.

Supplementary Fig. 5
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 2nd half of 2020 (July–December), by sex and age group.

Supplementary Fig. 6
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 1st half of 2021 (January–June), by sex and age group.

Supplementary Fig. 7
Prevalence of sedative-hypnotic prescriptions for the entire South Korean population in the 2nd half of 2021 (July–December), by sex and age group.

Supplementary Fig. 8
Top 6 commonly used sedative-hypnotics drug combinations by number of prescriptions half-yearly, 2019–2021.

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