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Analysis of Prescription Trends for Narcotic Appetite Suppressants: Utilizing the Narcotics Information Management System

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Purpose: The aim of this study was to systematically analyze the prescription trends of medical narcotic appetite suppressants in South Korea.

Materials and Methods: Data was extracted from the Narcotics Information Management System dataset from 2020, which encompasses nationwide information concerning the use of medical narcotics. The selected variables for this study included the types of prescribed medical narcotic appetite suppressants, gender, age, region, and the category of medical institution. Regional prescription trends were compared by utilizing the defined daily doses for statistical purposes (S-DDD).

Results: The prescription of medical narcotic appetite suppressants was predominantly for females (94%), with the highest prescription rates identified in the 30–40 age group. The majority of these prescriptions were dispensed by clinics. Within the category of narcotic appetite suppressants, phentermine and phendimetrazine were found to have higher prescription rates. Notably, the region of Daegu recorded the highest S-DDD value (12.66) in phentermine consumption.

Conclusion: Our findings underscore the need for governmental policy and guidance to address the risks linked to the long-term use of medical narcotic appetite suppressants. This is crucial to ensure their safe and efficacious prescription and administration.

Key Words: Medical narcotic appetite suppressant, prescription trend, S-DDD

INTRODUCTION

According to the 2020 Obesity Fact Sheet issued by the Korean Society for the Study of Obesity, the prevalence of obesity in Koreans rose from 32.6% in 2009 to 38.5% in 2018, with a notable surge among younger individuals.[1]

In alignment with the 2022 Obesity Treatment Guidelines published by the Korean Society for the Study of Obesity, non-pharmacological interventions, including dietary therapy, exercise, and behavioral therapy, are the cornerstone of obesity treatment.[2] Pharmacological interventions, specifically appetite suppressants, are regarded as supplementary treatments for individuals having a body mass index (BMI) of 25 kg/m^2 or more, or a BMI of 23 kg/m^2 with other risk factors such as hypertension, diabetes, or dyslipidemia, among Koreans aged 19 years and above.[3] The primary objective in prescribing appetite suppressants is a 5%–10% weight loss after initiation of pharmacological treatment, particularly those categorized as medical narcotic appetite suppressants, warranting strict adherence to safety and appropriateness due to potential abuse and dependency.[3,4] However, tracking the appropriateness of non-reimbursable prescriptions for medical narcotics in South Korea, especially those related to plastic surgery and cosmetics, presents significant challenges. Due to the persistent misuse of medical narcotics, there has been a growing demand for the establishment of a system with a defined reporting framework. In response, the Narcotics Information Management System

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(NIMS) was launched in 2018.[5] The NIMS serves as a comprehensive platform for reporting and managing the entire process, ranging from manufacturing and importation to distribution, compounding, and administration for end-users. This system requires the reporting of handling and usage records to the Commissioner of the Ministry of Food and Drug Safety, as mandated by the Narcotics Control Act.[5] In addition, the Korea Disease Control and Prevention Agency (KDCA) strengthened the guidelines for the safe use of these substances in light of potential risks in 2020.[3] South Korea has authorized five medical narcotic appetite suppressants, including phentermine, phendimetrazine, diethylpropion, mazindol, and phentermine/topiramate. Among these, four drugs—phentermine, phendimetrazine, diethylpropion, mazindol—are sanctioned for short-term usage within a 4-week span and can be extended to a maximum of 3 months, if necessary.[3] Long-term administration of these medications has been associated with cardiovascular complications and psychological disorders, such as depression and suicidal tendencies.[6-8] A recent KDCA report highlighted an increase in instances of utilization extending beyond 3 months, underscoring inappropriate prescribing habits.[9] Consequently, the long-term use of medical narcotic appetite suppressants has led to amplified adverse effects, including the risk of dependency and psychological disturbances.[10]

Despite the current understanding, there remains a dearth of fundamental research on the prescription patterns of narcotic appetite suppressants within the country. In an attempt to fill this gap, the current study focused on the analysis of prescription trends of medical narcotic appetite suppressants across various regions and age groups, utilizing data sourced from the NIMS. Additionally, we aimed to offer insights into safe prescription practices and strategies to prevent the misuse of medical narcotic appetite suppressants.

MATERIALS AND METHODS

Data source

Data pertaining to the prescription of medical narcotic appetite suppressants were retrieved from NIMS for the year 2020.[5] The NIMS encompasses nationwide data on medical narcotics, covering aspects such as manufacturing, compounding, prescription, and administration, as reported by medical institutions and pharmacies engaged in narcotics handling. Included within the data were details on the specific type of medication, gender, age group (segmented into 10-year intervals), region, and the category of medical institution responsible for prescribing the medication.

Ethical approval was obtained from the KDCA Institutional Review Board Ethics Committee, and a waiver for informed consent pertaining to the management of retrospective data was approved by the Institutional Review Board of Yonsei University (7001988-202206-HR-1609-01E).

Data collection

Data was compiled from the NIMS between January 1, 2020, and December 31, 2020. Variables in this study encompassed prescribed medical narcotic appetite suppressants, gender, age groups (stratified by 10-year intervals), region, and the type of medical institution. Medical institutions were classified into general hospitals, hospitals, nursing hospitals, clinics, and other healthcare facilities, including dental hospitals, oriental medicine hospitals, and public health centers. The prescribing institution's location was utilized to segment the data into 17 regional local government units within South Korea. Within the NIMS dataset, individual-specific and daily prescription records are withheld for research to prevent the disclosure of patient-identifying information. Instead, aggregate data are provided, delineating the total quantity of medications prescribed according to gender, age group (organized into 10-year intervals), region, and prescribing medical institution, on a monthly basis.

Statistical analyses

The quantification of appetite suppressant usage was determined through the application of the internationally accepted measure, the defined daily doses for statistical purposes (S-DDD) rule (equation 1). The term S-DDD, replacing the prior term "defined daily doses (DDD)," is utilized by the International Narcotics Control Board (INCB) as a specialized unit of measurement for statistical analysis, and it is not indicative of a suggested prescription dose.[11] The method of using S-DDD is shown in equation 1 below.

$$\text{S-DDD per 1000 inhabitants per day} = \frac{\text{Total amount of medication (mg)}}{\text{S-DDD (mg)} \times 365 \times \text{total population}} \times 1000$$

Within this equation, the denominator incorporates the S-DDD value representing the quantity of the medication ingested by 1000 adults in a solitary day, as symbolized by DDD values in accordance with INCB protocols. The consumption of medical appetite suppressants prescribed in 2020 was computed, and in order to approximate the dosage details that were not supplied by NIMS, the recommended single dosage (mg) by KDCA was aggregated by ingredient, then translated into the total amount of medication. The total population in the denominator was derived from the 2020 population statistics as provided by Statistics Korea.[12] The resultant computations delineated the prescribed quantities of medical narcotic appetite suppressants, segregating them by medication, age demographic, geographical area, and medical institution type, as sourced from NIMS. Moreover, the relative prescription rates were analyzed by employing S-DDD. Specifically for phenter-

mine, an international comparison of consumption rates was undertaken, referencing data from the INCB annual report.[11]

All descriptive statistical analyses were performed using STATA 16 (Stata Corp, College Station, TX, USA).

RESULTS

In this study, five distinct types of medical narcotic appetite suppressants were identified, with four typically recommended for short-term prescription not exceeding a span of 12 weeks, usually limited to 4 weeks. An exception is phentermine/topiramate, which has gained approval in South Korea for long-term administration in obesity treatment (Table 1). Of the prescribed medical appetite suppressants, females received 94% of them. The age demographics were mainly focused on individuals in their 30s (32.7%) and 40s (32.3%), trailed by those in their 50s and 20s (Supplementary Table 1, only online). Notably, despite the restriction against administering medical narcotic appetite suppressants to those under 16 years old, prescriptions of diethylpropion, phentermine, and phendimetrazine were found in individuals under the age of 10. Among teenagers, diethylpropion prescription rates were elevated (11.6%) relative to other age cohorts. The prescription rates of phentermine and phendimetrazine were substantial across all ages, but an analysis showed that when adjusting for the dosage frequency, phentermine's prescription quantity was more significant. Geographically, prescriptions were predominantly observed in Seoul's capital area and Gyeonggi-province, with Daegu showing a higher prescription rate among regional metropolitan regions. Clinics were the primary setting for prescription (97.5%). With respect to the type of medical institutions, general hospitals exhibited a higher prescription rate for phentermine/topiramate (27.4%), whereas clinics presented increased prescription rates for phendimetrazine and phentermine (Table 2).

The study also compared the estimated S-DDD of medical narcotic appetite suppressants across 17 regional local government units, employing NIMS data from 2020 (Fig. 1 and Table 3). Daegu led the nationwide metropolitan cities in prescriptions per capita for both genders (S-DDD=15.66), which translates to roughly 16 out of every 1000 individuals taking 15 mg of phentermine daily (Table 3). The S-DDD values were also detected to be more elevated in regions such as Daegu and Jeollabuk-province as opposed to Seoul, Gyeonggi-province, and Incheon. Daegu, where phentermine's prescription rate was elevated (S-DDD=15.66), also had an increased prescription rate for phendimetrazine (S-DDD=7.51). In Chungcheongnam-province, both phentermine and phendimetrazine had S-DDD values exceeding 9, emphasizing the regional variations in prescription patterns.

To assess the potential seasonal effects on the prescription patterns of narcotic appetite suppressants for weight loss, we compared the monthly prescription proportions relative to the annual prescription volume for each medication (Fig. 2 and Table 4). Among the short-term approved narcotic appetite suppressants, such as phentermine and phendimetrazine, there was a relatively consistent distribution throughout the year, despite a slightly elevated prescription proportion from May to July. Conversely, mazindol exhibited a distinct pattern, with prescriptions escalating from March, reaching a peak in July, and subsequently declining. For the long-term approved medication phentermine/topiramate, a different trajectory was observed, with usage gradually increasing and stabilizing at a consistent level from July onwards.

DISCUSSION

Medical narcotic appetite suppressants should be administered with prudence, adhering to the healthcare provider's prescription guidelines.[8,13] In particular, the four medications sanctioned for short-term use are generally recommended for up to 4 weeks but can be extended to a maximum of 12 weeks if required. Despite these recommendations, the 2022 report from the Ministry of Food and Drug Safety revealed that 1.6 million patients were prescribed medical narcotic appetite suppressants, with a substantial portion receiving prescriptions extending beyond 3 months.[14] Even with the compulsory registration of all narcotics consumption through the NIMS, instances of misuse have escalated.[15] The findings of this study reflect governmental concerns. Between January and December 2020, roughly 250 million prescriptions for medical appetite suppressants were logged with NIMS. Women aged 30–40 years exhibited a higher prescription rate. Analysis of the National

Table 1. Characteristics of Medical Narcotic Appetite Suppressants

Medication	Duration	S-DDD (mg)*	Recommended single dose (mg)†	Prescription for children (Aged 16 years and below)†
Phentermine	Short	15	37.5	Do not administer
Phendimetrazine	Short	70	35.0	Do not administer
Diethylpropion	Short	75	25.0	Do not administer
Mazindol	Short	1	0.5	Do not administer
Phentermine/topiramate	Long	NA	Initial 3.75/23 mg for 2 weeks, and then 7.5/46 mg for 12 weeks†	Do not administer

*Defined daily doses for statistical purposes (S-DDD) as per the International Narcotics Control Board; †Guidelines for medical narcotic appetite suppressants as detailed in the Korea Disease Control and Prevention Agency report.

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Table 2. Prescription Distribution of Medical Narcotic Appetite Suppressants

Variables	Mazindol	Diethylpropion	Phendimetrazine	Phentermine	Phentermine /topiramate	Total
Gender						
Male	20890 (0.1)	980757 (6.9)	8055179 (56.6)	4692860 (33.0)	480064 (3.4)	14229750
Female	419644 (0.2)	13271143 (5.7)	137524832 (58.7)	79280768 (33.8)	3717731 (1.6)	234214118
Age						
Under 10 years	0 (0.0)	63 (31.0)	119 (58.6)	21 (10.3)	0 (0.0)	203
10 years	2219 (0.2)	113627 (11.6)	594248 (60.6)	248601 (25.4)	21125 (2.2)	979820
20 years	57143 (0.1)	2877960 (7.4)	24282846 (62.3)	11255704 (28.9)	488736 (1.3)	38962389
30 years	134932 (0.2)	4677815 (5.8)	47970572 (59.1)	27150070 (33.5)	1215894 (1.5)	81149283
40 years	149236 (0.2)	4079640 (5.1)	46477384 (57.8)	28230674 (35.1)	1422283 (1.8)	80359217
50 years	75414 (0.2)	2010618 (5.3)	21454644 (56.9)	13402412 (35.5)	782302 (2.1)	37725390
60 years	20608 (0.2)	470415 (5.4)	4546123 (52.1)	3434519 (39.4)	246924 (2.8)	8718589)
70 years	983 (0.2)	20461 (3.9)	244506 (46.5)	240514 (45.7)	19726 (3.7)	526190
Over 80 years	0 (0.0)	1303 (5.7)	9573 (42.0)	11111 (48.7)	806 (3.5)	22793
Region						
Seoul	48114 (0.1)	3252753 (6.9)	28788662 (61.2)	13765773 (29.3)	1165211 (2.5)	47020513
Busan	9396 (0.1)	437279 (3.5)	6230078 (50.5)	5381160 (43.7)	267044 (2.2)	12324957
Daegu	6815 (0.1)	315059 (1.5)	13306079 (64.1)	6938463 (33.5)	169267 (0.8)	20735683
Incheon	15218 (0.1)	250539 (2.2)	6337703 (56.2)	4503701 (39.9)	176806 (1.6)	11283967
Gwangju	2908 (0.1)	271284 (4.8)	2950303 (52.1)	2187781 (38.6)	254176 (4.5)	5666452
Daejeon	4859 (0.1)	2593743 (26.7)	4230815 (43.6)	2718599 (28.0)	151974 (1.6)	9699990
Ulsan	7281 (0.1)	95672 (1.7)	3171636 (57.6)	2153080 (39.1)	73937 (1.3)	5501606
Sejong-si	0 (0.0)	1730 (0.4)	165873 (37.6)	254466 (57.7)	18623 (4.2)	440692
Gyeonggi	211661 (0.4)	3180033 (5.7)	30133468 (54.1)	21241910 (38.2)	911016 (1.6)	55678088
Gangwon	1014 (0.1)	164242 (2.1)	5871750 (76.5)	1534621 (20.0)	102002 (1.3)	7673629
Chungcheongbuk	77785 (0.8)	949379 (9.8)	5866787 (60.5)	2726608 (28.1)	77835 (0.8)	9698394
Chungcheongnam	2130 (0.1)	1652919 (8.5)	13987214 (72.0)	3558825 (18.4)	192027 (1.0)	19393115
Jeollabuk	3533 (0.1)	183435 (2.3)	3567698 (44.7)	4120943 (51.7)	95896 (1.2)	7971505
Jellanam	1701 (0.1)	261506 (3.3)	4400077 (56.2)	3046507 (38.8)	126176 (1.6)	7835967
Gyeongsangbuk	16621 (0.3)	151061 (2.4)	2929739 (46.9)	3036017 (48.5)	121893 (1.9)	6255331
Gyeongsangnam	27991 (0.2)	401744 (2.1)	12466680 (66.4)	5656949 (30.2)	213066 (1.1)	18766430
Jeju	3510 (0.1)	89526 (3.6)	1175459 (47.1)	1148228 (46.0)	80847 (3.2)	2497570
Medical institution						
Hospital	1969 (0.1)	189920 (5.0)	1624281 (42.4)	1815541 (47.3)	197211 (5.2)	3828922
General hospital	741 (0.1)	59290 (3.2)	259713 (14.0)	1024636 (55.3)	507691 (27.4)	1852071
Nursing hospital	524 (0.1)	66304 (16.3)	186164 (45.6)	150646 (36.9)	4338 (1.1)	407976
Clinics	437300 (0.2)	13931644 (5.8)	143456880 (59.2)	80907736 (33.4)	3478410 (1.4)	242211970
Others	0 (0.0)	4743 (3.3)	52977 (37.1)	75064 (52.5)	10146 (7.1)	142930

Data are presented as n (%).

Health and Nutrition Examination Survey showed that although obesity rates are elevated in males, the majority of prescriptions for appetite suppressants are predominantly among females.[16] There is also an increased utilization rate of medications intended for short-term use compared to phentermine/topiramate, which is approved for extended use. This may indicate a trend toward focusing on temporary weight reduction.[17] As per the 2021 INCB report, South Korea's use of short-term appetite suppressants, such as phentermine, ranks third globally, trailing only New Zealand (S-DDD=12.11) and Chile (S-DDD=11.74), and is one of the principal importers of phentermine, following United States.[11] Among the four short-term appetite suppressants, phentermine exhibited the highest prescription dosage. This can be attributed to its ease of administration, with a daily maintenance dose of 30 mg (Phentermine HCl 37.5 mg) and an initial dose of 15 mg. Additionally, phentermine is preferred over mazindol due to its perceived safety. Mazindol has been associated with pulmonary arterial hypertension.[18] According to the INCB report comparing the S-DDD of phentermine, Daegu's prescription rate was nearly double the national average in South Korea.

Analyzing the reasons for the higher prescription rates of ap-

petite suppressants in Daegu compared to other regions presents challenges. However, a long-term study on cardiovascular disease mortality in South Korea has revealed regional differences in mortality rates. Specifically, elevated mortality rates were observed in areas such as Busan, Ulsan, and Gyeongnam.[19]

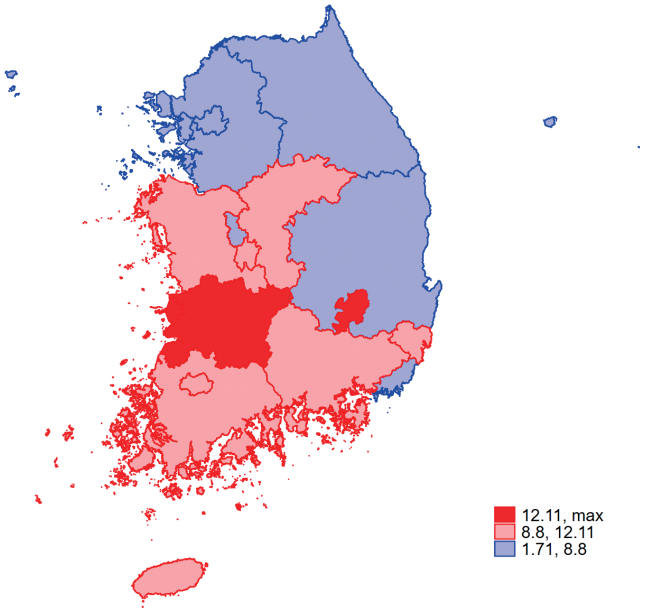

Fig. 1. Phentermine consumption in S-DDD* per 1000 inhabitants per day. Classification by phentermine consumption: Ranked first in New Zealand (S-DDD=12.11), third in South Korea (S-DDD=8.8), with the baseline being the second highest in Singapore within Asia (S-DDD=1.71) according to non-amphetamine substances in the International Narcotics Control Board annual report. *S-DDD as per the International Narcotics Control Board. S-DDD, defined daily doses for statistical purposes.

Furthermore, while the density of healthcare institutions prescribing medical narcotics per capita is higher in Daegu than in Busan and Incheon, there remains a significant knowledge gap when trying to explain the elevated rates in Daegu relative to Seoul, which boasts the highest concentration of healthcare facilities.[12]

A study on the off-label use of pharmaceuticals reported that among patient prescribed beyond the approved scope, cosmetic and plastic surgery patients constitute 26.8%.[20] Additionally, an analysis of voluntarily posted online prescription data for weight loss medications revealed that an average of seven drugs were prescribed concurrently.[21] These findings emphasize the importance of considering various factors, such as regional disparities in population composition, economic status, and healthcare resources. This includes examining the prescribing patterns of community-based primary care physicians regarding narcotic appetite suppressants.

Consequently, there is a pressing need for further research to analyze the accumulated data on narcotic appetite suppressant prescriptions over the years.

To the best of our knowledge, this study represents the first attempt to analyze the entire prescription pattern of medical narcotic appetite suppressants, taking into account geographical, gender, and drug-specific variations. Additionally, we undertook an effort to compare the INCB report's S-DDD values with domestic regional pharmaceutical consumption rates.

Our study presents several limitations. First, the primary purpose of NIMS is to gather information concerning the utilization of medical narcotics. Consequently, it does not provide specifics regarding prescriptions for medical narcotic appetite suppressants based on obesity status. Moreover, the dataset does

Table 3. Consumption of Medical Narcotic Appetite Suppressants in S-DDD* Per 1000 Inhabitants Per Day

Variables	Mazindol	Diethylpropion	Phendimetrazine	Phentermine
Seoul	0.014	0.31	4.06	7.76
Busan	0.008	0.12	2.51	8.67
Daegu	0.008	0.12	7.51	15.66
Incheon	0.014	0.08	2.95	8.38
Gwangju	0.005	0.17	2.78	8.24
Daejeon	0.009	1.61	3.94	10.13
Ulsan	0.017	0.08	3.81	10.34
Sejong-si	0.000	0.00	0.66	4.03
Gyeonggi	0.043	0.22	3.09	8.72
Gangwon	0.002	0.10	5.22	5.46
Chungcheongbuk	0.133	0.54	5.03	9.35
Chungcheongnam	0.003	0.71	9.04	9.20
Jeollabuk	0.005	0.09	2.70	12.49
Jellanam	0.003	0.13	3.25	9.01
Gyeongsangbuk	0.017	0.05	1.52	6.29
Gyeongsangnam	0.023	0.11	5.10	9.26
Jeju	0.014	0.12	2.40	9.36

*S-DDD as per the International Narcotics Control Board. S-DDD, defined daily doses for statistical purposes.

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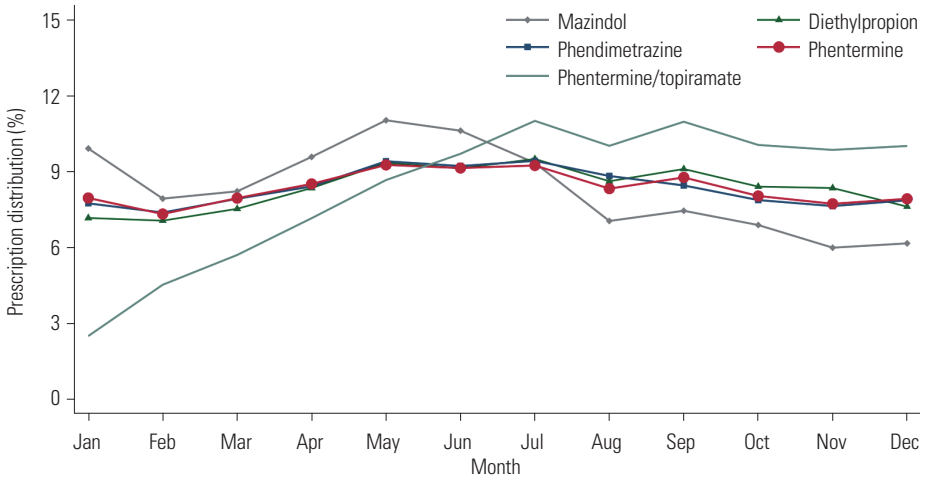

Fig. 2. Seasonal distribution of medical narcotic appetite suppressants.

Table 4. Prescription Distribution (%) of Medical Narcotic Appetite Suppressants

Month	Mazindol	Diethylpropion	Phendimetrazine	Phentermine	Phentermine/topiramate
2020.01	9.9	7.2	7.7	7.9	2.5
2020.02	7.9	7.0	7.4	7.4	4.5
2020.03	8.2	7.5	7.9	7.9	5.7
2020.04	9.6	8.3	8.4	8.5	7.1
2020.05	11.0	9.3	9.4	9.2	8.7
2020.06	10.6	9.1	9.2	9.2	9.7
2020.07	9.3	9.5	9.4	9.2	11.0
2020.08	7.0	8.6	8.8	8.3	10.0
2020.09	7.4	9.1	8.4	8.8	11.0
2020.10	6.9	8.4	7.9	8.0	10.0
2020.11	6.0	8.3	7.6	7.7	9.8
2020.12	6.1	7.6	7.9	7.9	10.0

not allow for the determination of the specific types of medications prescribed to a patient or the frequency of such prescriptions. It delivers aggregated data, merging factors, such as age, gender, location, and medical institution information to researchers. Instead of providing individual-specific data, this aggregation is conducted to safeguard against the exposure of personal information associated with narcotics prescriptions. As a result, we were unable to access individual-level information specifically for appetite suppressants and their potential misuse. However, we strived to mitigate these limitations by referencing governmental announcements, parliamentary submissions, and INCB reports.[11,14,17] Second, the S-DDD used for regional comparison is a technical unit of measurement for the purpose of statistical analysis and is not a recommended therapeutic dosage applied in clinical settings.[11] While the S-DDD is not a standard prescription unit in clinical practice, it has been frequently employed in prior research to quantify the usage of narcotic pharmaceuticals.[22,23] In this study, the S-DDD was similarly used to assess and analyze the usage patterns of medical narcotic appetite suppressants. Third, this study has inherent limitations as it is an analysis of the short-term prescription patterns of medical narcotics over 1 year, so it is challenging to explain the relatively high rate of prescription of narcotic appetite suppressants in a specific region. If future research permits the use of data spanning multiple years, a comparative study could assess whether the prescription rate of medical appetite suppressants remains consistently high in specific regions or periods. Additionally, this approach could enable an analysis of potential regional differences in population composition, socioeconomic status, and healthcare-related resources. Through such investigations, we can emphasize the critical importance of targeted medication safety education and vigilance against pharmaceutical misuse, particularly in regions or seasons experiencing an increase in prescription volumes.

Prevention of chronic diseases, such as hypertension, diabetes, and hyperlipidemia, requires concerted efforts from healthcare professionals in the context of obesity treatment.[24,25] For safe weight reduction, proper prescription and well-informed guidance concerning not only the efficacy of the medication but also potential adverse effects tied to the usage of medical nar-

cotic appetite suppressants are vital. As exemplified by the withdrawal of lorcaserin due to an elevated cancer risk, it becomes imperative for healthcare practitioners to prescribe and dispense narcotic appetite suppressants with caution, considering the uncertain safety profile for extended usage.[26] This cautious approach is necessitated, in part, due to a global lack of safety information, as most countries impose restrictions on the long-term use of specific medical narcotic appetite suppressants, such as phendimetrazine and amfepramone.[6,13]

Furthermore, the implementation of policies encouraging healthy lifestyle habits during childhood and adolescence is essential for preventing the progression to adult obesity.[27] Tailoring interventions for specific populations, such as postmenopausal women and economically vulnerable groups, is equally vital. In conclusion, there is an urgent need for governmental policies and guidance concerning the risks tied to long-term usage, ensuring the safe and effective prescription and administration of medical narcotic appetite suppressants.

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AUTHOR CONTRIBUTIONS

Conceptualization: Kyung Sun Oh and Euna Han. Data curation: Kyung Sun Oh. Formal analysis: Kyung Sun Oh. Funding acquisition: Euna Han. Investigation: Kyung Sun Oh and Euna Han. Methodology: Kyung Sun Oh and Euna Han. Supervision: Euna Han. Validation: Euna Han. Visualization: Kyung Sun Oh and Euna Han. Writing—original draft: Kyung Sun Oh. Writing—review & editing: Euna Han. Approval of final manuscript: all authors.

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