

# Pediatric Codeine Prescriptions in Outpatient and Inpatient Settings in Korea

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Codeine, an opioid alkaloid derived from opium, was first identified in 1833.<sup>1</sup> Codeine is a prodrug that is converted into morphine by cytochrome P-450 2D6 (CYP2D6) in the liver and binds to the  $\mu$ -opioid receptor in the central nervous system, thereby producing its analgesic effect.<sup>2,3</sup> Codeine has long been used in children as an analgesic and antitussive agent, and it was the most frequently used opioid medication among European children and adolescents in the early 2000s.<sup>4</sup> However, codeine toxicity has been linked to pediatric deaths.<sup>5</sup> Life-threatening or fatal toxicity of codeine was attributed to ultrarapid CYP2D6 metabolizers.<sup>6,7</sup>

Owing to safety concerns, in 2012 the World Health Organization deleted codeine from its list of recommended analgesics based on the risk associated with metabolic rate differences and the insufficient pharmacological effect due to its lower metabolism in children younger than 12 years.<sup>8</sup> Subsequently, the European Medicines Agency, the Medicines and Healthcare Products Regulatory Agency of the United Kingdom, and Health Canada also issued safety letters and guidelines recommending against the use of codeine in children younger than 12 years based on its opioid toxicity risk and suggesting a change in the drug labeling.<sup>9-11</sup> In 2013, the FDA added a black box warning to the label of codeine-containing products to restrict the postoperative use of codeine for children, which was elevated to a contraindication in 2017 alerting that codeine should not be used to treat pain or cough in children younger than 12 years.<sup>12</sup> Following the initiatives of other countries, the regulatory authority in Korea also issued a safety letter to warn about the risk of codeine use in children and, in November 2014, changed the drug label so that codeine is contraindicated in children younger than 12 years.<sup>13,14</sup>

Despite repeated warnings regarding weak opioids such as codeine, the off-label use of codeine in young patients appears to persist, emphasizing the urgency of the need to address the issue of its contraindicated use.<sup>15,16</sup> Characteristics of patients (eg, age) and healthcare providers (eg, specialty) were shown to influence opioid analgesic use and off-label prescribing to children in the United States.<sup>17,18</sup> In the United States, codeine prescriptions in the emergency department (ED) were associated with age of the patient and geographic region of the prescriber.<sup>19</sup> Odds of pediatric

## ABSTRACT

**OBJECTIVES:** To examine the extent of codeine prescriptions for children younger than 12 years in Korea and to investigate characteristics associated with pediatric codeine use.

**STUDY DESIGN:** A retrospective observational study was conducted to examine codeine prescriptions and patients' characteristics.

**METHODS:** We used the Korea Health Insurance Review and Assessment Service National Patient Sample database. The study participants were patients younger than 12 years who were prescribed codeine as inpatients or outpatients between 2011 and 2016. Pediatric codeine use was defined as codeine prescribed at least once for a child younger than 12 years. The frequency and proportion of pediatric codeine users were analyzed by age group (0-2, 3-6, or 7-11 years), sex, year, region, diagnosis, type of medical institution, and coprescribed medication. Logistic regression analyses were performed to identify characteristics associated with pediatric codeine use.

**RESULTS:** Of all patients younger than 12 years, 518,895 (55.8%) and 16,337 (1.7%) were treated with codeine in outpatient and inpatient settings, respectively. Odds of pediatric codeine prescriptions were highest for outpatients at clinics [adjusted odds ratio [OR], 1.19; 95% CI, 1.16-1.21] and public hospitals [adjusted OR, 1.56; 95% CI, 1.28-1.91] and for inpatients at public hospitals [adjusted OR, 8.38; 95% CI, 6.64-10.58].

**CONCLUSIONS:** Codeine was frequently prescribed for pediatric outpatients in Korea, especially in primary care clinics. Efforts to limit codeine use in children are required to prevent the occurrence of codeine-related adverse events.

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codeine use were higher in children outside of the Northeast United States, with poor physical health status, and with health insurance.<sup>20</sup> In Australia, codeine use was higher in areas that were more remote and those with higher percentages of males.<sup>21</sup> We reasoned that the characteristics of pediatric codeine use differ by patient setting, because inpatient use of codeine is mostly for management of postoperative pain but it is usually used as an antitussive agent in the outpatient setting.<sup>5</sup> Therefore, this study aims to examine the patterns of prescribing codeine for children younger than 12 years and to identify characteristics associated with pediatric codeine prescriptions in outpatient and inpatient settings in Korea using population-based health insurance claims data. In addition, we sought to understand if a change in prescribing practice occurred after the label change for codeine in Korea.

## METHODS

### Data

The patterns of prescribing codeine were analyzed using Health Insurance Review and Assessment Service National Patient Sample (HIRA-NPS) data. The primary aim of the HIRA-NPS database is to construct sample data representative of the Korean population for researchers to access by compiling patient visit and prescription data from National Health Insurance claims data. The data are anonymized by replacing personal information with random unique identifiers. The database includes information on general characteristics of the patient (age and sex), medical services (inpatient and outpatient procedures and inpatient prescriptions), diagnoses (specialty codes, diagnosis codes, and names), outpatient prescriptions (generic code, dose, and prescribed days), and medical institution (type, number of beds, and region).

The HIRA-NPS database contains claims data on a stratified random sample of 3% of all patients covered by the National Health Insurance system; the mandatory health insurance system covers approximately 98% of all inhabitants of Korea.<sup>22</sup> Stratified by sex and age, the patient sample was divided into a total of 32 strata (2 for sex and 16 for age) before random extraction. Different patients are selected for the sample data each year, and the patient samples are updated annually because they are developed through the accumulation of claims data over a yearlong cycle. HIRA, a government agency, has constructed and maintained the database annually since 2009. The database is publicly available to qualified researchers through HIRA's website.

### Study Participants

The study participants were patients younger than 12 years of age who received care as inpatients or outpatients in Korea between January 1, 2011, and December 31, 2016. The study drugs were drugs that contain codeine phosphate as the only analgesic and

## TAKEAWAY POINTS

- ▶ Of patients younger than 12 years in Korea, 55.8% and 1.7% were treated with codeine in outpatient and inpatient settings, respectively.
- ▶ Children were more likely to be treated with codeine in the outpatient setting at clinics and public hospitals.
- ▶ Efforts to limit codeine use in children are needed to prevent the occurrence of codeine toxicity events.

antitussive agent or codeine combination products that contain acetaminophen or ibuprofen as an active ingredient and are approved and listed as reimbursable drugs. Unlike in the United States and some European countries where low-strength codeine products are sold as over-the-counter medications, all codeine-containing products are sold as prescription-only medications in Korea. Inpatient prescriptions of codeine were analyzed separately from outpatient prescriptions owing to differences in dosage and the use of codeine for the management of postoperative pain.

### Measurements

Pediatric patients were defined as patients younger than 12 years. Pediatric codeine use was defined as the prescribing of codeine for children younger than 12 years. The proportion of pediatric patients who received a prescription for codeine was calculated by dividing the number of codeine users younger than 12 years by the number of total pediatric patients. The proportion of pediatric codeine users was calculated by patient setting (outpatient vs inpatient). The frequency and proportion of pediatric codeine use were analyzed by age group (0-2, 3-6, and 7-11 years), year, region, diagnosis, type of medical institution, and coprescribed medication.

The quarterly proportion of patients treated with codeine was plotted for inpatients and outpatients younger than 12 years. In addition, the quarterly proportion of patients treated with antibiotics was plotted to examine if it coincided with the proportion of codeine prescriptions according to seasonality. The numbers of pediatric patients and of pediatric codeine users were calculated by age group, sex, region, and clinical specialty. Pediatric patients were divided into 3 age groups (0-2, 3-6, and 7-11 years). Region was classified as metropolitan, city, or rural. Based on the classification of administrative regions provided by the government, we classified 5 megacities with surrounding satellite towns as metropolitan areas. Clinical specialties were grouped into pediatrics and nonpediatrics. The type of medical institution was divided into tertiary hospitals, general hospitals, clinics, and public hospitals.

### Statistical Analysis

The Mantel-Haenszel  $\chi^2$  test was performed for categorical data. Multivariate logistic regression was performed to identify characteristics associated with pediatric codeine prescriptions in each patient setting (outpatient and inpatient). Independent variables were sex, region, diagnosis, type of medical institution, and

coprescribed medication. An adjusted odds ratio (OR) with 95% CI was calculated for each variable. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc; Cary, North Carolina). The study protocol was approved by the Sungkyunkwan University Institutional Review Board (IRB No. 2016-10-015).

## RESULTS

A total of 929,358 and 957,746 patients younger than 12 years were treated in outpatient and inpatient settings, respectively, between 2011 and 2016 (Table 1). Of these patients, 518,895 (55.8%) and 16,337 (1.7%) patients were codeine users in those settings. The mean ages of these users were 5.5 and 4.2 years, respectively. Infants 2 years and younger comprised 22.7% and 40.3% of all pediatric codeine users in the outpatient and inpatient settings, respectively. In the outpatient setting, 51.1% of pediatric codeine users were treated in metropolitan areas. The most frequent diagnoses for pediatric codeine users were acute bronchitis (83.4% of outpatients and 91.0% of inpatients) and acute upper respiratory infection (81.0% and 88.6%, respectively). Antibiotics were coprescribed in 76.8% and 73.7% of outpatients and inpatients, respectively. In the outpatient and inpatient settings, 82.9% and 48.1% of pediatric codeine users were treated at clinics.

In both outpatient and inpatient settings, boys were as likely to be prescribed codeine as girls (Table 2). The odds of pediatric codeine prescribing in the outpatient setting were higher in nonmetropolitan areas than in metropolitan regions. Children diagnosed with acute upper respiratory infection were 1.62 to 2.22 times more likely to be prescribed codeine than those without the diagnosis. Pediatric outpatients were more likely to receive codeine at clinics (adjusted OR, 1.19; 95% CI, 1.16-1.21) and public hospitals (adjusted OR, 1.56; 95% CI, 1.28-1.91) than at tertiary hospitals; inpatients were more likely to receive codeine at public hospitals (adjusted OR, 8.38; 95% CI, 6.64-10.58) than at tertiary hospitals. The odds of pediatric codeine prescriptions were increased with coprescribing of antibiotics but were decreased with coprescribing of opioid analgesics in both settings.

The proportion of pediatric patients treated with codeine showed little change in the temporal trend (Figure). The proportion of patients prescribed antibiotics tended to fluctuate together with the proportion of pediatric outpatients prescribed codeine. There appears to be seasonality for the proportion of outpatient codeine users.

## DISCUSSION

By analyzing population-based National Health Insurance claims data, we showed that 55.8% and 1.7% of patients younger than 12 years were treated with codeine in the outpatient and inpatient settings, respectively. The extent of codeine prescriptions for children appears to be remarkably higher in Korea than in other countries. Between 2000 and 2005, the prescription rate of codeine for children younger than 12 years by primary care providers in the United Kingdom was 0.11 patients per 1000 person-years, whereas the rate was 1.32 in adolescent patients aged 12 to 17 years.<sup>4</sup> The prescription rate

of codeine for children in the ED in the United States was 3.3% in patients aged 3 to 7 years and 4.5% in those aged 8 to 12 years.<sup>19</sup> Another US study showed that although an acetaminophen–codeine combination was among the most frequently used drugs among all hospitalized patients, it was not frequently used for patients younger than 12 years.<sup>23</sup>

We showed that codeine was frequently prescribed in primary care clinics in the Korean outpatient setting. Codeine was frequently prescribed for treatment of upper respiratory infections, acute bronchitis, and asthma. Moreover, children who were prescribed antibiotics were more likely to be prescribed codeine than those who were not. Simultaneous fluctuations in the proportion of codeine users in the outpatient setting and the proportion of antibiotic users revealed that codeine was used to treat upper respiratory infections. These findings suggest that codeine was used as an antitussive agent. The prevalence of bronchitis and asthma is high among children with the common symptom of cough and, therefore, codeine is commonly used in children as an antitussive agent.<sup>24</sup> Codeine has long been recommended as an antitussive agent that acts in the central nervous system against acute and chronic cough among children.<sup>25-27</sup> However, evidence exists that codeine should not be used for cough due to pneumonia in infants owing to the risk of toxicity.<sup>28</sup> Our findings and those of other studies suggest that physicians should be guided against prescribing codeine for children in the outpatient setting based on recent evidence and international guidelines.

Our findings showed that in both outpatient and inpatient settings, the proportion of pediatric patients who were prescribed codeine was lower in 2013 than in 2011 and 2012, which may be attributable to a safety letter issued by the Ministry of Food and Drug Safety of Korea in 2012.<sup>13</sup> After a slight uptick in 2014, the proportion fell back to even lower levels in 2015 and 2016, suggesting the possible impact of the label change in November 2014. Nonetheless, the extent of codeine prescriptions for children younger than 12 years remained substantial; approximately half of pediatric outpatients were treated with codeine in 2015 and 2016 after the label change. These findings highlight the need for more efforts to reduce pediatric codeine use in Korea. Similarly, since the release of the 2006 guidelines on codeine use among children by the American Academy of Pediatrics in the United States, prescribing of codeine for children and adolescents 17 years and younger did not decrease much.<sup>19</sup> In contrast, the prescription rate of codeine decreased by approximately 60% in Italy after the issuance of a safety letter against use of codeine in infants younger than 2 years in 2007.<sup>29</sup>

The results of the logistic regression analysis showed that pediatric codeine use tends to be greater in public hospitals than in tertiary hospitals in both outpatient and inpatient settings and that outpatient codeine use is higher in clinics and in tertiary hospitals. Our findings also showed that pediatric outpatients are more likely to be treated with codeine in metropolitan areas than in nonmetropolitan areas; the reverse is true for pediatric inpatients. These findings highlight the areas of intervention for clinical practice change. Efforts to improve prescribing behaviors should be directed

**TABLE 1.** Characteristics of Pediatric Codeine Users in Outpatient and Inpatient Settings, 2011-2016\*

Characteristic	Patients Younger Than 12 Years		Codeine Users Younger Than 12 Years		Proportion, % (codeine users / patients)	
	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient
Number of users younger than 12 years	929,358	957,746	518,895	16,337	55.8	1.7
Mean (SD) age in years	5.8 (3.3)	5.8 (3.3)	5.5 (3.2)	4.2 (3.1)		
Age group in years						
0-2	203,756 (21.9)	208,705 (21.8)	117,919 (22.7)	6584 (40.3)	57.9	3.2
3-6	322,667 (34.7)	328,318 (34.3)	196,007 (37.8)	5764 (35.3)	60.7	1.8
7-11	402,935 (43.4)	420,723 (43.9)	204,969 (38.5)	3989 (24.4)	50.9	0.9
Sex						
Male	481,776 (51.8)	495,936 (51.8)	268,953 (51.8)	8835 (54.1)	55.8	1.8
Female	447,582 (48.2)	461,810 (48.2)	249,942 (48.2)	7502 (45.9)	55.8	1.6
Year						
2011	156,556 (16.8)	161,462 (16.9)	90,394 (17.4)	2903 (17.8)	57.7	1.8
2012	144,084 (15.5)	147,959 (15.4)	84,061 (16.2)	2605 (15.9)	58.3	1.8
2013	125,628 (13.5)	129,948 (13.6)	70,068 (13.5)	1727 (10.6)	55.8	1.3
2014	169,363 (18.2)	174,256 (18.2)	101,116 (19.5)	3637 (22.3)	59.7	2.1
2015	167,402 (18.0)	173,015 (18.1)	83,814 (16.2)	2744 (16.8)	50.1	1.6
2016	166,325 (17.9)	171,106 (17.9)	89,442 (17.2)	2721 (16.7)	53.8	1.6
Region						
Metropolitan	463,048 (49.8)	479,429 (50.1)	265,305 (51.1)	5270 (32.3)	57.3	1.1
City	193,225 (20.8)	200,817 (21.0)	106,795 (20.6)	4265 (26.1)	55.3	2.1
Rural	272,828 (29.4)	277,369 (29.0)	146,653 (28.3)	6800 (41.6)	53.8	2.5
Clinical specialty						
Pediatrics	760,064 (81.8)	841,441 (87.9)	447,031 (86.2)	15,604 (95.5)	58.8	1.9
Not pediatrics	169,294 (18.2)	116,305 (12.1)	71,864 (13.8)	733 (4.5)	42.4	0.6
Diagnosis						
Acute upper respiratory infection (J00-J06)	696,818 (75.0)	715,027 (74.7)	432,812 (83.4)	14,868 (91.0)	62.1	2.1
Acute bronchitis (J20-J22)	660,270 (71.0)	663,659 (69.3)	420,148 (81.0)	14,467 (88.6)	63.6	2.2
Otitis media (H65-H67)	199,340 (21.4)	204,954 (21.4)	132,490 (25.5)	5740 (35.1)	66.5	2.8
Pneumonia (J12-J18)	96,659 (10.4)	110,021 (11.5)	66,602 (12.8)	7260 (44.4)	68.9	6.6
Asthma (J45-J46)	108,628 (11.7)	111,039 (11.6)	75,011 (14.5)	3878 (23.7)	69.1	3.5
Influenza (J09-J11)	3591 (0.4)	4539 (0.5)	2276 (0.4)	290 (1.8)	63.4	6.4
Insurance type						
Employee or self-employed insured	909,833 (97.9)	937,374 (97.9)	507,366 (97.8)	15,692 (96.1)	55.8	1.7
Medical aid beneficiary	19,525 (2.1)	20,372 (2.1)	11,529 (2.2)	645 (3.9)	59.0	3.2
Type of medical institution						
Tertiary hospital	64,154 (6.9)	111,236 (11.6)	34,963 (6.7)	4356 (26.7)	54.5	3.9
General hospital	100,460 (10.8)	104,491 (10.9)	53,258 (10.3)	3967 (24.3)	53.0	3.8
Clinic	763,846 (82.2)	736,288 (76.9)	430,213 (82.9)	7865 (48.1)	56.3	1.1
Public hospital	641 (0.1)	1158 (0.1)	319 (0.1)	115 (0.7)	49.8	9.9
Coproscripted medication						
Antibiotic	454,743 (48.9)	65,321 (6.8)	398,382 (76.8)	12,040 (73.7)	87.6	18.4
Opioid analgesic	1607 (0.2)	9933 (1.0)	1303 (0.3)	597 (3.7)	81.1	6.0
NSAID	322,821 (34.7)	57,575 (6.0)	268,879 (51.8)	10,332 (63.2)	83.3	17.9
Acetaminophen	340,503 (36.6)	42,180 (4.4)	291,166 (56.1)	8588 (52.6)	85.5	20.4

NSAID indicates nonsteroidal anti-inflammatory drug.

\*Except for rows of number of users and age, results are presented as n (%).

**TABLE 2.** ORs of Pediatric Codeine Prescriptions in Outpatient and Inpatient Settings

Characteristic	Outpatient		Inpatient	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
<b>Sex</b>				
Male	1.00 (0.99-1.01)	1.01 (1.00-1.02)	1.10 (1.07-1.13)	1.01 (0.97-1.04)
Female	Reference	Reference	Reference	Reference
<b>Region</b>				
Metropolitan	Reference	Reference	Reference	Reference
City	0.92 (0.91-0.93)	0.91 (0.90-0.92)	1.95 (1.87-2.03)	1.29 (1.23-1.35)
Rural	0.87 (0.86-0.88)	0.87 (0.86-0.89)	2.26 (2.18-2.35)	1.57 (1.50-1.63)
<b>Diagnosis</b>				
Acute upper respiratory infection (J00-J06)	2.79 (2.76-2.82)	2.22 (2.20-2.25)	3.49 (3.31-3.68)	1.62 (1.53-1.72)
Acute bronchitis (J20-J22)	3.02 (2.99-3.05)	1.70 (1.68-1.73)	3.48 (3.32-3.66)	1.34 (1.27-1.41)
Otitis media (H65-H67)	1.76 (1.74-1.78)	0.97 (0.96-0.99)	2.02 (1.95-2.09)	0.92 (0.89-0.96)
Pneumonia (J12-J18)	1.86 (1.84-1.89)	1.03 (1.01-1.05)	6.53 (6.33-6.74)	1.65 (1.59-1.71)
Asthma (J45-J46)	1.89 (1.87-1.92)	1.43 (1.40-1.45)	2.42 (2.34-2.51)	1.59 (1.53-1.66)
Influenza (J09-J11)	1.37 (1.28-1.47)	1.68 (1.55-1.84)	3.99 (3.54-4.49)	1.73 (1.50-2.01)
<b>Type of medical institution</b>				
Tertiary hospital	Reference	Reference	Reference	Reference
General hospital	0.94 (0.92-0.96)	0.82 (0.79-0.84)	0.97 (0.93-1.01)	0.87 (0.83-0.92)
Clinic	1.08 (1.06-1.09)	1.19 (1.16-1.21)	0.27 (0.26-0.28)	0.67 (0.64-0.70)
Public hospital	0.83 (0.71-0.97)	1.56 (1.28-1.91)	2.71 (2.23-3.29)	8.38 (6.64-10.58)
<b>Coprescribed medication</b>				
Antibiotic	20.77 (20.54-21.00)	10.46 (10.33-10.60)	46.71 (45.06-48.41)	9.43 (8.96-9.92)
Opioid analgesic	3.40 (3.00-3.85)	0.79 (0.68-0.91)	3.79 (3.48-4.12)	0.77 (0.70-0.85)
NSAID	7.11 (7.03-7.18)	1.56 (1.53-1.58)	32.57 (31.50-33.66)	3.41 (3.26-3.57)
Acetaminophen	9.36 (9.26-9.46)	2.71 (2.70-2.74)	29.95 (28.99-30.94)	2.84 (2.72-2.96)

NSAID indicates nonsteroidal anti-inflammatory drug; OR, odds ratio.

toward clinics where a majority of pediatric patients were treated with codeine in the outpatient setting. Furthermore, efforts should be focused on outpatient use of codeine in the metropolitan areas.

### Strengths and Limitations

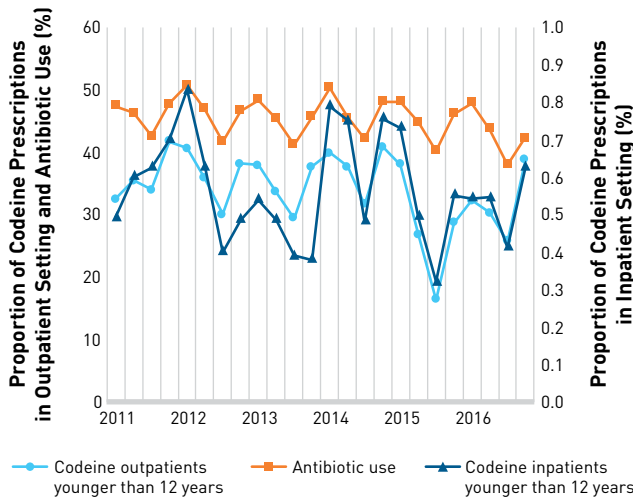
By using population-based insurance claims data, this study analyzed the patterns of codeine prescriptions in children younger than 12 years in Korea. All drugs containing codeine in Korea are

prescription-only medications and use of these drugs is recorded in the HIRA database used for this study. This makes it possible to accurately measure children's exposure to these drugs. Nonetheless, this study also has limitations. First, although we showed that the proportions of pediatric patients treated with codeine tended to decrease in 2015 and 2016, these findings are only descriptive. Second, it is possible that codeine may have been prescribed as a nonreimbursable drug in the ED. Furthermore, the use of codeine for which claims have not been filed to the payer would not have been captured in the HIRA database. If children younger than 12 years visit the ED more frequently than older patients, this study may have underestimated the use of codeine prescriptions for children. Third, our finding of the high proportion of pediatric patients who were prescribed codeine in the outpatient setting should be interpreted with caution due to the actual practice of patient care in Korea. All patients who receive injectable drugs are classified as inpatient, and injectable use is high in Korea.

Despite these limitations, this study generated valuable evidence that codeine has been widely prescribed for children younger than 12 years in Korea, especially in the outpatient setting, even after the 2014 label change. Our findings suggest that various efforts to further limit pediatric use of codeine should be developed and implemented. One such measure shown to be effective in the United States was a clinical intervention program including prescriber education.<sup>30</sup> The effective use of nonopioid analgesics may significantly reduce or even eliminate the need for opioids such as codeine.<sup>15</sup> Healthcare providers should be guided on alternative pain management in children based on recent evidence on safety and efficacy.<sup>31</sup> Based on our findings, such efforts to restrict prescriptions of codeine among young patients should not only reach major sources of

prescriptions, such as metropolitan areas, but also include general hospitals and clinics in nonmetropolitan areas in Korea. Meanwhile, informing parents of pediatric patients about the risks of pediatric codeine use may also be helpful to influence clinical practice. In addition, it is important on the nationwide level to systematically monitor codeine use and harms in the pediatric population and to develop policy measures to encourage healthcare providers to comply with contraindication of codeine in pediatric patients for

**FIGURE.** Trends of Antibiotics and Codeine Use Proportion in Inpatient and Outpatient Settings in Korea, 2011-2016



analgesic and antitussive effects; an example would be limiting reimbursement for off-label use of codeine.

## CONCLUSIONS

The guidelines published by many international and national organizations based on risk-benefit assessment of codeine recommend that codeine should not be prescribed for children younger than 12 years. This study showed that codeine was frequently prescribed for children younger than 12 years despite the actions taken to restrict the use of codeine in that age group in Korea as well as in many other countries. Children were more likely to be treated with codeine at clinics and public hospitals in the outpatient setting. Our findings suggest that codeine is used for its antitussive effect among children in the outpatient setting. Further efforts to limit codeine use, especially as an antitussive agent in primary care clinics in the outpatient setting, are needed to prevent the occurrence of codeine toxicity events among children younger than 12 years. ■

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