Brief Report

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Trends in the prescription of constipation medications in Japan (fiscal years 2019-2023): A nationwide baseline study prior to the 2023 clinical guidelines

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SUMMARY: Constipation is a common gastrointestinal disorder that markedly affects health and quality of life. In Japan, magnesium-based and contact laxatives have long been widely prescribed. Since the launch of lubiprostone in November 2012, several new agents with novel mechanisms have been introduced, and their use has increased. However, to our knowledge, no nationwide study has examined their use. This study aimed to analyze nationwide trends and regional differences in the prescription of medications for constipation. We used data from the Japanese National Health Insurance Claims and Specific Health Checkup Database Open Data from fiscal years (FYs) 2019 to 2023, covering the period when all currently available constipation medications were on the market in Japan, and prior to the inclusion of the drug selection flowchart in the Evidence-Based Clinical Guidelines for Chronic Constipation 2023. Prescription trends were evaluated using defined daily doses per 1,000 inhabitants per day (DID), and regional variations were assessed using standardized claim ratios (SCRs). The DID for contact laxatives decreased during the study period, whereas the DID for other constipation medications increased. Magnesium oxide showed the smallest regional variation, whereas polyethylene glycol and linaclotide showed the largest variations in FY 2019 and FY 2023, respectively. Throughout the 5-year period, the highest SCRs for contact laxatives were observed in Akita, Iwate, and Aomori prefectures. Our findings provide a comprehensive nationwide picture of evolving constipation treatment patterns and regional variations in Japan, establishing baseline data for evaluating the impact of guideline dissemination and evidence accumulation on clinical practice.

Keywords: constipation, contact laxatives, daily dose per 1,000 inhabitants per day, standardized claim ratio

1. Introduction

Constipation is a condition in which defecation is difficult, unsatisfactory, or infrequent. While constipation is a commonly occurring condition, chronic constipation may affect long-term prognosis, as it is associated with an increased risk of cardiovascular disease and mortality (*1-3*) as well as an elevated risk of developing Parkinson's disease (*4*) and kidney disease (*5*). In Japan, magnesium-based and contact laxatives have been predominantly used for the treatment of constipation. However, since the launch of lubiprostone in November 2012, multiple therapeutic agents with novel mechanisms of action have been developed, and their use has increased.

In the Evidence-Based Clinical Guidelines for Chronic Constipation 2023, published by the Japanese Society of Gastroenterology in July 2023, a flowchart of the diagnosis of chronic constipation and the associated therapeutic drug selection was presented (*6*). Prior to this publication, physicians provided empirical treatments in the absence of clearly defined treatment algorithms. In addition, previous surveys investigating the actual usage of constipation medications in Japan have suggested regional variations in the use of magnesium-based and contact laxatives (*7*). However, to date, no study has been conducted on the actual usage patterns of lubiprostone or subsequently launched medications, including linaclotide, elobixibat, naldemedine, and polyethylene glycol.

Recently, the Ministry of Health, Labour and Welfare (MHLW) published the Japanese National Health Insurance Claims and Specific Health Checkup Database Open Data (NDB-OD) online, providing several summary files based on the NDB data. The NDB-OD (including prescription data from April 1, 2014, to March 31, 2015) was first released in October 2016 and has been updated annually thereafter (*8*). Since NDB-OD can be used to understand Japanese healthcare in a simple and comprehensive manner, the number of studies utilizing NDB-OD has been increasing (*6,9,10*).

Furthermore, epidemiological studies using NDB-OD may be useful for monitoring the actual usage patterns of medications (*10*).

This study aimed to examine the real-world use of constipation medications in Japan over a 5-year period from fiscal years (FYs) 2019 to 2023. This study period encompasses both the time before and after the introduction of the drug selection flowchart in the Evidence-Based Clinical Guidelines for Chronic Constipation 2023, which were published in July 2023, and predominantly precedes their publication. This would allow us to establish baseline data for evaluating the impact of guideline dissemination and evidence accumulation on clinical practice.

2. Materials and Methods

2.1. Data source

We obtained the 6th, 7th, 8th, 9th, and 10th NDB-OD datasets from the MHLW website (*https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000177182.html*; accessed July 7, 2025); the collection periods corresponded to FYs 2019 (April 1, 2019, to March 31, 2020), 2020 (April 1, 2020, to March 31, 2021), 2021 (April 1, 2021, to March 31, 2022), 2022 (April 1, 2022, to March 31, 2023), and 2023 (April 1, 2023, to March 31, 2024), respectively. The NDB-OD provides information about pharmaceuticals with high prescription volumes, categorized by three-digit therapeutic classification codes, and low-frequency products are excluded. Furthermore, the actual prescription volumes of oral medications with prescription volumes ≤ 1,000 are anonymized. Two types of files containing data on prescribed oral medications were available: one stratified by sex and 5-year age groups and the other categorized by the 47 prefectures in Japan. In this study, we extracted records for sennoside, sodium picosulfate, magnesium oxide, polyethylene glycol, lubiprostone, linaclotide, elobixibat, and naldemedine prescribed to inpatients and outpatients both within hospitals and at external pharmacies.

2.2. Assessing the time trend of constipation medication use nationwide in Japan

To compare the use of constipation medications in each FY, the defined daily dose (DDD) per 1,000 inhabitants per day (DID) was calculated according to the DDD of the World Health Organization (WHO) (ATC / DDD Index 2025: *https://atcddd.fhi.no/atc_ddd_index/*).

DID = (constipation medications (g, mg, μg) × 1000)/(WHO DDD or assumed DDD (g, mg, μg) × population × 365)

However, the WHO has not established a DDD for sennosides, lubiprostone, or elobixibat, and that for magnesium oxide (7 g) is considerably higher than the standard daily dose in Japan (2 g). Therefore, in this study, the assumed DDDs for these drugs were based on the dosages specified in the Japanese package inserts. The WHO DDDs and assumed DDDs for each constipation medication are presented in Table 1. Population data for each year were obtained from e-Stat (*https://www.e-stat.go.jp/*).

2.3. Constipation medication prescribing across regions

Based on previous reports (*9,11*), the standardized claim ratios (SCRs), adjusted for both sex ratio and age distribution, were calculated as an index showing the level of medical claims in the target prefectures relative to all of Japan (100 for Japan). This index was calculated using the following formula,

SCR = (Observed number of claims / Expected number of claims) × 100,

where the observed number of claims is the total number of claims in a target prefecture in a year, and the expected number of claims is the number of claims in a year if the situation of submitting claims (sex- and age-specific claims rates) for all of Japan is assumed for the population in the target prefecture. The expected number of claims was calculated using the following formula,

Expected number of claims = ∑ [(population of a sex and age group in a target prefecture) × (sex and age specific claim rate of the sex and age group in whole Japan)],

where sex- and age-specific groups comprised 36 groups of various combinations of sex (males, females)

Table 1. Target constipation medications, ATC codes, and defined daily doses

Drugs	WHO ATC code (Classification)	WHO DDD	Daily dosage indicated in the Japanese package insert	WHO DDD or assumed DDD value used to calculate DID
Sennosides	A06AB06 (Contact laxatives)	NA	12 –24 mg	12 mg
Sodium picosulfate	A06AB08 (Contact laxatives)	5 mg	5 –7.5 mg	5 mg
Magnesium oxide	A06AD02 (Osmotically acting laxatives)	7 g	2 g	2 g
Polyethylene glycol	A06AD15 (Osmotically acting laxatives)	10 g	13.125 g	10 g
Lubiprostone	A06AX03 (Other drugs for constipation)	NA	48 μg	48 μg
Linaclotide	A06AX04 (Other drugs for constipation)	0.29 mg	0.5 mg	0.29 mg
Elobixibat	A06AX09 (Other drugs for constipation)	NA	10 mg	10 mg
Naldemedine	A06AH05 (Other drugs for constipation)	0.2 mg	0.2 mg	0.2 mg

WHO, World health Organization; ATC, Anatomical Therapeutic Chemical; DDD, defined daily dose.

and age groups (aged 0-4, 5-9,…., 85 and over).

2.4. Statistical analyses

Trends in the consumption of constipation medications were evaluated using linear regression analysis. Statistical significance was set at $p < 0.05$. To assess regional variation, the coefficient of variation (CV) of SCRs and the Pearson correlation coefficient between FYs 2019 and 2023 were calculated. All statistical analyses were performed using Microsoft Excel 2018 (Microsoft Corp., Redmond, WA, USA) and JMP Student Edition 18 (SAS Institute, Inc., Cary, NC, USA).

2.5. Ethics

The data used in this study were obtained from the NDB-OD, a publicly available and fully anonymized dataset. We consulted our institutional ethics committee regarding the ethical handling of this study. Based on the consultation, it was confirmed that the NDB-OD consists solely of statistical information from which all correspondence to specific individuals has been completely eliminated, and therefore falls outside the scope of the ethical guidelines stipulated by our institution. Accordingly, formal ethical review and informed consent were not required.

3. Results and Discussion

Chronic constipation is a highly prevalent gastrointestinal disorder frequently encountered in gastroenterology and various medical specialties (*12*). Studies investigating the impact of various functional gastrointestinal disorders (including constipation) on survival have reported that chronic constipation is associated with a significantly higher risk of reduced survival than other disorders, warranting careful clinical consideration (*13*). Therefore, standardizing constipation treatment is important, and it is necessary to understand the current situation. The present study elucidated the trends and regional variations in the use of constipation medication in Japan from FY 2019 to FY 2023 using the NDB-OD.

The DIDs for constipation medications are shown in Table 2. Among them, sennosides had the highest DID, followed by magnesium oxide, and this ranking remained consistent over the 5-year period. The use of contact laxatives (sennosides [from 23.58 to 19.39, $p < 0.001$] and sodium picosulfate [from 7.18 to 6.66, $p = 0.016$]) consistently declined, whereas the use of other medications for constipation consistently increased. Polyethylene glycol showed the highest rate of increase in DID (slope = 0.562, $p < 0.001$) among all constipation medications. The DID of naldemedine, which is indicated for opioid-induced constipation (OIC), also showed a modest increase (slope = 0.047, $p = 0.005$).

These findings suggest that the emergence of new drugs for chronic constipation and their increased utilization may have contributed to the decline in the use of contact laxatives. Contact laxatives take effect within a few hours, but they can cause side effects such as watery diarrhea, abdominal pain, dehydration, and electrolyte imbalance (*14*). The long-term use of contact laxatives can also lead to tolerance and dependence; therefore, they should be prescribed with caution (*15*). In addition, the chronic use of sennosides has been reported to be associated with the development of melanosis coli, colorectal adenoma, and/or carcinoma (*16-18*). Therefore, the use of contact laxatives should be kept to a minimum and, whenever possible, administered on an as-needed basis or for short-term use. Magnesium oxide, an osmotically acting laxative, was also frequently used in Japan during the study period, and its DID increased slightly from 17.00 to 17.65 ($p = 0.032$). Cases of hypermagnesemia associated with magnesium oxide use have been reported in patients with impaired renal function and older patients; therefore, it is necessary to appropriately monitor serum magnesium levels and symptoms of hypermagnesemia (*19,20*). Another osmotically acting laxative, polyethylene glycol, also showed an increase in the DID (from 0.70 to 3.00, $p < 0.001$). Polyethylene glycol has been available for prescription in Japan since 2018, and it can be administered to children aged 2 years or older. Moreover, polyethylene glycol is minimally absorbed and does not carry specific warnings for patients with impaired renal function. Polyethylene glycol is a relatively new drug, and its cost is higher than that of magnesium oxide. Therefore, polyethylene glycol is primarily considered a feasible treatment option for patients for whom magnesium oxide

Table 2. Time trends in the nationwide utilization of constipation medications (defined daily doses per 1,000 inhabitants per day)

Drugs	FY 2019	FY 2020	FY 2021	FY 2022	FY 2023	Slope	95% CI	*p*-value
Sennosides	23.58	22.58	21.77	20.63	19.39	-1.033	-1.179 to -0.887	< 0.001
Sodium picosulfate	7.18	7.04	7.08	6.84	6.66	-0.124	-0.206 to -0.042	0.016
Magnesium oxide	17.00	17.24	17.62	17.64	17.65	0.170	0.027 to 0.313	0.032
Polyethylene glycol	0.70	1.44	2.03	2.46	3.00	0.562	0.461 to 0.663	< 0.001
Lubiprostone	2.03	2.14	2.28	2.37	2.51	0.119	0.106 to 0.132	< 0.001
Linaclotide	1.16	1.36	1.56	1.67	1.80	0.159	0.121 to 0.197	< 0.001
Elobixibat	0.77	1.12	1.45	1.73	1.99	0.305	0.269 to 0.341	< 0.001
Naldemedine	0.17	0.19	0.23	0.28	0.36	0.047	0.027 to 0.067	0.005

therapy is inappropriate or insufficiently effective. In recent years, lubiprostone (chloride channel (ClC-2) activator), linaclotide (guanylate cyclase-C agonist), and elobixibat (ileal bile acid transporter inhibitor) have been approved for insurance coverage, thereby expanding the treatment options for chronic constipation. However, an established strategy for selecting drugs for patients with specific clinical characteristics is currently unavailable, and further investigation is required in this regard (*6*). Osmotically acting and contact laxatives are considered the preferred treatments for OIC. Strong evidence supports the efficacy of naldemedine, a peripheral μ-opioid receptor antagonist, in the treatment of OIC (*21*); however, owing to cost-effectiveness concerns, physicians differ in their opinions regarding its use as a first-line therapy (*6*).

The SCRs for each constipation medication in the 47 prefectures during FYs 2019 and 2023 are displayed in a box plot in Figure 1. A heat map illustrating the SCRs for each constipation medication across the 47 prefectures in FYs 2019 and 2023 is presented in Figure 2. Magnesium oxide exhibited the least regional variation. The largest regional differences were observed for polyethylene glycol in FY 2019 and linaclotide in FY 2023. The highest SCR for linaclotide was observed in Tokushima in both years, at 198.4 in FY 2019 and 270.6 in FY 2023. Akita, Iwate, and Aomori had the highest utilization of contact laxatives (sennosides and sodium picosulfate). The CV of SCRs was similar between FYs 2019 and 2023 (CV = 0.129 and 0.123, respectively), and a strong correlation was observed between prefecture-level SCRs in these years (r = 0.964), indicating that the magnitude and pattern of regional variation remained largely unchanged over time. Box plots illustrating the 5-year changes in the SCRs for all constipation medications across each prefecture are presented in Supplementary Figures S1-8 (*https://www.ddtjournal.com/action/getSupplementalData.php?ID=295*).

This study clarifies regional differences in prescribing constipation medications across 47 prefectures in Japan. Previous studies have shown that the prevalence of constipation increases with age in both men and women, and it is higher in women than in men (*7,22*). As such, the SCR was used as an age- and sex-adjusted index in this study. Among the examined constipation medications, the SCR for magnesium oxide exhibited the smallest regional variation. The SCRs for contact laxatives were particularly high in Akita, Iwate, and Aomori, all of which are located at higher latitudes and have lower average temperatures. Previous studies using the NDB-OD have shown that the use of contact laxatives is associated with lower ambient temperature (*7*). Johanson was the first to report cold temperature as a global environmental risk factor for constipation (*23*). Consistent with these findings, the SCRs for all constipation medications

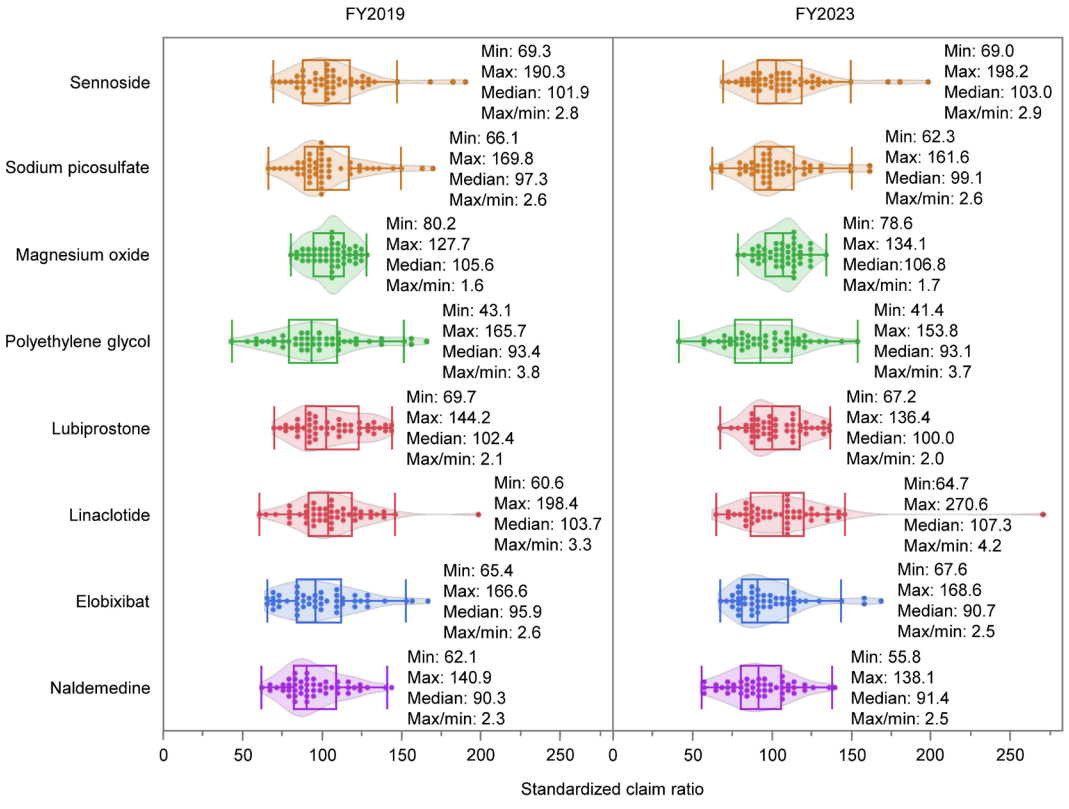

Figure 1. Regional variation in standardized claim ratios for constipation medications across Japan's 47 prefectures: Box plots for FYs 2019 and 2023. Sennosides and sodium picosulfate: contact laxatives; magnesium oxide and polyethylene glycol: osmotically acting laxatives; lubiprostone and linaclotide: intestinal secretagogues; elobixibat: ileal bile acid transporter inhibitor; naldemedine: peripherally acting μ-opioid receptor antagonist.

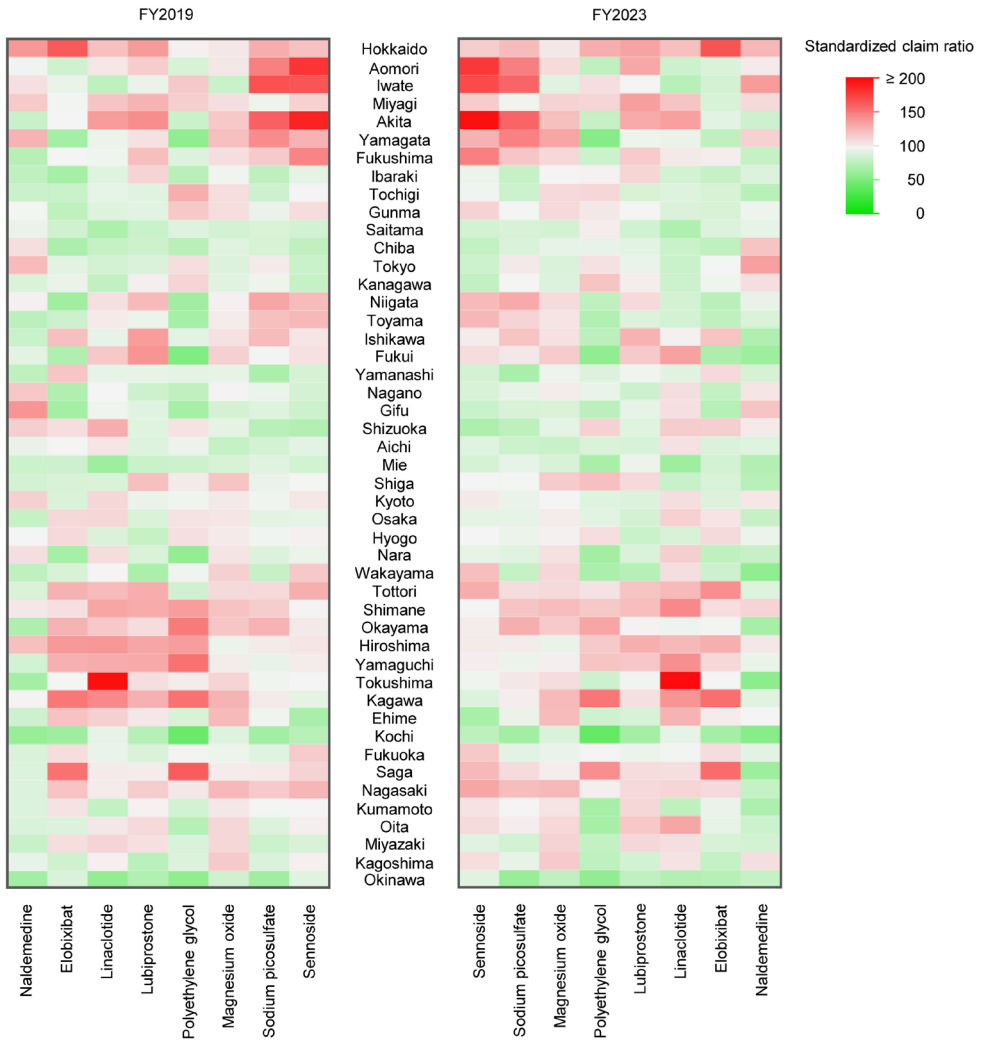

Figure 2. Regional variation in standardized claim ratios for constipation medications across Japan's 47 prefectures: Heat maps for FYs 2019 and 2023.

investigated were > 100 in Hokkaido, which has the lowest average temperature, whereas the SCRs were < 100 for Okinawa, which has the highest average temperature (average temperature data for Japan were obtained from e-Stat [*https://www.e-stat.go.jp/*]).

This study has several limitations. First, the investigation was limited to the eight constipation medications listed in Table 1, and herbal medicines, suppositories, and other constipation-related medications were excluded. Second, for drugs without an established WHO DDD, or those whose WHO DDD substantially differed from the dosages indicated in the Japanese package inserts, assumed DDDs were set specifically for this study. Third, several potential confounding factors, such as other diseases or medications related to constipation and regional characteristics, were not considered in the analysis. Fourth, because this study focused solely on prescribed medications, it did not fully capture the actual burden of constipation in Japan. An internet survey of the general Japanese population reported that among those who had used laxatives, 67.5% had purchased over-the-counter (OTC) drugs from pharmacies (*24*). Therefore, some constipation medications are available both as prescription and OTC drugs, while others are used exclusively as prescription drugs. Consequently, comparing these two groups based on DID was not appropriate.

In conclusion, despite its limitations, this study elucidates the trends and regional differences in the use of constipation medication in Japan from FYs 2019 to 2023. In July 2023, the Evidence-Based Clinical Guidelines for Chronic Constipation 2023 were released in Japan, and these included a drug selection flowchart. The findings of this study are expected to serve as baseline data for future evaluations of the standardization of constipation treatment through the dissemination of guidelines and accumulation of evidence.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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