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Time-Series Analysis of Triptan Prescription for Migraine in Japan Using NDB Open Data (FY2014–FY2022)

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Background: Migraine impairs daily functioning, and concerns persist about underdiagnosis, inappropriate pharmacotherapy, and medication-overuse headache (MOH). Triptan access has widened in Japan, with stepped-care guidance, yet avoiding overuse remains difficult. **Methods:** Using NDB Open Data Releases 1–9 (FY2014–FY2022), we quantified annual outpatient and community-pharmacy triptan prescriptions. Volumes were stratified by sex, drug, and 5-year age bands, and absolute/percentage changes were calculated versus FY2014. To contextualize age-structure shifts, we referenced total patient counts for ICD-10 G43 from the e-Stat Patient Survey (2014, 2017, 2020, 2023). Associations between sex and drug were tested by chi-square on contingency tables aggregated across releases. **Results:** Total prescriptions approximately doubled by FY2022 (31,095,293 tablets), comprising 6,219,190 for males and 24,876,103 for females (~4-fold female predominance). All five triptans increased, with the largest gains for rizatriptan (~2.3×) and eletriptan (~2.2×). The greatest increases occurred in males aged 15–19 years (~2.78×) and 60–64 years (~2.73×) and in females aged 55–59 years (~2.58×) and 15–19 years (~2.56×). The modal age band shifted from 40–44 years in FY2014 to 45–49 years in FY2022. Sex-by-drug distribution differed significantly (χ^2 , $p < 0.0001$); in FY2022, rizatriptan predominated in males (followed by sumatriptan) and eletriptan in females (followed by rizatriptan). **Conclusions:** From 2014 to 2022, triptan use in Japan rose with persistent female predominance, growth among adolescents (particularly males) and middle-to-older adults, and an older peak age. Findings suggest contributions from expanded care-seeking, rising social burden, chronification, and MOH. Multilevel actions—early diagnosis, rational use with MOH prevention, school/workplace support, timely specialist referral, and proactive pharmacist engagement—are warranted.

Key words migraine, triptans, NDB Open Data, medication-overuse headache, prescription

INTRODUCTION

Migraine is a complex neurological disorder characterized by recurrent attacks and associated symptoms including severe pulsating headaches, photophobia, phonophobia, and nausea.¹⁾ In recent years, migraine has affected approximately 15.2% of the global population, and its prevalence has increased.^{2,3)} According to the Global Burden of Disease (GBD) study, in age-stratified disability-adjusted life years (DALYs) across neurological conditions, migraine ranks second among individuals aged 20–59 years and first among those aged 5–19 years.⁴⁾

Despite its substantial impact on daily life, migraine care remains insufficient, and many individuals do not receive appropriate treatment.^{5,6)} In Japan, an estimated 8.4 million

people have migraines, and 74.2% report a high degree of interference with their daily activities.⁷⁾ Moreover, approximately 70% of the patients have never sought medical care,⁸⁾ and approximately 50% rely solely on over-the-counter medications.⁷⁾ Underdiagnosis and undertreatment are common challenges in Japan, East Asia, Canada, Germany, the United Kingdom, and other countries.^{5-7,16)} Inadequate headache management may precipitate medication-overuse headache (MOH), necessitating careful attention.

Parallel to the recent increase in disease burden, multiple countries have reported rising volumes of triptan prescriptions.^{9,10)} Japan's Clinical Practice Guideline for Headache 2021 recommends a stepped-care approach while administering acute treatment, advising triptan use for moderate-to-severe attacks or mild-to-moderate attacks when

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nonsteroidal anti-inflammatory drugs are ineffective.¹¹⁾ Simultaneously, MOH related to triptan overuse has been highlighted both domestically and internationally, and is recognized as a global challenge.^{12,13)}

Although population-based studies of triptan use have been conducted in other countries, evidence from Japan remains limited. While medication overuse represents an individual-level problem, prescribing behaviors are shaped by healthcare policies and broader social trends. Accordingly, analyzing temporal changes in national prescription volumes provides valuable insight into these population-level determinants. Therefore, this study aimed to characterize the time-series trends in triptan prescription volumes in Japan using the NDB Open Data, the only publicly available aggregated claims-based dataset derived from health insurance claims.

METHODS

Data Source and Outcome This repeated cross-sectional study involved a secondary analysis of publicly available aggregated data. We used the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) Open Data, which has been fully operational since April 2013. Releases 1 through 9 were analyzed (FY2014:

April 2014–March 2015 to FY2022: April 2022–March 2023) using aggregated tables of outpatient, out-of-hospital dispensing quantities by pharmacological class, stratified by sex and age¹⁴⁾. We included the five triptan agents approved in Japan for the acute treatment of migraine: sumatriptan, zolmitriptan, eletriptan, rizatriptan, and naratriptan (Table 1).

The primary outcome was the annual quantity of dispensed triptan agents (fiscal-year notation; e.g., FY2014 = April 2014–March 2015), obtained from the NDB Open Data aggregated tables for outpatient, out-of-hospital dispensing by pharmacological class. Analyses were stratified by sex, individual agent, and 5-year age bands in accordance with the category definitions used in Releases 1–9. As a reference indicator, total patient counts were extracted from the national Patient Survey (e-Stat) by sex × 5-year age group × disease subcategory for 2014, 2017, 2020, and 2023 to characterize shifts in age structure; the investigated disease subcategory corresponded to ICD-10 G43 (migraine).

Statistical Analysis

Trends in Total Prescription Volume (NDB Open Data, Releases 1–9)

For the nine-year period from FY2014 to FY2022, we described annual trends in the total dispensed volume of triptan agents by sex and individual agents (Fig. 1A, 1B).

Table 1. Triptan Medications Approved in Japan for Acute Migraine Treatment

Generic name	Brand name	Approval date in Japan	Approval date in Japan (GE)	Dosage form	Tmax (hr)	t1/2 (hr)
Sumatriptan	IMIGRAN®	2001.6.20	2012.8.15	50 mg tablet	1.8 ± 0.9	2.2 ± 0.3
Zolmitriptan	Zomig®	2002.3.15	2015.2.16	2.5 mg tablet	3.00	2.40
	Zomig® RM	2002.3.15	2015.2.16	2.5 mg tablet Rapid Melt	2.98	2.90
Eletriptan	RELPAx®	2002.4.11	2018.8.15	20 mg tablet	1.0 ± 0.32	3.20
	Maxalt®	2003.7.17	2017.2.15	10 mg tablet	1.0 ± 0.6	1.6 ± 0.3
Rizatriptan	Maxalt RPD®	2003.7.17	2017.2.15	10 mg tablet Rapidly Disintegrating	1.3 ± 0.7	1.7 ± 0.3
Naratriptan	Amerge®	2008.1.25	2020.2.17	2.5 mg tablet	2.68 ± 1.34	5.05 ± 1.71

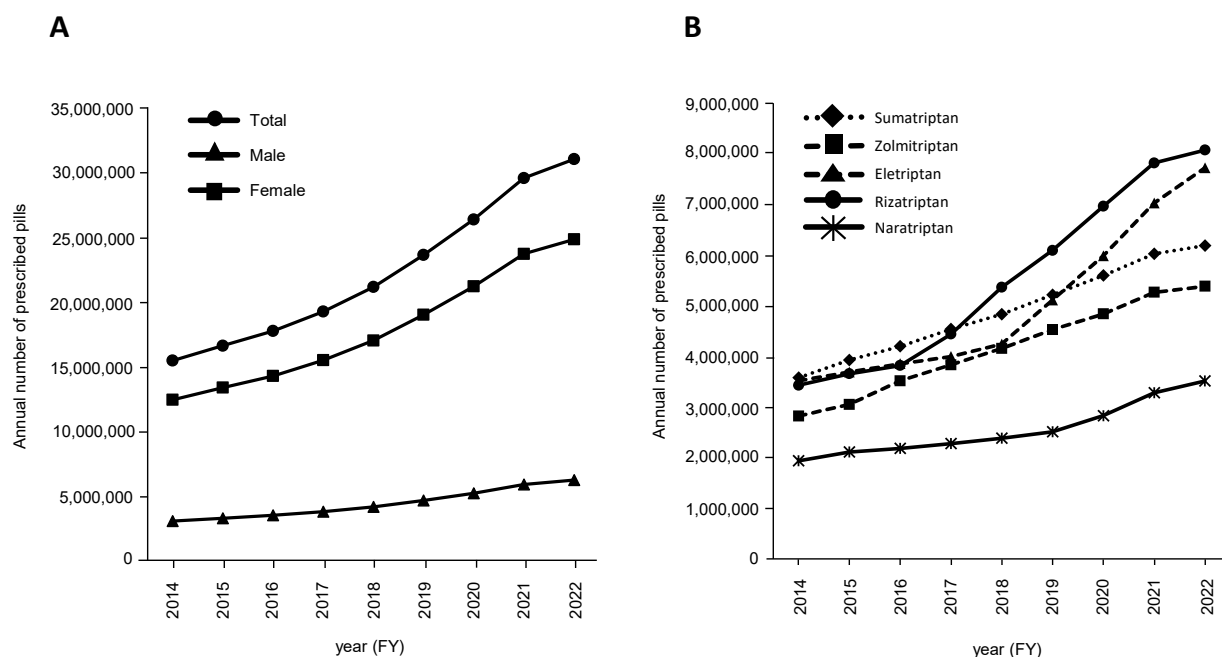


Fig. 1. Trends in Annual Triptan Prescription Volumes in Japan (FY2014–FY2022)

(A) Number of tablets dispensed by sex. (B) Number of tablets dispensed by triptan agent (sumatriptan, rizatriptan, zolmitriptan, eletriptan, naratriptan). Data source: NDB Open Data Japan, Releases 1–9. Counts reflect tablets dispensed, not unique patients. FY = fiscal year (April–March).

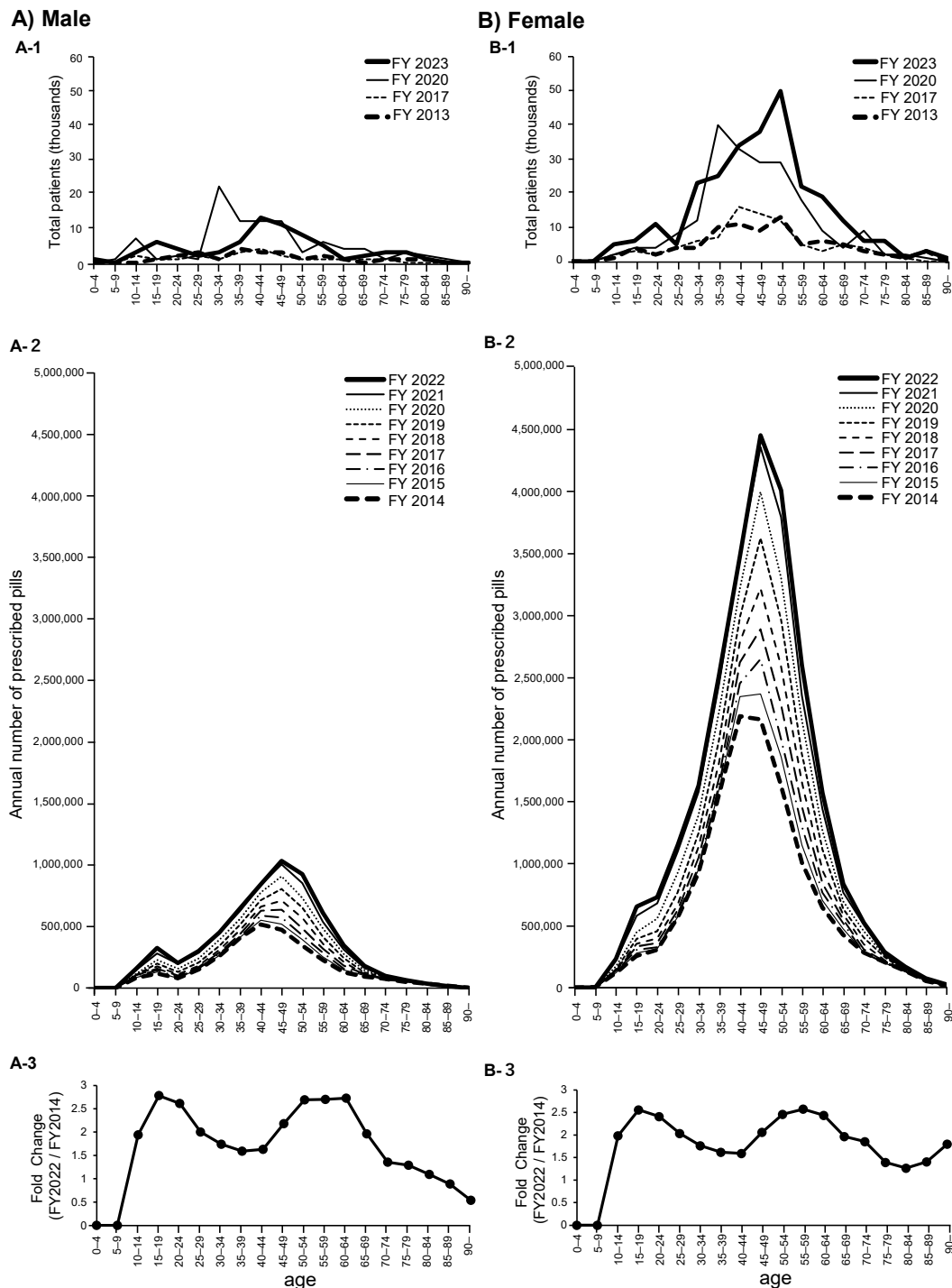


Fig. 2. Age-Specific Changes in Triptan Use in Japan, FY2014–FY2022

(A) Males; (B) Females. Subpanels: (1) Annual number of patients with migraine (ICD-10 G43); (2) Annual number of triptan tablets dispensed; (3) Fold change in dispensed tablets (FY2022 relative to FY2014). Data sources: e-Stat Patient Survey (2014, 2017, 2020, 2023) for patient counts; NDB Open Data Japan, Releases 1–9, for prescriptions. Prescription volumes are shown by 5-year age groups. Counts reflect tablets dispensed, not unique patients. FY = fiscal year (April–March).

Trends by 5-Year Age Bands

For the same period, we aggregated dispensing quantities by sex \times 5-year age band and observed age band-specific annual trends and percentage changes (Fig. 2A, 2B). In addition, we referenced the age composition of all patients corresponding to ICD-10 G43 from the national Patient Survey (e-Stat) for 2014, 2017, 2020, and 2023, juxtaposing changes

in the age distribution of prescriptions with changes in patient distribution.¹⁵⁾

Association between Sex and Drug Used

We summed the dispensed quantities across Releases 1–9 to construct a contingency table of sex (male/female) \times drug (five agents) and assessed the independence using a chi-square test with visualization via mosaic plots (Fig. 3A, 3B).

Ethical Considerations This study was a secondary analysis of publicly available aggregate data that did not contain individual-level information. No personally identifiable data were handled and institutional review board approval was not required.

RESULTS

The total dispensed volume aggregated across 5-year age bands in FY2022 was 31,095,293 tablets, which is approximately double the volume in FY2014. In terms of sex, the volumes approximately doubled for both males (6,219,190 tablets) and females (24,876,103 tablets), and the volume for females was approximately four times that for males in FY2022 (Fig. 1A).

All five triptan agents showed an upward trend in prescription volume from FY2014 to FY2022. The largest increase was observed for rizatriptan ($\sim 2.3\times$), followed by eletriptan ($\sim 2.2\times$) (Fig. 1B). In relation to the 5-year age bands, the greatest increase in total dispensed volume over the 9 years occurred in males aged 15–19 years ($\sim 2.78\times$), followed by those aged 60–64 years ($\sim 2.73\times$); in females, the highest increase was observed in those aged 55–59 years ($\sim 2.58\times$), followed by those aged 15–19 years ($\sim 2.56\times$) (Fig. 2A, 2B). The modal age group shifted from 40–44 years in FY2014 to 45–49 years in FY2022, indicating a rightward shift in the peak age.

In the contingency table of sex (male/female) \times agent (five triptans) aggregated across FY2014–FY2022, the distribution differed significantly between the sexes (chi-square test, $p < 0.0001$) (Fig. 3A, 3B). In FY2022, the most dispensed agent was rizatriptan in males, followed by sumatriptan, and eletriptan in females, followed by rizatriptan (Fig. 3A, 3B).

DISCUSSION

Using NDB Open Data, we found that the total dispensed volume of triptan agents approximately doubled over the nine fiscal years from FY2014 (Release 1) to FY2022 (Release 9). In FY2022, the volumes dispensed to males and females were 6,219,190 and 24,876,103 tablets, respectively. These findings suggest that a growing number of patients in Japan seek care at medical institutions and receive migraine-specific treatments.

Regarding sex differences, consistent with prior studies that reported that migraine prevalence in women is approximately 3.6 times that in men,⁷⁾ our study found that the dispensed volume was approximately four times higher among women than among men. This female-skewed prescription may reflect multiple factors, including differences in care-seeking behavior, attack frequency and severity, treatment preferences, and diagnostic thresholds. At the same time, our outcome measure was the number of tablets dispensed; therefore, the total volume can be influenced by longer treatment durations, dosing regimens, formulation or strength selection, and the diffusion of generics, and thus does not directly equate to patient counts.

According to the age-stratified analyses, the largest relative increase was observed among males aged 15–19 years ($\sim 2.78\times$), followed by females aged 15–19 years ($\sim 2.56\times$). This escalation from adolescence into early adulthood indicates a growing migraine burden among the youth and is consistent with international findings based on the GBD 2021 database, which reports the most rapid increases in prevalence and DALYs among individuals under 20 years of age, with growth projected to continue through 2050, particularly in males.¹⁶⁾ The pronounced uptick in prescription volumes among younger males in Japan supports the view that this global trajectory is unfolding domestically.

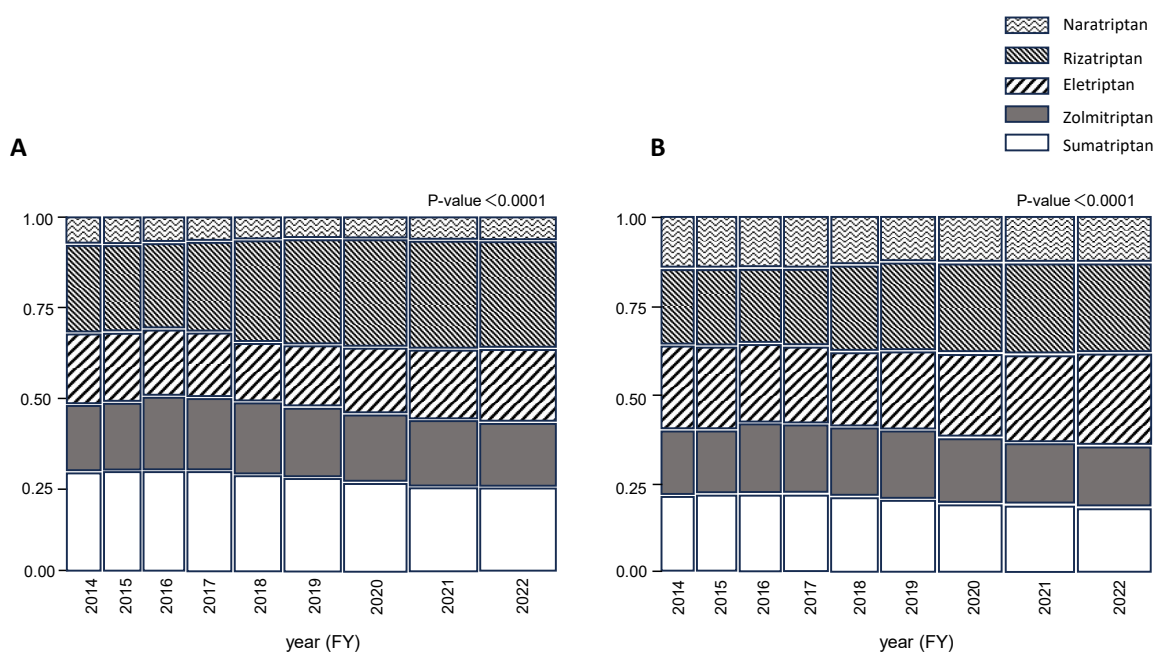


Fig. 3. Cross-Tabulations of Annual Triptan Dispensing by Fiscal Year and Agent, with Chi-Square Test Results, Stratified by Sex: (A) Males; (B) Females

Each cell displays the number of tablets dispensed and the corresponding row and column percentages. χ^2 tests assess the independence between fiscal year and triptan agent within each sex, and p-values are shown. Data source: National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) Open Data, Releases 1–9 (FY2014–FY2022). Counts represent the number of tablets dispensed, not unique patients. FY = fiscal year (April–March).

Migraine prevalence peaks at 30–39 years in Japan⁷⁾ and 35–49 years globally (i.e., the working-age population).¹⁷⁾ Attacks in this age range directly reduce labor productivity, thus increasing socioeconomic costs through absenteeism (i.e., frequent or habitual absence from work) and presenteeism (i.e., working while symptomatic with reduced efficiency). Together with the growing burden on younger cohorts, this observation raises concerns about an overall increase in the impact of migraines, highlighting the need for multilayered interventions such as early diagnosis, self-management education, optimization of acute treatment, and reasonable accommodation in schools and workplaces.

In this study, the year-on-year increase in triptan prescription even among individuals aged ≥ 50 years is noteworthy. From FY2014 to FY2022, the largest increase among women occurred at ages 55–59 years (~ 2.58 -fold), whereas among men, the second-largest increase was at ages 60–64 years (~ 2.73 -fold). Prior research in Japan identified fatigue and physical/psychological stress as major triggers of migraines.¹⁸⁾ Coupled with the progression of a super-aging society, the increasing social burdens in this cohort—balancing employment with caregiving, family care, and grandchild care—may have heightened care-seeking and treatment demands, contributing to the observed increase in prescriptions. The marked increase among women aged 55–59 years also supports the hypothesis that menopausal transition-related hormonal changes, alongside comorbid sleep disturbances and anxiety, may influence migraine activity.

In Japan, over the nine fiscal years from Release 1 (FY2014) to Release 9 (FY2023), the peak age band for triptan dispensing shifted from 40–44 years to 45–49 years for both sexes. In contrast, global data for 2021 show a clear age-sex pattern in migraine prevalence, peaking at 35–39 years in both men and women,¹⁹⁾ and Japanese reports likewise indicate the highest prevalence among women in their 30s⁷⁾ and in people of both sexes aged 30–39 years.¹⁷⁾ Despite the prevalence peaking at 30–39 years, the dispensing peak shifted to the older 45–49 years band during the study period, suggesting the influence of the problems faced by Japan's super-aging society, namely, increasing social burdens (e.g., balancing employment with caregiving and family responsibilities) that may delay or prolong treatment needs.

A plausible explanation for this rightward shift is that a subset of patients aged 35–39 years progressed to experiencing chronic migraines and continued to use triptan thereafter. In headache specialty clinics, chronic migraine is the most frequent phenotype of daily headaches. A systematic review estimated that approximately 2% of the global population has chronic migraine and the prevalence is 2.5–6.5 times higher in women than in men.¹¹⁾ Many triptan users present inadequate responses to over-the-counter analgesics and are subsequently prescribed triptans in clinical settings.²⁰⁾ MOH is a modifiable risk factor for progression to chronic migraine. Our findings indicating an increase in triptan dispensing that is consistent with international trends underscore the importance of robust medication management in preventing MOH. MOH is a major global concern that has become increasingly salient in Japan.²⁰⁾ Pharmacists can play a pivotal role in this context by systematically reviewing medication use, educating patients about MOH, and facilitating referrals to headache specialists when appropriate.

Regarding the agents, the most dispensed triptan in FY2022

was rizatriptan for men (followed by sumatriptan) and eletriptan for women (followed by rizatriptan). Eletriptan and rizatriptan demonstrated greater analgesic efficacy than other triptans, which may partly account for their higher dispensing volumes.²¹⁾ The largest sex difference was observed for naratriptan; its demonstrated efficacy as short-term prophylaxis for menstrual migraines (1 mg twice daily) suggests the intention to target female patients.^{22,23)} Many women report increased attack frequency around menstruation, with episodes that are more severe, longer-lasting, and treatment-refractory than at other times.

Recently, monoclonal antibodies targeting the calcitonin gene-related peptide (CGRP) or the CGRP receptor have emerged as preventive therapies for migraine. In Japan, galcanezumab was approved in January 2021, followed by fremanezumab and the CGRP receptor antibody, erenumab, in June 2021. In Korea, where CGRP-related agents were introduced in 2019, a reduction in triptan use was observed.⁹⁾ Future investigations should assess preventive strategies and patient education and incorporate international comparisons.

This study had several limitations. First, as this study was an ecological analysis based on aggregated NDB data, we could not directly assess individual-level clinical information, such as attack frequency and severity, concomitant medications, or treatment response. Second, because our primary outcome was the number of tablets dispensed, the underlying number of patients was unknown; therefore, claim-based quantities may not match the actual intake, and within-patient switching among triptans could not be captured. We were also unable to disentangle system- and market-level influences of dose adjustments, longer prescription durations, formulation/strength differences, drug price revisions, changes in guidelines or insurance coverage, and diffusion of generics on the total volume, and for some agents, the domestically recommended dose is lower than typical international doses, potentially inflating apparent quantities. Third, changes in data inclusion/extraction procedures and coding across Releases 1–9 may have biased the time-series comparisons.

In light of these issues, future studies should employ individual-level data to conduct stratified analyses by age, sex, and severity; link prescription with healthcare utilization and school/work outcomes; and evaluate the effects of guideline revisions and pricing policies.

In Japan, triptan prescriptions have risen markedly over the past nine years, characterized by a persistent female predominance and notable growth among younger cohorts, particularly males. These patterns align with international increases in migraine prevalence and disease burden^{13,16)} and point to the need for coordinated action across clinical practice (early diagnosis and optimization of acute therapy), public health (school and workplace interventions and education), and policy (access, pricing, and guideline development). While findings in older adults suggest rising social burdens and possible chronification, substantial uncertainty remains in younger populations. Pharmacists can play a pivotal role by promoting appropriate use, providing structured education on MOH, and facilitating specialist referral, thereby helping curb unnecessary medication use. Given the paucity of adolescent-focused migraine research in Japan, future studies should prioritize youths and extend beyond triptans to include preventive agents, such as lomerizine, CGRP-targeted therapies, and newer options including gepants.

CONCLUSION

This study shows that triptan prescription in Japan increased consistently from 2014 to 2022, with a persistent female predominance, marked growth among younger cohorts (particularly males) and middle aged-to-older adults, and a rightward shift in the age peak. These patterns suggest contributions from multiple factors, including changes in care-seeking and sickness behavior, rising social burden, chronification, and MOH. Agent-specific differences align with sex-related indications and treatment preferences, highlighting the need for coordinated actions across clinical practice, public health, and policy, such as early diagnosis, rational use, MOH prevention, support in schools and workplaces, and facilitated referral to specialists with the active involvement of pharmacists. Major limitations include the use of aggregated rather than individual-level data, reliance on dispensed tablet counts, and the limited ability to disentangle system/market factors or changes in data curation. Future studies should leverage linked individual-level datasets for finer stratification and evaluate how preventive agents, CGRP-targeted therapies, and agents shape prescription trends, alongside international comparisons.

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Conflict of interest Emi Nomura, Yuka Kanamori, Shota Aoki, and Kota Hosoe are employed by Pinokio Shoji Co., Ltd., Pinokio Pharmacy. Mari Iwata is employed by Yanaizu Pharmacy. The authors declare no other conflicts of interest related to this work.

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