

Prescription volume and costs of over-the-counter-like drugs in Japan by patient and healthcare facility characteristics: A nationwide descriptive study

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Abstract

Introduction

“Over-the-counter (OTC)-like drugs” are prescription medicines that contain the same or similar active ingredients as OTC drugs but receive reimbursement under Japan’s universal health insurance system. Despite ongoing policy discussions regarding the potential exclusion of these drugs from insurance coverage or increased patient cost-sharing, evidence describing their real-world prescription volume and costs is limited. We aimed to characterize the use of representative OTC-like drugs in Japan and examine variations by patient and healthcare facility characteristics.

Methods

This nationwide descriptive study was conducted using two claims-based data sources. From the National Database of Health Insurance Claims Open Data, we summarized the overall annual prescription volume and costs, further stratified by sex and age group, for fiscal years (FYs) 2018–2023. Using the DeSC database, we performed additional stratified analyses by comorbidity burden, health insurance type, and healthcare facility type. Five OTC-like drug categories were examined: oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs, topical anti-inflammatory patches, second-generation antihistamines, and heparinoid-containing topical preparations.

Results

In FY2023, the five OTC-like drug categories accounted for 17.4 billion prescriptions nationwide (139.6 per capita) and total costs of 288.1 billion yen (2317.0 yen per capita).

Heparinoid-containing topical preparations and topical anti-inflammatory patches comprised the largest prescription volumes, whereas second-generation antihistamines and topical anti-inflammatory patches accounted for the highest costs. Prescription volume and costs were higher among females and increased markedly with age, particularly for topical anti-inflammatory patches. Per capita values also increased with greater comorbidity burden, being the highest among individuals covered by the Medical Care System for the Advanced Elderly. Clinics showed higher per capita prescription volume and costs than hospitals.

Conclusions

The use of representative OTC-like drugs in Japan is large and varies considerably by patient and healthcare facility characteristics. These findings provide important evidence to inform future policy discussions on OTC-like drugs.

Key words

Cost-sharing; Health policy; Japan; Over-the-counter-like drugs; Prescription patterns

Introduction

Over-the-counter (OTC) drugs are medications that can be purchased without a prescription, as they have been deemed safe and effective for the self-treatment of mild conditions when used according to label directions¹. In Japan, there exists a distinct category of medications, called “*OTC-like drugs*,” which generally refer to prescription medications that contain the same or similar active ingredients as OTC drugs but require a physician’s prescription and are reimbursed by public health insurance. These OTC-like drugs include common therapeutic categories such as analgesics, antipyretics, antihistamines, topical anti-inflammatory patches, and moisturizers, many of which are also available without a prescription in other countries.

In Japan, a policy debate has emerged regarding whether OTC-like drugs should be excluded from public health insurance coverage or subject to increased patient copayments². Proponents of this policy argue that excluding these medications from insurance coverage would promote self-medication and reduce national healthcare expenditures, thereby alleviating the financial burden of insurance premiums, particularly for younger populations. However, medical professional organizations and patient advocacy groups have raised concerns about the potential adverse consequences of such policy changes. These include increased out-of-pocket costs for patients who would need to purchase more expensive OTC alternatives, reduced access to necessary medications, particularly among economically or medically vulnerable individuals, and a potential increase in disease progression resulting from delayed or forgone healthcare consultations. Despite the ongoing policy discussion, evidence regarding the prescription volume and costs of OTC-like drugs in Japan is limited, including how these prescriptions are

distributed across patient subgroups with varying comorbidity burdens and across different types of healthcare facilities. Such evidence is essential for informing evidence-based policy decisions and understanding the potential implications of insurance coverage changes on specific patient populations and healthcare settings.

To address this evidence gap, we aimed to describe the prescription volume and costs of representative OTC-like drugs in Japan, both overall and stratified by patient and healthcare facility characteristics. Specifically, our objectives were as follows: 1) to quantify the prescription volume and costs for each drug category; 2) to stratify these measures by patient characteristics, including sex, age group, Charlson Comorbidity Index (CCI) category³, the presence of comorbidities of major causes of death in Japan, and health insurance type; and 3) to examine the prescription volume and costs across healthcare facility types, including clinics, non-university hospitals, and university hospitals.

Methods

Data source

Two data sources were used for this study: 1) the National Database of Health Insurance Claims (NDB) Open Data and 2) the DeSC database. The NDB is a nationwide administrative claims database covering approximately 99% of hospitals in Japan and contains various types of information, including age, sex, disease diagnoses coded according to the International Classification of Diseases, 10th Revision (ICD-10), procedures, and medications in both inpatient and outpatient settings⁴. Although the NDB is an important data source for epidemiological research, access is limited due to a

multistep application process that requires a certain amount of time⁵. In parallel, the Ministry of Health, Labour, and Welfare of Japan, which administers the NDB, provides an open-access, publicly available version known as the NDB Open Data⁴. While the NDB Open Data does not include patient- or facility-level information, it contains aggregated medication data, including prescription volumes for each fiscal year (FY), for both the overall database population and stratified by sex and age group.

The DeSC database is a large-scale health insurance claims database in Japan^{5,6}. Five types of public health insurance are operational in Japan: 1) the municipality-based National Health Insurance for non-employees; 2) Japan Health Insurance Association-managed insurance for employees of small companies; 3) association- or union-managed insurance for employees of large companies; 4) Mutual Aid Association-managed insurance for civil servants; and 5) the Advanced Elderly Medical Service System for individuals aged 75 years or above. While the NDB consolidates information from all five insurance types, the DeSC database collects information from the first, third, and fifth types. The data elements contained in the DeSC database are similar to those in the NDB.

We selected the NDB Open Data as the primary data source to quantify national prescription volumes and costs for each study drug and stratify these data by sex and age group. Because the NDB Open Data provides aggregated data without information required for more detailed stratification, prescription volumes and costs could not be further stratified by CCI category, the presence of comorbid conditions corresponding to major causes of death in Japan, insurance type, or healthcare facility type. We used the

DeSC database to enable these stratified analyses. For both the NDB Open Data and DeSC database, we extracted data from FYs 2018 through 2023 (April 2018 to March 2024).

Study drugs

We focused on five representative OTC-like drug categories: oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations. The analysis was limited to outpatient prescriptions because inpatient drug costs are often integrated into bundled reimbursement systems, making it difficult to isolate and calculate the specific costs of individual drugs. The WHO-ATC codes for each drug category are provided in Supplementary Table 1.

Analysis using the NDB Open Data

Using information extracted from the NDB Open Data, we calculated the annual total prescription volume and costs for each study drug category for each FY. We further stratified these data by sex and age group (≤ 64 , 65–74, and ≥ 75 years). Additionally, we calculated the per capita prescription volume and costs for each study drug. For these calculations, the total prescription volume and costs for each study drug category in each FY were divided by either the total estimated population of Japan or the estimated number of individuals in each stratum in that year⁷.

Analysis using the DeSC database

Using the DeSC database, we first calculated the total prescription volume and costs for each study drug category in each FY, to describe the overall prescription patterns captured in the DeSC database and facilitate comparison with the NDB Open Data. Thereafter, we stratified these data by CCI category (0, 1–2, and ≥ 3), presence of one of the leading causes of death in Japan, health insurance type, and healthcare facility type.

The CCI is a weighted score that sums assigned points for 17 categories of chronic conditions and can predict both short-term and long-term outcomes, including mortality and functional status^{3,8}. The ICD-10 codes for the 17 chronic conditions were obtained from a previous study⁸. We limited our analysis to chronic conditions, viz. malignant neoplasms, heart diseases, cerebrovascular diseases, renal diseases, and Alzheimer's disease, from among Japan's ten leading causes of death in 2024⁹. The ICD-10 codes for these conditions were defined in accordance with the national mortality survey and are presented in Supplementary Table 2¹⁰. A condition was considered to be present if the corresponding diagnostic code appeared during the FY, both for calculating the CCI and identifying chronic conditions. Health insurance types included the National Health Insurance, Health Insurance for employees of large companies, and the Medical Care System for the Advanced Elderly. Healthcare facilities were categorized into clinics, non-university hospitals, and university hospitals.

For the stratified analyses, we also calculated the per capita prescription volume and costs for each study drug. For these calculations, the total prescription volume and costs for each study drug category in each FY were divided by the corresponding denominator population in the year: individuals with a CCI of 0, 1–2, or ≥ 3 ; individuals with each of

the above-mentioned chronic conditions; individuals enrolled in each insurance type; and individuals who visited each type of facility. A separate denominator was estimated for the respective FY. In the stratified analyses, results were primarily reported as per capita values for strata with substantial differences in population size, to ensure interpretable comparisons.

To evaluate the representativeness of the individual composition within the DeSC database relative to the general Japanese population, we summarized the number and proportion of individuals by health insurance type in the DeSC database. According to national statistics reported in Japan in 2022, the nationwide distribution was as follows: National Health Insurance (25.4 million; 20.9%), Health Insurance for employees of small companies (40.3 million; 33.2%), Health Insurance for employees of large companies (28.4 million; 23.4%), Mutual Aid Associations for civil servants (8.7 million; 7.2%), and Medical Care System for the Advanced Elderly (18.4 million; 15.2%)¹¹.

Results

Results from the NDB Open Data

Overall prescription volume and costs

The ranking of OTC-like drug categories by total prescription volume changed over time (Table 1 and Figure 1). In FY2018, the three most frequently prescribed drug categories were topical anti-inflammatory patches, heparinoid-containing topical preparations, and second-generation antihistamines. By FY2023, this ranking shifted to heparinoid-containing topical preparations, topical anti-inflammatory patches, and second-generation antihistamines. In FY2023, the total prescription volumes (per capita values)

of the three leading categories were 5.8 billion (46.9), 4.4 billion (35.5), and 3.9 billion (31.7) for heparinoid-containing topical preparations, topical anti-inflammatory patches, and second-generation antihistamines, respectively. The total volume (per capita value) for the five study drug categories in FY2023 was 17.4 billion (139.6).

In contrast, the ranking of drug categories by total prescription costs remained unchanged throughout the study period, with second-generation antihistamines, topical anti-inflammatory patches, and heparinoid-containing topical preparations consistently accounting for the highest costs. In FY2023, the total costs (per capita values) were 109.2 billion yen (877.8 yen) for second-generation antihistamines, 85.6 billion yen (688.2 yen) for topical anti-inflammatory patches, and 66.1 billion yen (531.7 yen) for heparinoid-containing topical preparations. The total costs (per capita values) for the five study drug categories in FY2023 were 288.1 billion yen (2317.0 yen).

Sex-specific prescription volume and costs

Across all fiscal years and all drug categories, females consistently had higher total prescription volume and total costs than males, both in absolute terms and on a per capita basis (Supplementary Table 3, Figure 2).

In FY2023, the three leading drug categories by total prescription volume differed by sex. Among males, the top three categories were heparinoid-containing topical preparations, second-generation antihistamines, and topical anti-inflammatory patches, with total volumes (per capita values) of 2.6 billion (43.2), 1.7 billion (28.4), and 1.6 billion (26.5), respectively. In contrast, among females, the top three categories were heparinoid-

containing topical preparations, topical anti-inflammatory patches, and second-generation antihistamines, with corresponding values of 3.2 billion (50.3), 2.8 billion (43.9), and 2.2 billion (34.8). The total volume (per capita value) for the five study drug categories in FY2023 was 7.1 billion (117.3) for males, and 10.3 billion (160.6) for females.

The top three drug categories accounting for the majority of the total prescription costs in FY2023 were identical for males and females: second-generation antihistamines, topical anti-inflammatory patches, and heparinoid-containing topical preparations. Among males, the total costs (per capita values) were 46.4 billion yen (767.5 yen) for antihistamines, 31.1 billion yen (514.3 yen) for patches, and 29.2 billion yen (483.4 yen) for heparinoids. The corresponding values among females were 62.7 billion yen (981.7 yen), 54.5 billion yen (852.7 yen), and 36.9 billion yen (577.5 yen), respectively. The total costs (per capita values) for the five study drug categories in FY2023 were 116.5 billion yen (1925.3 yen) for males, and 171.6 billion yen (2687.3 yen) for females.

Age-group-specific prescription volume and costs

In FY2023, the drug category with the highest per capita prescription volume varied by age group (Supplementary Table 4, Figure 3). Among individuals aged 0–64 years, the per capita volume (48.6) was the highest for heparinoid-containing topical preparations. Among those aged 65–74 years and ≥ 75 years, topical anti-inflammatory patches ranked the highest, with per capita volumes of 61.7 and 118.9, respectively. The total per capita volume for the five study drug categories in FY2023 were 106.7 in the 0–64 years age group, 154.7 in the 65–74 years group, and 271.8 in the ≥ 75 years group.

The leading drug category by per capita prescription costs also differed by age group. In the 0–64 years age group, second-generation antihistamines accounted for the highest per capita cost (848.1 yen), whereas topical anti-inflammatory patches accounted for the highest per capita costs in the 65–74 year and ≥ 75 year age groups (1192.6 yen and 2351.2 yen, respectively). The total costs per capita for the five study drug categories in FY2023 were 1747.8 yen in the 0–64 years age group, 2729.4 yen in the 65–74 years group, and 4481.2 yen in the ≥ 75 years group.

Comparison of the youngest (0–64 years) and oldest (≥ 75 years) age groups revealed that the per capita prescription volume and costs for topical anti-inflammatory patches were more than tenfold higher in the oldest group, while the corresponding per capita values for second-generation antihistamines and heparinoid-containing topical preparations were similar for these age groups.

Results from the DeSC database

Overall prescription volume and costs

In the analysis of the whole population from the DeSC database, the ranking of OTC-like drug categories by total prescription volume and total costs differed from that observed in the NDB Open Data (Supplementary Table 5 and Supplementary Figure 1). Additionally, the per capita prescription volumes and costs were consistently smaller than those estimated from the NDB Open Data.

In FY2023, the three leading drug categories by total prescription volume were topical

anti-inflammatory patches, heparinoid-containing topical preparations, and second-generation antihistamines, with total volumes (per capita values) of 80.0 million (8.5), 25.0 million (2.7), and 23.1 million (2.5), respectively. In contrast, the ranking by total prescription costs was as follows: topical anti-inflammatory patches, second-generation antihistamines, and heparinoid-containing topical preparations, with corresponding costs (per capita values) of 1.6 billion yen (170.6 yen), 0.68 billion yen (72.2 yen), and 0.33 billion yen (35.1 yen).

The total volume (per capita value) and costs (per capita value) for the five study drug categories in FY2023 were 155.3 million (16.5) and 2.94 billion yen (312.1 yen), respectively.

CCI-specific prescription volume and costs

Across all study drug categories, both per capita total prescription volume and costs increased with higher CCI categories (Supplementary Table 6 and Supplementary Figure 2).

The total volume per capita for the five study drug categories in FY2023 were 6.9 in the CCI=0 category, 36.7 in the CCI=1–2 category, and 49.1 in the CCI $\geq$ 3 category. Moreover, the total per capita costs for the five study drug categories in FY2023 were 130.7 yen in the CCI=0 category, 699.3 yen in the CCI=1–2 category, and 915.1 in the CCI $\geq$ 3 category.

Major-disease-specific prescription volume and costs

The total per capita volume for the five study drug categories in FY2023 was 45.2 in patients with malignant neoplasms, 47.8 in patients with heart diseases, 43.0 in patients with cerebrovascular diseases, 47.9 in patients with renal diseases, and 27.4 in patients with Alzheimer's disease. Additionally, the total per capita costs for the five study drug categories in FY2023 were 837.4 yen for patients with malignant neoplasms, 898.4 yen for patients with heart diseases, 808.1 yen for patients with cerebrovascular diseases, 879.7 yen for patients with renal diseases, and 493.3 yen for patients with Alzheimer's disease (Supplementary Table 7 and Supplementary Figure 3).

Health-insurance-specific prescription volume and costs

National Health Insurance accounted for approximately 45–55%, Health Insurance for approximately 7–10%, and the Medical Care System for the Advanced Elderly for approximately 35–45% of individuals in the DeSC database (Supplementary Table 8).

The total volume per capita for the five study drug categories in FY2023 was 7.0 in individuals covered by the National Health Insurance, 12.3 in individuals covered by Health Insurance, and 26.4 in individuals covered by the Medical Care System for the Advanced Elderly (Supplementary Table 9 and Supplementary Figure 4). Additionally, the total costs per capita for the five study drug categories in FY2023 were 131.8 yen for individuals covered by the National Health Insurance, 227.5 yen for individuals covered by Health Insurance, and 499.2 yen for individuals covered by the Medical Care System for the Advanced Elderly.

Healthcare-facility-specific prescription volume and costs

The total per capita volume for the five study drug categories in FY2023 was 30.9, 11.6, and 12.1 for individuals visiting clinics, non-university hospitals, and university hospitals, respectively (Supplementary Table 9 and Supplementary Figure 5). The total costs per capita for the five study drug categories in FY2023 were 589.3, 209.9, and 232.8 yen for individuals visiting clinics, non-university hospitals, and university hospitals, respectively.

Discussion

Using both nationwide claims data in an aggregated manner and individual-level data, this study provides a contemporary comprehensive description of the scale and distribution of prescription use of representative OTC-like drugs in Japan. We found that these drugs accounted for a substantial volume of prescriptions and healthcare expenditures, with an annual national prescription volume of approximately 17.4 billion prescriptions and total costs of 288.1 billion yen. Among the five drug categories examined, heparinoid-containing topical preparations, topical anti-inflammatory patches, and second-generation antihistamines accounted for the largest prescription volumes, whereas second-generation antihistamines and topical anti-inflammatory patches contributed the most to the total costs.

The prescription volume and cost varied markedly across population subgroups. Females consistently had higher per capita prescription volume and costs than males, and both measures increased substantially with advancing age. In particular, the per capita prescription volume and costs for topical anti-inflammatory patches were more than ten times higher among individuals aged ≥ 75 years compared with those aged 0–64 years,

whereas age-related differences were less pronounced for second-generation antihistamines and heparinoid-containing topical preparations.

Several features of the observed prescription patterns warrant consideration. The higher prescription volume and costs among older adults and individuals with a greater comorbidity burden likely reflect the higher prevalence of chronic symptoms and conditions for which these OTC-like drugs are commonly prescribed, such as pain, inflammation, allergic symptoms, and skin disorders. The marked age-related increase in the use of topical anti-inflammatory patches may be attributable to the high burden of musculoskeletal conditions in older populations¹² as well as the clinical preference for topical agents to reduce the risk of systemic adverse effects. This preference may be reflected in the substantially higher prescription volume of topical anti-inflammatory patches compared with oral NSAIDs among older adults. In contrast, the relatively modest age-related differences for second-generation antihistamines and heparinoid-containing topical preparations may reflect their use across a broader age range for conditions that are less strongly age-dependent.

Differences by healthcare facility type may also reflect variations in clinical practice patterns and patient case mix. The higher prescription volume and costs observed in clinics, compared with hospitals, may be related to the role of clinics as primary points of contact for patients with chronic, non-life-threatening conditions, for which OTC-like drugs are frequently prescribed. Similarly, differences across health insurance types are likely influenced by underlying differences in age distribution and comorbidity burden among insured populations, rather than by the type of insurance itself.

Amid the ongoing discussion about increasing patient cost-sharing for selected OTC-like drugs, the description of national prescription volume and costs across population subgroups provided by this study may serve as a useful reference for policy considerations. If patient cost-sharing were increased, the financial impact would not be uniform across the population, given the substantial differences in prescription volume and costs observed by age, comorbidity burden, and insurance type. Conversely, if current coverage policies remain unchanged, the observed trends may persist, with continued implications for healthcare expenditure. Importantly, the present study did not evaluate the effects of cost-sharing policies on prescribing behavior or health outcomes. If policy changes regarding patient cost-sharing for OTC-like drugs are implemented in the future, the present findings may serve as baseline data for evaluating subsequent changes in prescription patterns and healthcare expenditures.

This study has some limitations. First, some prescription volume values—generally those with fewer than 1000 prescriptions—were masked in the NDB Open Data, leading to slight underestimation of the prescription volume and costs. However, because these masked values accounted for only a very small proportion of total prescriptions, the magnitude of underestimation is likely minimal. Second, individuals included in the DeSC database may not be representative of the overall Japanese population. The proportion of individuals covered by the Medical Care System for the Advanced Elderly was higher in the DeSC database than in national statistics (35–45% vs. 15.2%), resulting in overrepresentation of older adults. This likely explains why the overall prescription volume and cost distributions observed in the DeSC database (Supplementary Figure 1)

resembled those among individuals aged ≥ 75 years in the NDB Open Data (Figure 3). Nevertheless, despite its limited representativeness for national-level estimates, the analyses of DeSC database provide valuable insights into differences in prescription patterns across patient subgroups and healthcare settings.

In conclusion, using the NDB Open Data, we showed that the five representative OTC-like drug categories accounted for 288.1 billion yen (2317.0 yen per capita) in prescription costs in fiscal year 2023. The three drug categories that contributed to the largest share of the total costs were second-generation antihistamines (109.2 billion yen; 877.8 yen per capita), topical anti-inflammatory patches (85.6 billion yen; 688.2 yen per capita), and heparinoid-containing topical preparations (66.1 billion yen; 531.7 yen per capita). The magnitude and composition of OTC-like drug use varied substantially by sex and age group.

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Author contributions

YK designed the research, collected the data, performed statistical analysis, and wrote the first draft. AO and AS designed the research and revised the first draft. HY revised the first draft and supervised the entire manuscript preparation. All authors have read and approved the final manuscript.

Conflicts of interest

YK and SA are members of the Department of Health Services Research, Graduate School of Medicine, which is a cooperative program between The University of Tokyo and Tsumura & Co. AO is a member of the Department of Prevention of Diabetes and Lifestyle-Related Diseases, which is a cooperative program between The University of Tokyo and Asahi Mutual Life Insurance Company.

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Approval by institutional review board

This study protocol was approved by the Institutional Review Board of the Graduate School of Medicine of the University of Tokyo [approval number: 2021010NI (April 23, 2021)], and the study was conducted in accordance with the principles of the Helsinki Declaration.

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Table 1. Annual prescription volume and costs for representative OTC-like drugs: Analysis of the NDB Open Data

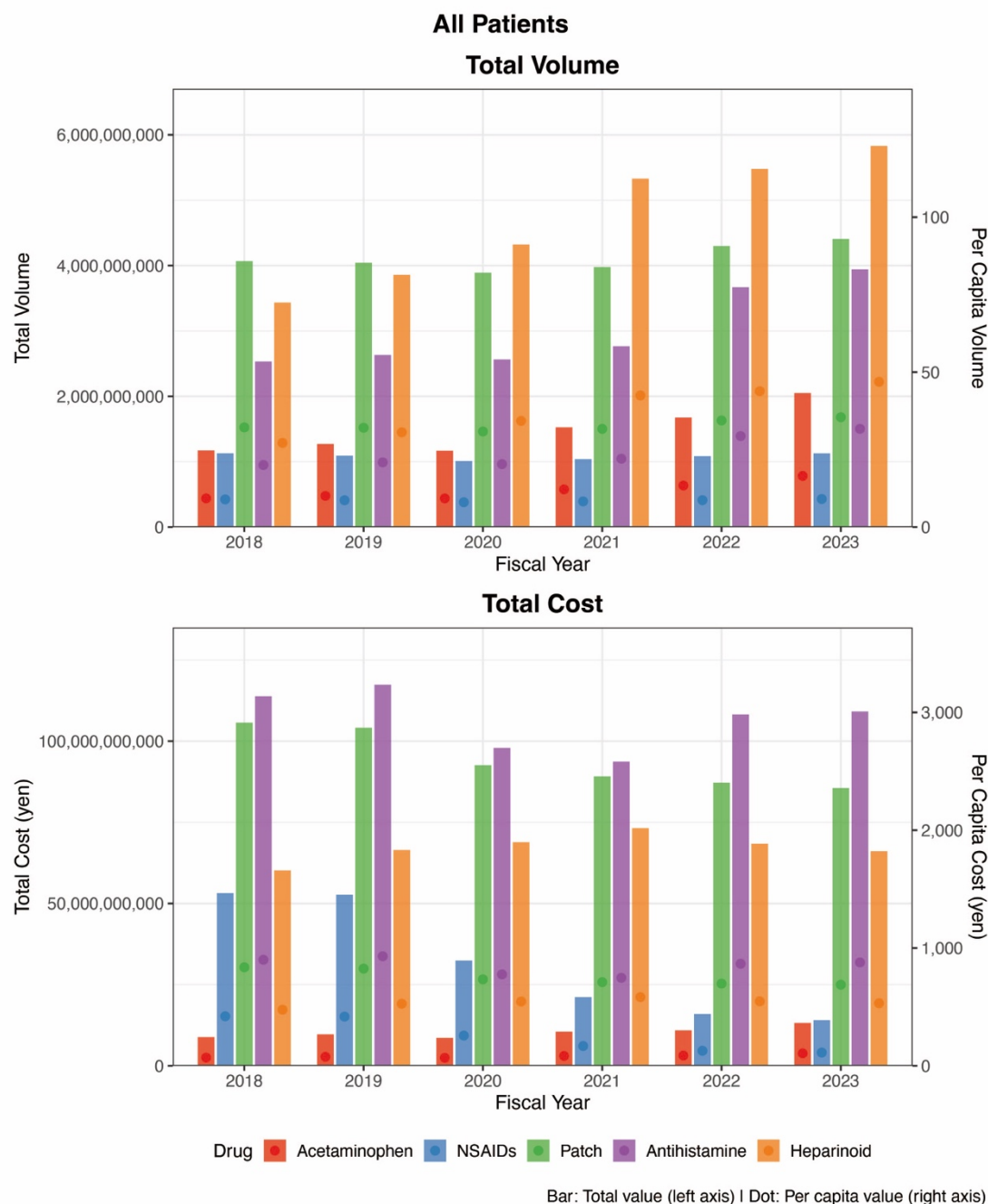
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	1,172,361,927 (9.27)	1,271,822,166 (10.08)	1,168,642,025 (9.26)	1,526,814,588 (12.17)	1,676,305,346 (13.42)	2,051,034,096 (16.49)
Oral single-agent NSAIDs	1,129,166,791 (8.93)	1,092,460,341 (8.66)	1,011,475,742 (8.02)	1,039,447,432 (8.28)	1,085,322,657 (8.69)	1,127,034,339 (9.06)
Topical anti-inflammatory patches	4,068,473,867 (32.18)	4,042,655,598 (32.04)	3,890,772,483 (30.84)	3,976,870,616 (31.69)	4,299,166,484 (34.41)	4,408,370,740 (35.45)
Second-generation antihistamines	2,533,579,664 (20.04)	2,633,672,516 (20.87)	2,564,071,236 (20.33)	2,766,832,502 (22.05)	3,669,767,294 (29.37)	3,942,289,252 (31.70)
Heparinoid-containing topical preparations	3,434,187,254 (27.16)	3,859,872,858 (30.59)	4,323,208,452 (34.27)	5,330,609,281 (42.47)	5,479,287,246 (43.85)	5,829,599,656 (46.88)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	8,854,322,769 (70.03)	9,690,837,462 (76.81)	8,607,294,322 (68.23)	10,530,335,287 (83.91)	10,947,761,096 (87.62)	13,222,687,319 (106.33)
Oral single-agent NSAIDs	53,200,465,798 (420.75)	52,721,026,492 (417.87)	32,431,739,701 (257.10)	21,129,402,655 (168.36)	15,973,591,045 (127.84)	14,055,393,929 (113.03)
Topical anti-inflammatory	105,724,091,731 (836.14)	104,111,034,573 (825.18)	92,607,334,275 (734.13)	89,138,361,899 (710.25)	87,203,485,407 (697.92)	85,576,637,271 (688.18)

patches						
Second-generation antihistamines	113,831,217,597 (900.26)	117,387,429,942 (930.41)	97,917,244,817 (776.22)	93,726,947,099 (746.82)	108,238,494,682 (866.28)	109,150,646,414 (877.76)
Heparinoid-containing topical preparations	60,199,963,644 (476.10)	66,470,607,447 (526.85)	68,899,530,697 (546.19)	73,212,820,092 (583.36)	68,423,704,093 (547.62)	66,114,679,727 (531.67)

The data in parentheses represent per capita values.

OTC: over-the-counter, NSAIDs: nonsteroidal anti-inflammatory drugs, NDB: National Database of Health Insurance Claims

Figure 1. Trends in prescription volume and costs of representative OTC-like drugs in the overall population: Analysis of the NDB Open Data

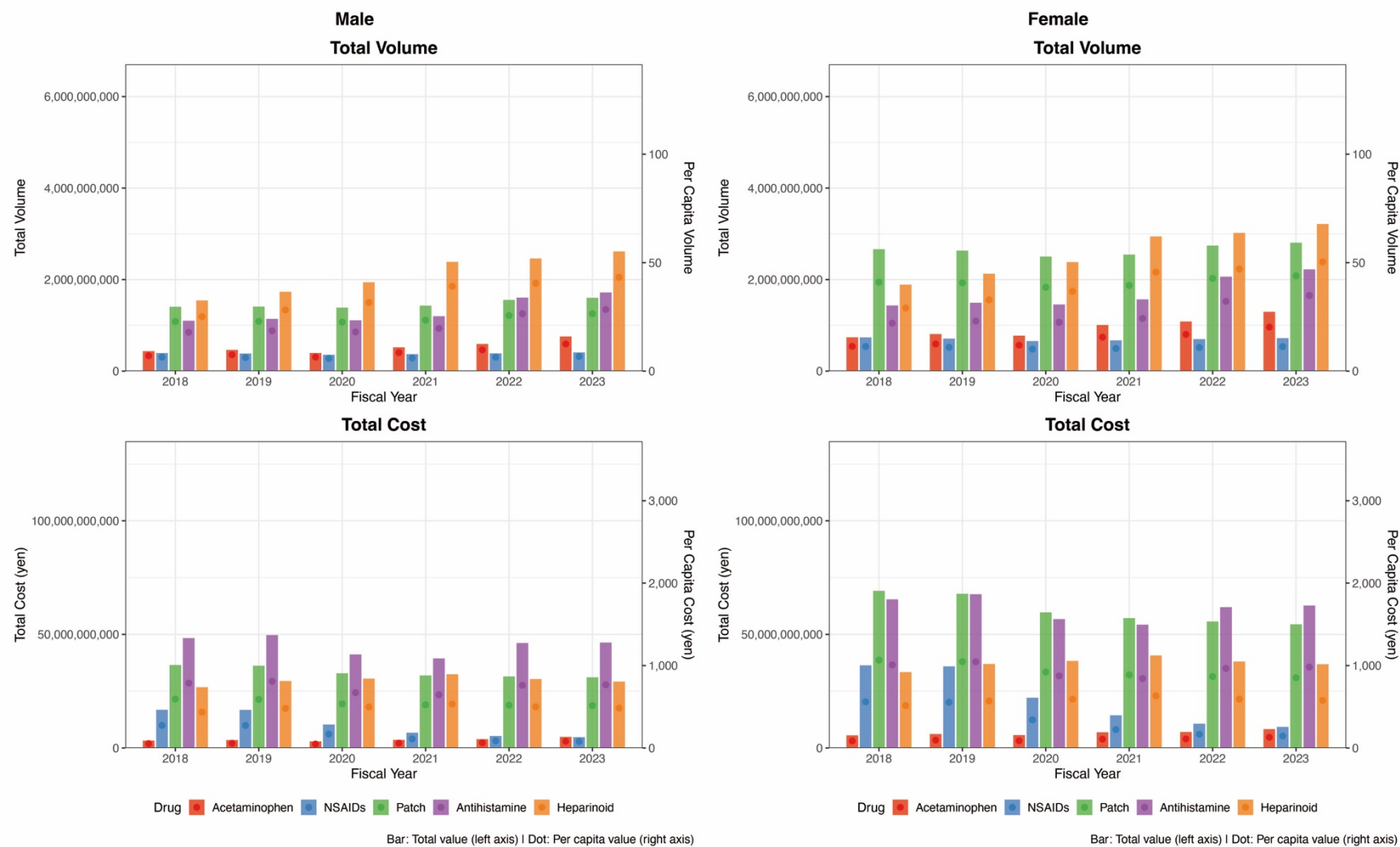


The upper panel depicts the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis), and the lower panel depicts the total prescription costs (bars, left y-axis) and per capita prescription costs (dots, right y-axis).

Note: Prescription volume and costs are presented for oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-

inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations. The per capita values were calculated by dividing the annual totals by the estimated Japanese population in each fiscal year.

Figure 2. Sex-specific trends in prescription volume and costs of representative OTC-like drugs: Analysis of the NDB Open Data

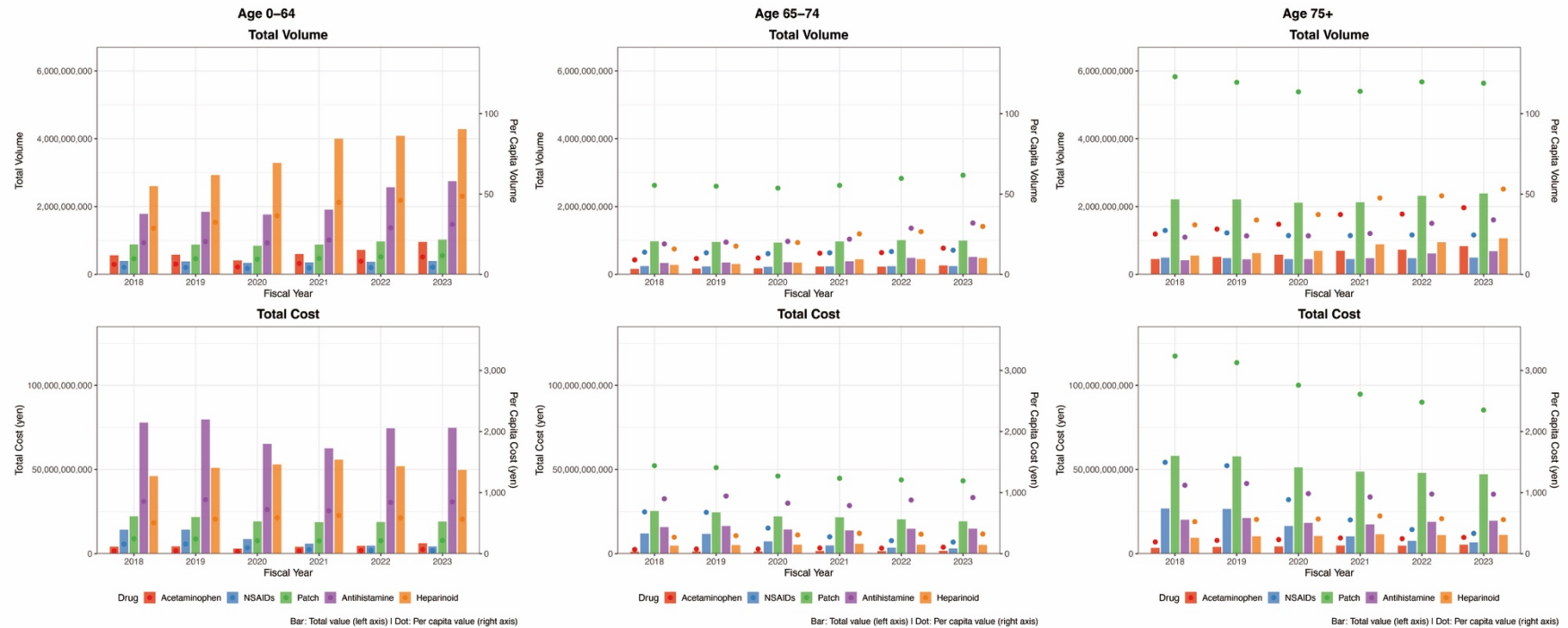


(A) Trends in the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among males.

(B) Trends in the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among .

Note: Prescription volume and costs are presented for oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations.

Figure 3. Age-group-specific trends in prescription volume and costs of representative OTC-like drugs: Analysis of the NDB Open Data



- (A) Trends in total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals aged 0–64 years.
- (B) Trends in total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals aged 65–74 years.
- (C) Trends in total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals aged ≥ 75 years.

Note: Prescription volume and costs are presented for oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations.

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Supplementary Table 1. WHO–ATC codes for the study drugs

Study drugs	WHO-ATC codes
Oral single-agent acetaminophen	N02BE01
Oral single-agent NSAIDs	M01AB, M01AC, M01AE, M01AG, M01AH
Topical anti-inflammatory patches*	M02AA, M02AB, M02AC, M02AX
Second-generation antihistamines**	R06AX24, R06AX22, R06AE07, R06AX26, R01AC08, R06AX13, R06AE09, R06AX29, R06AX27, R06AX28
Heparinoid-containing topical preparations***	Not applicable

NSAIDs, nonsteroidal anti-inflammatory drugs; WHO, World Health Organization; ATC, Anatomical Therapeutic Chemical classification

*Because some topical agents with the listed WHO-ATC codes are not patches, we have included only the products specifically categorized as patches.

**Bepotastine is a second-generation antihistamine used in Japan; however, no WHO-ATC code is assigned to this drug. Therefore, bepotastine was included in the second-generation antihistamines category based on its drug name rather than the WHO–ATC code.

***No WHO–ATC codes are assigned to heparinoid-containing topical preparations. Therefore, we included in this category those drugs whose product name contains “hirudoid” or “heparinoid.”

Supplementary Table 2. ICD-10 codes for the leading causes of death

Disease category	ICD-10 codes
Malignant neoplasms	C00–97
Heart diseases	I01–020, I05–09, I20–25, I27, I30–52
Cerebrovascular diseases	I60–69
Renal diseases	N17–19
Alzheimer disease	G30

ICD-10, International Classification of Diseases, 10th Revision

Supplementary Table 3. Annual prescription volume and costs of representative OTC-like drugs stratified by sex: Analysis of the NDB Open Data

Male						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	434,302,072 (7.06)	462,284,555 (7.53)	394,241,983 (6.43)	519,119,445 (8.51)	592,389,856 (9.75)	756,268,701 (12.50)
Oral single-agent NSAIDs	393,861,956 (6.40)	382,550,633 (6.23)	356,064,746 (5.80)	368,317,556 (6.04)	387,248,060 (6.37)	407,345,728 (6.73)
Topical anti-inflammatory patches	1,405,109,216 (22.84)	1,409,567,077 (22.95)	1,386,794,264 (22.60)	1,430,406,678 (23.44)	1,554,860,554 (25.59)	1,601,518,170 (26.47)
Second-generation antihistamines	1,099,829,456 (17.87)	1,140,519,149 (18.57)	1,108,920,552 (18.08)	1,199,696,921 (19.66)	1,605,496,489 (26.42)	1,717,876,172 (28.40)
Heparinoid-containing topical preparations	1,543,834,983 (25.09)	1,732,173,388 (28.21)	1,941,248,831 (31.64)	2,387,082,394 (39.12)	2,459,930,507 (40.49)	2,614,579,277 (43.22)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	3,277,761,809 (53.27)	3,523,113,513 (57.37)	2,918,084,956 (47.56)	3,601,031,329 (59.01)	3,888,723,051 (64.00)	4,912,998,563 (81.22)
Oral single-agent NSAIDs	16,820,841,878 (273.37)	16,783,061,930 (273.29)	10,313,644,080 (168.11)	6,736,943,463 (110.41)	5,288,275,611 (87.04)	4,773,158,982 (78.91)
Topical anti-inflammatory patches	36,534,662,734 (593.75)	36,233,045,296 (590.01)	32,890,288,606 (536.11)	31,946,410,369 (523.55)	31,517,633,932 (518.74)	31,110,749,791 (514.30)

Second-generation antihistamines	48,384,127,421 (786.32)	49,688,790,377 (809.12)	41,184,273,165 (671.30)	39,426,021,127 (646.13)	46,225,133,211 (760.81)	46,427,641,534 (767.50)
Heparinoid-containing topical preparations	26,795,649,736 (435.48)	29,496,514,954 (480.31)	30,555,068,767 (498.05)	32,466,105,662 (532.07)	30,364,039,739 (499.75)	29,238,721,284 (483.35)
Female						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	738,034,717 (11.37)	809,494,871 (12.50)	774,379,776 (11.95)	1,007,663,087 (15.63)	1,083,883,388 (16.89)	1,294,743,841 (20.28)
Oral single-agent NSAIDs	735,209,968 (11.33)	709,845,879 (10.96)	655,335,211 (10.11)	671,045,989 (10.41)	697,977,069 (10.87)	719,599,875 (11.27)
Topical anti-inflammatory patches	2,663,290,851 (41.03)	2,633,020,569 (40.66)	2,503,911,937 (38.64)	2,546,403,101 (39.49)	2,743,450,126 (42.74)	2,806,000,301 (43.94)
Second-generation antihistamines	1,433,690,610 (22.09)	1,493,106,014 (23.06)	1,455,068,459 (22.46)	1,567,044,165 (24.30)	2,062,846,425 (32.14)	2,222,900,380 (34.81)
Heparinoid-containing topical preparations	1,890,263,091 (29.12)	2,127,616,138 (32.86)	2,381,814,241 (36.76)	2,943,413,824 (45.65)	3,019,234,285 (47.04)	3,214,887,643 (50.34)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	5,576,360,944 (85.91)	6,167,427,130 (95.24)	5,689,064,224 (87.80)	6,929,106,981 (107.46)	7,058,836,105 (109.97)	8,309,544,849 (130.12)
Oral single-agent NSAIDs	36,378,066,529 (560.43)	35,936,823,623 (554.96)	22,116,691,173 (341.32)	14,391,264,469 (223.18)	10,684,148,845 (166.45)	9,281,367,986 (145.34)

Topical anti-inflammatory patches	69,188,223,487 (1065.89)	67,876,731,595 (1048.19)	59,715,802,968 (921.58)	57,190,852,187 (886.91)	55,673,030,692 (867.33)	54,453,091,493 (852.71)
Second-generation antihistamines	65,444,274,687 (1008.22)	67,696,650,341 (1045.41)	56,730,668,183 (875.51)	54,297,955,963 (842.05)	61,979,793,034 (965.58)	62,690,440,534 (981.70)
Heparinoid-containing topical preparations	33,403,590,077 (514.61)	36,973,402,331 (570.96)	38,343,188,928 (591.74)	40,745,869,942 (631.89)	38,058,714,764 (592.92)	36,875,126,583 (577.45)

The data in parentheses represent per capita values.

OTC: over-the-counter, NDB: National Database of Health Insurance Claims, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Table 4. Annual prescription volume and costs of representative OTC-like drugs stratified by age: Analysis of the NDB Open Data

Age ≤64 years						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	562,515,986 (6.19)	579,705,445 (6.42)	410,573,984 (4.56)	601,194,602 (6.73)	721,787,643 (8.14)	955,506,716 (10.84)
Oral single-agent NSAIDs	394,844,792 (4.35)	382,191,871 (4.23)	338,421,258 (3.76)	353,668,303 (3.96)	370,861,732 (4.18)	392,743,389 (4.46)
Topical anti-inflammatory patches	882,676,071 (9.71)	879,161,485 (9.74)	843,386,926 (9.36)	879,309,821 (9.85)	971,442,433 (10.95)	1,024,033,177 (11.62)
Second-generation antihistamines	1,784,923,105 (19.64)	1,843,085,929 (20.42)	1,761,328,192 (19.54)	1,907,730,413 (21.37)	2,569,311,886 (28.96)	2,745,318,179 (31.15)
Heparinoid-containing topical preparations	2,603,314,010 (28.65)	2,929,772,573 (32.45)	3,286,576,418 (36.47)	4,001,216,968 (44.81)	4,085,121,555 (46.05)	4,282,891,723 (48.60)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	4,182,482,132 (46.03)	4,343,349,046 (48.11)	2,993,967,873 (33.22)	4,106,926,352 (46.00)	4,668,225,666 (52.62)	6,158,537,509 (69.88)
Oral single-agent NSAIDs	14,293,941,753 (157.31)	14,314,684,255 (158.56)	8,693,439,106 (96.47)	5,953,119,481 (66.67)	4,740,106,414 (53.43)	4,320,269,209 (49.02)
Topical anti-inflammatory patches	22,218,337,424 (244.51)	21,793,753,385 (241.40)	19,161,795,980 (212.63)	18,739,005,100 (209.87)	18,806,373,469 (212.00)	19,104,112,886 (216.77)

Second-generation antihistamines	77,877,080,117 (857.04)	79,719,895,342 (883.03)	65,223,264,726 (723.75)	62,581,875,912 (700.91)	74,489,739,050 (839.69)	74,742,075,676 (848.09)
Heparinoid-containing topical preparations	46,029,778,556 (506.56)	50,987,653,105 (564.77)	52,991,914,061 (588.02)	55,832,211,319 (625.31)	51,956,765,121 (585.69)	49,709,459,990 (564.05)
Age 65–74 years						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	158,764,205 (9.02)	171,391,962 (9.85)	177,696,398 (10.20)	230,764,204 (13.16)	228,383,876 (13.54)	263,197,595 (16.30)
Oral single-agent NSAIDs	243,168,982 (13.81)	233,509,002 (13.42)	224,427,570 (12.88)	235,428,587 (13.42)	239,531,276 (14.20)	242,508,351 (15.02)
Topical anti-inflammatory patches	975,029,825 (55.39)	953,911,163 (54.84)	934,770,255 (53.65)	971,050,765 (55.36)	1,007,293,631 (59.70)	995,849,656 (61.67)
Second-generation antihistamines	333,238,654 (18.93)	348,345,770 (20.03)	357,139,243 (20.50)	384,132,085 (21.90)	484,648,899 (28.73)	515,498,082 (31.92)
Heparinoid-containing topical preparations	277,556,473 (15.77)	305,093,212 (17.54)	344,639,828 (19.78)	442,066,521 (25.20)	447,787,605 (26.54)	481,415,766 (29.81)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	1,223,391,366 (69.50)	1,334,825,072 (76.74)	1,332,263,886 (76.46)	1,620,705,750 (92.40)	1,520,521,191 (90.12)	1,715,639,272 (106.24)
Oral single-agent NSAIDs	12,031,643,811 (683.50)	11,772,323,880 (676.80)	7,296,049,432 (418.71)	4,844,290,641 (276.17)	3,587,758,385 (212.65)	3,068,415,321 (190.01)

Topical anti-inflammatory patches	25,356,273,804 (1440.45)	24,500,240,136 (1408.55)	22,144,204,062 (1270.83)	21,645,421,685 (1233.99)	20,373,773,138 (1207.55)	19,259,144,834 (1192.59)
Second-generation antihistamines	15,813,921,166 (898.37)	16,422,084,036 (944.12)	14,403,125,993 (826.58)	13,813,379,139 (787.49)	14,818,851,374 (878.31)	14,828,090,960 (918.20)
Heparinoid-containing topical preparations	4,750,419,304 (269.86)	5,117,762,373 (294.23)	5,343,153,478 (306.64)	5,853,281,093 (333.69)	5,373,465,471 (318.48)	5,206,338,956 (322.39)
Age ≥75 years						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	451,056,598 (25.09)	520,682,019 (28.16)	580,351,376 (31.20)	694,823,727 (37.21)	726,101,725 (37.50)	832,308,232 (41.46)
Oral single-agent NSAIDs	491,058,149 (27.32)	476,695,639 (25.78)	448,551,130 (24.11)	450,266,655 (24.11)	474,832,121 (24.52)	491,693,864 (24.49)
Topical anti-inflammatory patches	2,210,694,172 (122.97)	2,209,514,997 (119.50)	2,112,549,019 (113.57)	2,126,449,194 (113.88)	2,319,574,615 (119.79)	2,387,635,637 (118.94)
Second-generation antihistamines	415,358,307 (23.10)	442,193,464 (23.92)	445,521,576 (23.95)	474,878,588 (25.43)	614,382,129 (31.73)	679,960,291 (33.87)
Heparinoid-containing topical preparations	553,227,591 (30.77)	624,923,740 (33.80)	691,846,826 (37.19)	887,212,729 (47.52)	946,255,632 (48.87)	1,065,159,430 (53.06)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	3,448,249,255 (191.81)	4,012,366,524 (217.00)	4,280,917,420 (230.13)	4,802,506,207 (257.20)	4,758,812,300 (245.76)	5,348,366,630 (266.42)

Oral single-agent NSAIDs	26,873,322,844 (1494.87)	26,632,877,419 (1440.39)	16,440,846,714 (883.82)	10,330,797,810 (553.28)	7,644,559,657 (394.78)	6,665,842,438 (332.05)
Topical anti-inflammatory patches	58,148,274,994 (3234.59)	57,815,783,370 (3126.87)	51,300,091,532 (2757.77)	48,752,835,771 (2611.01)	48,010,518,016 (2479.37)	47,200,583,564 (2351.21)
Second-generation antihistamines	20,137,400,825 (1120.18)	21,243,461,340 (1148.92)	18,288,550,629 (983.15)	17,328,722,039 (928.06)	18,896,335,820 (975.85)	19,547,915,431 (973.74)
Heparinoid-containing topical preparations	9,419,041,953 (523.95)	10,364,501,808 (560.55)	10,563,190,156 (567.85)	11,526,483,192 (617.31)	11,092,523,911 (572.84)	11,198,048,921 (557.81)

The data in parentheses represent per capita values.

OTC: over-the-counter, NDB: National Database of Health Insurance Claims, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Table 5. Annual prescription volume and costs of representative OTC-like drugs: Analysis of the DeSC database

Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	22,783,971 (2.76)	27,538,223 (3.05)	29,776,372 (2.94)	36,054,437 (3.41)	35,144,893 (3.39)	13,668,555 (1.45)
Oral single-agent NSAIDs	29,973,998 (3.63)	31,330,864 (3.47)	32,468,487 (3.21)	31,684,075 (3.00)	30,999,190 (2.99)	13,673,912 (1.45)
Topical anti-inflammatory patches	179,838,243 (21.78)	199,179,487 (22.06)	202,382,635 (20.01)	194,766,686 (18.45)	175,587,797 (16.96)	79,958,254 (8.50)
Second-generation antihistamines	42,955,847 (5.20)	47,075,913 (5.21)	51,218,421 (5.06)	50,273,617 (4.76)	50,009,582 (4.83)	23,064,637 (2.45)
Heparinoid-containing topical preparations	40,528,480 (4.91)	46,952,942 (5.20)	53,485,402 (5.29)	59,569,950 (5.64)	58,099,113 (5.61)	24,973,368 (2.65)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	170,166,457 (20.60)	206,662,145 (22.89)	224,465,333 (22.19)	236,762,020 (22.42)	232,053,305 (22.41)	87,910,101 (9.34)
Oral single-agent NSAIDs	1,427,137,564 (172.80)	1,530,855,564 (169.56)	1,251,907,159 (123.77)	891,257,938 (84.41)	601,515,367 (58.09)	234,045,499 (24.88)
Topical anti-inflammatory patches	4,515,194,510 (546.72)	4,971,647,300 (550.67)	4,789,612,579 (473.53)	4,418,321,669 (418.44)	3,740,691,821 (361.23)	1,605,342,706 (170.63)
Second-generation antihistamines	1,986,286,483 (240.51)	2,063,715,936 (228.58)	2,006,109,073 (198.33)	1,762,634,734 (166.93)	1,563,173,613 (150.95)	679,162,175 (72.19)

Heparinoid-containing	731,609,185	831,409,602	915,917,502	914,134,000	813,897,263	329,877,839
topical preparations	(88.59)	(92.09)	(90.55)	(86.57)	(78.60)	(35.06)

Data in parentheses represent per capita values.

**Supplementary Table 6. Annual prescription volume and costs for representative OTC-like drugs stratified by CCI categories:
Analysis of the DeSC database**

CCI = 0						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	6,279,581 (1.37)	7,042,202 (1.42)	7,500,829 (1.30)	9,642,393 (1.58)	9,270,212 (1.59)	3,568,244 (0.52)
Oral single-agent NSAIDs	9,675,511 (2.11)	10,150,186 (2.04)	11,054,302 (1.92)	10,794,411 (1.77)	10,145,969 (1.74)	4,343,493 (0.63)
Topical anti-inflammatory patches	57,785,319 (12.62)	63,339,679 (12.73)	68,454,484 (11.88)	65,615,922 (10.78)	57,456,141 (9.84)	24,530,086 (3.58)
Second-generation antihistamines	15,032,314 (3.28)	15,926,163 (3.20)	18,748,572 (3.25)	17,739,788 (2.91)	17,223,905 (2.95)	7,412,468 (1.08)
Heparinoid-containing topical preparations	12,788,185 (2.79)	14,612,733 (2.94)	17,997,723 (3.12)	19,515,677 (3.21)	18,219,089 (3.12)	7,216,646 (1.05)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	46,500,170 (10.15)	52,567,352 (10.56)	56,415,665 (9.79)	63,023,321 (10.35)	60,896,045 (10.43)	22,884,506 (3.34)
Oral single-agent NSAIDs	439,090,948 (95.86)	474,928,147 (95.43)	407,522,956 (70.72)	293,604,131 (48.23)	191,735,084 (32.84)	72,632,278 (10.61)
Topical anti-inflammatory patches	1,438,547,878 (314.05)	1,567,446,472 (314.97)	1,607,360,380 (278.93)	1,474,727,090 (242.28)	1,215,407,068 (208.19)	489,857,867 (71.56)

Second-generation antihistamines	688,398,946 (150.28)	690,947,588 (138.84)	728,054,154 (126.34)	616,710,924 (101.32)	533,266,329 (91.34)	216,203,193 (31.59)
Heparinoid-containing topical preparations	227,583,888 (49.68)	255,009,775 (51.24)	300,842,509 (52.21)	290,118,546 (47.66)	245,311,038 (42.02)	92,802,022 (13.56)
CCI = 1–2						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	7,314,706 (3.42)	8,850,473 (3.82)	9,287,713 (3.81)	11,236,043 (4.51)	10,739,123 (4.34)	4,209,424 (2.99)
Oral single-agent NSAIDs	10,649,404 (4.98)	10,934,110 (4.72)	11,148,309 (4.57)	10,835,484 (4.35)	10,539,126 (4.25)	4,573,534 (3.25)
Topical anti-inflammatory patches	62,607,802 (29.26)	68,961,204 (29.76)	68,781,328 (28.20)	65,955,719 (26.48)	59,343,655 (23.96)	27,065,977 (19.22)
Second-generation antihistamines	15,308,249 (7.16)	16,813,006 (7.26)	17,347,009 (7.11)	17,168,012 (6.89)	17,123,823 (6.91)	7,971,230 (5.66)
Heparinoid-containing topical preparations	13,167,078 (6.15)	15,093,531 (6.51)	16,208,108 (6.64)	18,207,996 (7.31)	17,565,163 (7.09)	7,782,192 (5.53)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	54,488,728 (25.47)	66,230,519 (28.58)	69,839,665 (28.63)	73,656,947 (29.57)	70,823,349 (28.59)	27,070,798 (19.22)
Oral single-agent NSAIDs	509,285,531 (238.05)	536,109,752 (231.34)	434,258,900 (178.02)	307,366,535 (123.41)	206,621,418 (83.41)	78,635,740 (55.83)

Topical anti-inflammatory patches	1,569,859,185 (733.78)	1,718,391,672 (741.51)	1,624,499,091 (665.96)	1,492,903,322 (599.41)	1,261,388,784 (509.22)	542,477,357 (385.18)
Second-generation antihistamines	707,446,210 (330.67)	735,977,038 (317.58)	678,850,330 (278.29)	601,230,086 (241.40)	533,705,007 (215.45)	233,751,550 (165.97)
Heparinoid-containing topical preparations	237,487,746 (111.01)	266,524,931 (115.01)	278,672,678 (114.24)	279,165,024 (112.09)	245,393,287 (99.06)	103,002,253 (73.14)
CCI ≥3						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	9,189,684 (5.97)	11,645,548 (6.71)	12,987,830 (6.79)	15,176,001 (7.66)	15,135,558 (7.42)	5,890,887 (5.10)
Oral single-agent NSAIDs	9,649,083 (6.27)	10,246,568 (5.91)	10,265,876 (5.37)	10,054,180 (5.07)	10,314,095 (5.06)	4,756,885 (4.12)
Topical anti-inflammatory patches	59,445,122 (38.63)	66,878,604 (38.56)	65,146,823 (34.06)	63,195,045 (31.89)	58,788,001 (28.81)	28,362,191 (24.56)
Second-generation antihistamines	12,615,284 (8.20)	14,336,744 (8.27)	15,122,840 (7.91)	15,365,817 (7.76)	15,661,854 (7.68)	7,680,939 (6.65)
Heparinoid-containing topical preparations	14,573,217 (9.47)	17,246,678 (9.94)	19,279,571 (10.08)	21,846,277 (11.03)	22,314,861 (10.94)	9,974,530 (8.64)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	69,177,559 (44.96)	87,864,274 (50.66)	98,210,003 (51.34)	100,081,752 (50.51)	100,333,911 (49.18)	37,954,797 (32.86)

Oral single-agent NSAIDs	478,761,085 (311.16)	519,817,665 (299.70)	410,125,303 (214.41)	290,287,272 (146.51)	203,158,865 (99.58)	82,777,481 (71.67)
Topical anti-inflammatory patches	1,506,787,447 (979.30)	1,685,809,156 (971.95)	1,557,753,108 (814.38)	1,450,691,257 (732.17)	1,263,895,969 (619.48)	573,007,482 (496.09)
Second-generation antihistamines	590,441,327 (383.74)	636,791,310 (367.14)	599,204,589 (313.26)	544,693,724 (274.91)	496,202,277 (243.21)	229,207,432 (198.44)
Heparinoid-containing topical preparations	266,537,551 (173.23)	309,874,896 (178.66)	336,402,315 (175.87)	344,850,430 (174.05)	323,192,938 (158.41)	134,073,564 (116.08)

Data in parentheses represent per capita values.

CCI: Charlson Comorbidity Index, OTC: over-the-counter, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Table 7. Annual prescription volume and costs of representative OTC-like drugs by the presence of Japan's leading causes of death: Analysis of the DeSC database

With malignant neoplasms						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	4,354,337 (5.62)	5,444,527 (6.22)	6,260,540 (6.27)	7,292,523 (7.07)	7,233,067 (6.85)	2,875,880 (4.92)
Oral single-agent NSAIDs	3,987,424 (5.15)	4,232,207 (4.84)	4,417,614 (4.43)	4,405,280 (4.27)	4,481,739 (4.25)	1,989,366 (3.40)
Topical anti-inflammatory patches	25,644,375 (33.11)	29,125,939 (33.30)	29,599,916 (29.66)	29,303,154 (28.39)	27,192,543 (25.76)	12,969,467 (22.18)
Second-generation antihistamines	5,236,616 (6.76)	6,162,249 (7.04)	6,753,452 (6.77)	6,950,305 (6.73)	7,210,312 (6.83)	3,445,439 (5.89)
Heparinoid-containing topical preparations	7,819,254 (10.09)	9,204,360 (10.52)	10,547,803 (10.57)	12,091,509 (11.72)	12,201,861 (11.56)	5,166,325 (8.83)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	32,990,318 (42.59)	41,321,126 (47.24)	47,639,293 (47.73)	48,508,958 (47.00)	48,373,302 (45.83)	18,690,339 (31.96)
Oral single-agent NSAIDs	197,685,017 (255.21)	215,674,919 (246.55)	173,964,428 (174.31)	125,434,555 (121.54)	87,420,454 (82.82)	34,196,098 (58.47)
Topical anti-inflammatory patches	653,443,052 (843.58)	736,279,278 (841.68)	707,380,769 (708.80)	672,212,984 (651.35)	584,433,108 (553.69)	262,244,248 (448.40)

Second-generation antihistamines	244,804,298 (316.04)	273,271,580 (312.39)	267,586,078 (268.12)	246,799,386 (239.14)	228,719,820 (216.69)	103,703,819 (177.32)
Heparinoid-containing topical preparations	144,429,227 (186.46)	167,159,384 (191.09)	186,750,761 (187.13)	194,157,774 (188.13)	179,338,401 (169.91)	70,895,849 (121.22)
With heart diseases						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	10,677,691 (5.19)	13,528,341 (5.92)	15,375,848 (5.91)	18,058,223 (6.74)	17,839,954 (6.61)	6,660,958 (4.48)
Oral single-agent NSAIDs	12,876,738 (6.26)	13,496,259 (5.91)	13,942,155 (5.36)	13,451,770 (5.02)	13,570,902 (5.03)	6,085,817 (4.10)
Topical anti-inflammatory patches	84,472,871 (41.08)	93,966,513 (41.15)	94,495,219 (36.34)	90,716,740 (33.87)	82,982,076 (30.76)	38,402,687 (25.85)
Second-generation antihistamines	15,601,116 (7.59)	17,494,090 (7.66)	18,743,602 (7.21)	18,920,774 (7.06)	19,165,043 (7.10)	8,933,402 (6.01)
Heparinoid-containing topical preparations	16,223,821 (7.89)	19,032,765 (8.33)	21,721,664 (8.35)	24,595,070 (9.18)	24,802,514 (9.19)	10,895,274 (7.33)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	80,139,262 (38.97)	101,893,985 (44.62)	115,986,135 (44.61)	118,731,860 (44.33)	117,874,481 (43.70)	42,775,277 (28.79)
Oral single-agent NSAIDs	638,662,662 (310.60)	684,059,276 (299.56)	556,448,593 (214.00)	390,291,170 (145.73)	269,143,886 (99.77)	106,719,238 (71.83)

Topical anti-inflammatory patches	2,130,660,489 (1036.20)	2,356,202,549 (1031.83)	2,249,625,391 (865.18)	2,071,825,861 (773.57)	1,778,611,685 (659.32)	774,428,937 (521.26)
Second-generation antihistamines	727,036,280 (353.58)	771,723,076 (337.95)	739,633,591 (284.45)	665,695,899 (248.55)	601,962,422 (223.14)	265,419,510 (178.65)
Heparinoid-containing topical preparations	294,363,931 (143.16)	337,685,261 (147.88)	374,497,028 (144.03)	381,529,758 (142.45)	353,339,740 (130.98)	145,332,261 (97.82)
With cerebrovascular diseases						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	5,397,598 (4.74)	6,812,499 (5.47)	7,710,498 (5.52)	8,765,878 (6.20)	8,365,388 (5.99)	3,046,756 (3.99)
Oral single-agent NSAIDs	6,719,422 (5.90)	6,846,671 (5.50)	6,979,471 (4.99)	6,563,801 (4.64)	6,398,769 (4.58)	2,833,934 (3.71)
Topical anti-inflammatory patches	43,865,001 (38.52)	47,604,512 (38.22)	46,584,572 (33.33)	43,819,809 (31.00)	39,212,569 (28.08)	17,657,628 (23.12)
Second-generation antihistamines	7,818,283 (6.87)	8,625,508 (6.93)	9,081,505 (6.50)	8,945,340 (6.33)	8,860,304 (6.34)	4,028,856 (5.28)
Heparinoid-containing topical preparations	8,747,527 (7.68)	10,045,653 (8.07)	11,065,966 (7.92)	12,079,731 (8.54)	11,966,900 (8.57)	5,253,771 (6.88)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	40,474,373 (35.54)	51,303,223 (41.19)	58,127,911 (41.59)	57,531,072 (40.70)	55,346,818 (39.63)	19,526,747 (25.57)

Oral single-agent NSAIDs	337,326,894 (296.20)	352,037,098 (282.67)	282,391,742 (202.03)	193,890,265 (137.15)	129,814,408 (92.96)	50,357,827 (65.95)
Topical anti-inflammatory patches	1,115,730,453 (979.71)	1,202,372,981 (965.44)	1,116,431,934 (798.72)	1,004,779,741 (710.75)	842,839,313 (603.56)	357,124,849 (467.68)
Second-generation antihistamines	366,159,481 (321.52)	382,184,903 (306.87)	359,324,759 (257.07)	317,604,664 (224.66)	280,745,390 (201.04)	120,455,157 (157.75)
Heparinoid-containing topical preparations	158,556,251 (139.23)	178,905,148 (143.65)	190,698,514 (136.43)	186,699,684 (132.07)	170,282,827 (121.94)	69,590,668 (91.13)
With renal diseases						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	2,524,316 (7.57)	3,276,613 (8.50)	3,861,958 (8.61)	4,586,754 (9.55)	4,692,943 (9.17)	1,839,406 (6.14)
Oral single-agent NSAIDs	1,689,085 (5.07)	1,821,976 (4.73)	1,874,459 (4.18)	1,911,100 (3.98)	2,021,053 (3.95)	982,402 (3.28)
Topical anti-inflammatory patches	12,649,480 (37.94)	14,541,176 (37.74)	14,875,759 (33.18)	15,069,317 (31.37)	14,449,616 (28.25)	7,008,288 (23.38)
Second-generation antihistamines	2,595,815 (7.79)	2,995,840 (7.78)	3,295,576 (7.35)	3,505,995 (7.30)	3,703,152 (7.24)	1,799,554 (6.00)
Heparinoid-containing topical preparations	3,772,239 (11.31)	4,517,184 (11.72)	5,274,574 (11.76)	6,099,186 (12.70)	6,357,378 (12.43)	2,734,413 (9.12)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023

Oral single-agent acetaminophen	18,951,139 (56.84)	24,661,806 (64.01)	29,076,154 (64.85)	30,147,370 (62.75)	31,068,762 (60.74)	11,818,126 (39.43)
Oral single-agent NSAIDs	84,937,541 (254.76)	93,573,875 (242.88)	76,337,482 (170.25)	56,148,000 (116.88)	39,882,688 (77.97)	17,150,434 (57.22)
Topical anti-inflammatory patches	323,867,862 (971.41)	370,714,920 (962.23)	359,055,739 (800.80)	348,721,907 (725.89)	312,885,374 (611.68)	143,372,486 (478.36)
Second-generation antihistamines	120,960,156 (362.81)	133,106,767 (345.49)	130,795,265 (291.71)	124,829,861 (259.84)	117,533,918 (229.78)	54,394,609 (181.49)
Heparinoid-containing topical preparations	69,461,537 (208.34)	81,170,970 (210.69)	91,803,889 (204.75)	96,149,024 (200.14)	92,409,709 (180.66)	36,926,591 (123.21)
With Alzheimer's disease						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	1,601,109 (4.26)	2,078,136 (4.85)	2,326,209 (4.77)	2,646,446 (5.27)	2,609,781 (5.16)	900,306 (3.24)
Oral single-agent NSAIDs	1,650,480 (4.40)	1,787,524 (4.18)	1,822,142 (3.73)	1,722,603 (3.43)	1,707,102 (3.37)	762,676 (2.74)
Topical anti-inflammatory patches	8,174,147 (21.77)	9,201,621 (21.49)	9,040,797 (18.52)	8,513,196 (16.94)	7,615,164 (15.05)	3,313,659 (11.92)
Second-generation antihistamines	1,794,992 (4.78)	2,051,353 (4.79)	2,159,913 (4.42)	2,124,703 (4.23)	2,102,612 (4.15)	934,596 (3.36)
Heparinoid-containing topical preparations	2,467,814 (6.57)	2,915,506 (6.81)	3,277,961 (6.72)	3,543,910 (7.05)	3,629,756 (7.17)	1,714,253 (6.17)

Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	11,966,982 (31.88)	15,538,197 (36.29)	17,401,845 (35.65)	17,206,430 (34.25)	17,051,332 (33.69)	5,736,039 (20.64)
Oral single-agent NSAIDs	87,011,692 (231.77)	97,086,133 (226.76)	76,905,817 (157.55)	51,522,880 (102.55)	34,792,465 (68.74)	13,631,433 (49.05)
Topical anti-inflammatory patches	204,957,129 (545.95)	231,087,534 (539.75)	214,093,270 (438.60)	193,481,239 (385.11)	162,628,127 (321.30)	66,749,816 (240.21)
Second-generation antihistamines	83,750,705 (223.09)	90,111,718 (210.47)	84,277,697 (172.66)	75,328,386 (149.94)	66,704,963 (131.79)	28,084,993 (101.07)
Heparinoid-containing topical preparations	44,803,027 (119.34)	51,578,449 (120.47)	55,822,341 (114.36)	53,824,337 (107.13)	50,976,891 (100.71)	22,884,208 (82.35)

The data in parentheses represent per capita values.

OTC: over-the-counter, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Table 8. Number of individuals categorized by health insurance type in the DeSC database

	2018	2019	2020	2021	2022	2023
Total	8,258,708 (100.0%)	9,028,436 (100.0%)	10,114,795 (100.0%)	10,558,971 (100.0%)	10,355,350 (100.0%)	9,408,449 (100.0%)
National Health Insurance	4,323,938 (52.4%)	4,688,678 (51.9%)	5,213,161 (51.5%)	5,521,430 (52.3%)	5,165,407 (49.9%)	4,301,933 (45.7%)
Employees' health insurance	854,938 (10.4%)	845,090 (9.4%)	840,520 (8.3%)	838,140 (7.9%)	829,945 (8.0%)	662,029 (7.0%)
Medical Care System for the Advanced Elderly	3,079,832 (37.3%)	3,494,668 (38.7%)	4,061,114 (40.2%)	4,199,401 (39.8%)	4,359,998 (42.1%)	4,444,487 (47.2%)

Supplementary Table 9. Annual prescription volume and costs of representative OTC-like drugs stratified by health insurance types: Analysis of the DeSC database

National health insurance						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	6,821,466 (1.58)	7,504,441 (1.60)	7,120,832 (1.37)	9,323,625 (1.69)	8,687,937 (1.68)	3,231,379 (0.75)
Oral single-agent NSAIDs	8,258,882 (1.91)	8,406,474 (1.79)	8,903,700 (1.71)	8,802,628 (1.59)	7,723,052 (1.50)	2,848,336 (0.66)
Topical anti-inflammatory patches	38,629,089 (8.93)	40,536,315 (8.65)	42,376,606 (8.13)	41,433,892 (7.50)	33,492,509 (6.48)	12,243,668 (2.85)
Second-generation antihistamines	16,991,596 (3.93)	18,198,408 (3.88)	20,481,116 (3.93)	19,538,614 (3.54)	18,128,295 (3.51)	6,210,302 (1.44)
Heparinoid-containing topical preparations	14,261,569 (3.30)	16,381,343 (3.49)	19,150,864 (3.67)	20,707,821 (3.75)	18,672,976 (3.62)	5,417,489 (1.26)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	50,410,197 (11.66)	55,848,866 (11.91)	53,776,873 (10.32)	61,450,986 (11.13)	57,519,226 (11.14)	20,837,986 (4.84)
Oral single-agent NSAIDs	354,699,504 (82.03)	367,564,244 (78.39)	315,727,298 (60.56)	225,670,307 (40.87)	139,099,230 (26.93)	45,372,154 (10.55)
Topical anti-inflammatory patches	967,142,777 (223.67)	1,000,077,095 (213.30)	989,846,514 (189.87)	931,050,707 (168.62)	706,858,585 (136.84)	250,502,363 (58.23)

Second-generation antihistamines	780,103,673 (180.42)	797,438,951 (170.08)	797,016,157 (152.89)	683,601,486 (123.81)	565,275,253 (109.43)	180,272,968 (41.91)
Heparinoid-containing topical preparations	255,371,351 (59.06)	288,026,526 (61.43)	323,868,513 (62.13)	316,752,097 (57.37)	257,695,669 (49.89)	70,134,580 (16.30)
Employees' health insurance						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	1,075,146 (1.26)	1,027,941 (1.22)	618,240 (0.74)	991,409 (1.18)	1,031,199 (1.24)	1,050,042 (1.59)
Oral single-agent NSAIDs	683,437 (0.80)	640,408 (0.76)	529,210 (0.63)	523,577 (0.62)	443,635 (0.53)	438,110 (0.66)
Topical anti-inflammatory patches	2,323,293 (2.72)	2,227,017 (2.64)	2,037,371 (2.42)	1,997,366 (2.38)	1,566,301 (1.89)	1,472,189 (2.22)
Second-generation antihistamines	3,099,508 (3.63)	2,981,469 (3.53)	2,857,796 (3.40)	2,848,173 (3.40)	2,596,755 (3.13)	2,498,921 (3.77)
Heparinoid-containing topical preparations	2,591,230 (3.03)	2,874,640 (3.40)	2,918,433 (3.47)	3,374,183 (4.03)	2,838,348 (3.42)	2,655,066 (4.01)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	7,825,542 (9.15)	7,505,864 (8.88)	4,606,278 (5.48)	6,451,804 (7.70)	6,729,366 (8.11)	6,753,570 (10.20)
Oral single-agent NSAIDs	22,364,575 (26.16)	22,047,348 (26.09)	16,650,871 (19.81)	12,865,165 (15.35)	7,703,474 (9.28)	6,479,834 (9.79)

Topical anti-inflammatory patches	57,654,200 (67.44)	54,089,027 (64.00)	46,919,097 (55.82)	43,741,023 (52.19)	32,307,452 (38.93)	28,679,773 (43.32)
Second-generation antihistamines	146,824,058 (171.74)	134,683,575 (159.37)	115,593,806 (137.53)	102,949,385 (122.83)	82,665,090 (99.60)	73,504,652 (111.03)
Heparinoid-containing topical preparations	47,772,169 (55.88)	52,577,069 (62.21)	51,498,556 (61.27)	51,911,964 (61.94)	39,752,615 (47.90)	35,180,880 (53.14)
Medical care system for the advanced elderly						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	14,887,359 (4.83)	19,005,841 (5.44)	22,037,300 (5.43)	25,739,403 (6.13)	25,425,757 (5.83)	9,387,134 (2.11)
Oral single-agent NSAIDs	21,031,679 (6.83)	22,283,982 (6.38)	23,035,577 (5.67)	22,357,870 (5.32)	22,832,503 (5.24)	10,387,466 (2.34)
Topical anti-inflammatory patches	138,885,861 (45.10)	156,416,155 (44.76)	157,968,658 (38.90)	151,335,428 (36.04)	140,528,987 (32.23)	66,242,397 (14.90)
Second-generation antihistamines	22,864,743 (7.42)	25,896,036 (7.41)	27,879,509 (6.86)	27,886,830 (6.64)	29,284,532 (6.72)	14,355,414 (3.23)
Heparinoid-containing topical preparations	23,675,681 (7.69)	27,696,959 (7.93)	31,416,105 (7.74)	35,487,946 (8.45)	36,587,789 (8.39)	16,900,813 (3.80)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	111,930,718 (36.34)	143,307,415 (41.01)	166,082,182 (40.90)	168,859,230 (40.21)	167,804,713 (38.49)	60,318,545 (13.57)

Oral single-agent NSAIDs	1,050,073,485 (340.95)	1,141,243,972 (326.57)	919,528,990 (226.42)	652,722,466 (155.43)	454,712,663 (104.29)	182,193,511 (40.99)
Topical anti-inflammatory patches	3,490,397,533 (1133.31)	3,917,481,178 (1120.99)	3,752,846,968 (924.09)	3,443,529,939 (820.01)	3,001,525,784 (688.42)	1,326,160,570 (298.38)
Second-generation antihistamines	1,059,358,752 (343.97)	1,131,593,410 (323.81)	1,093,499,110 (269.26)	976,083,863 (232.43)	915,233,270 (209.92)	425,384,555 (95.71)
Heparinoid-containing topical preparations	428,465,665 (139.12)	490,806,007 (140.44)	540,550,433 (133.10)	545,469,939 (129.89)	516,448,979 (118.45)	224,562,379 (50.53)

The data in parentheses represent per capita values.

OTC: over-the-counter, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Table 10. Annual prescription volume and costs of representative OTC-like drugs stratified by healthcare facility types: Analysis of the DeSC database

Clinics						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	12,626,587 (2.03)	15,354,487 (2.29)	15,843,486 (2.18)	19,739,659 (2.66)	18,714,059 (2.55)	7,639,996 (1.91)
Oral single-agent NSAIDs	21,810,891 (3.51)	23,010,689 (3.43)	24,164,039 (3.32)	23,500,508 (3.17)	22,825,822 (3.11)	10,513,274 (2.63)
Topical anti-inflammatory patches	146,057,406 (23.53)	162,507,481 (24.22)	165,957,948 (22.80)	159,979,614 (21.56)	145,224,643 (19.79)	67,656,235 (16.95)
Second-generation antihistamines	34,983,348 (5.64)	38,236,839 (5.70)	41,637,102 (5.72)	40,478,513 (5.45)	40,334,754 (5.50)	19,074,037 (4.78)
Heparinoid-containing topical preparations	28,743,251 (4.63)	33,350,808 (4.97)	37,956,973 (5.22)	42,240,372 (5.69)	40,924,719 (5.58)	18,486,952 (4.63)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	93,870,925 (15.12)	114,754,790 (17.11)	118,897,429 (16.34)	128,793,931 (17.36)	122,331,865 (16.67)	48,375,781 (12.12)
Oral single-agent NSAIDs	957,076,012 (154.21)	1,041,413,882 (155.23)	868,443,041 (119.33)	633,972,672 (85.43)	432,495,966 (58.93)	173,767,458 (43.54)
Topical anti-inflammatory patches	3,626,635,134 (584.34)	4,019,799,792 (599.19)	3,901,619,584 (536.12)	3,603,958,815 (485.64)	3,076,379,645 (419.20)	1,347,154,643 (337.52)

Second-generation antihistamines	1,595,078,308 (257.01)	1,648,983,521 (245.80)	1,599,728,329 (219.82)	1,391,582,655 (187.52)	1,238,081,657 (168.71)	549,667,560 (137.72)
Heparinoid-containing topical preparations	503,245,416 (81.09)	572,180,821 (85.29)	626,112,359 (86.03)	618,961,339 (83.41)	542,753,813 (73.96)	233,138,722 (58.41)
Non-university hospitals						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	9,084,944 (2.44)	10,910,488 (2.68)	12,621,901 (2.89)	14,730,688 (3.26)	14,801,787 (3.29)	5,387,308 (2.22)
Oral single-agent NSAIDs	7,217,492 (1.94)	7,426,613 (1.82)	7,438,035 (1.70)	7,261,750 (1.61)	7,243,677 (1.61)	2,845,452 (1.17)
Topical anti-inflammatory patches	31,010,589 (8.34)	33,965,440 (8.34)	33,943,529 (7.76)	32,229,397 (7.13)	28,063,813 (6.23)	11,365,706 (4.67)
Second-generation antihistamines	6,589,660 (1.77)	7,370,685 (1.81)	8,117,225 (1.86)	8,214,881 (1.82)	8,106,843 (1.80)	3,437,115 (1.41)
Heparinoid-containing topical preparations	8,579,278 (2.31)	10,055,018 (2.47)	11,620,328 (2.66)	12,975,702 (2.87)	12,913,360 (2.87)	5,106,541 (2.10)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	67,690,730 (18.21)	81,644,281 (20.04)	94,852,854 (21.69)	96,586,321 (21.38)	98,020,145 (21.77)	35,278,352 (14.51)
Oral single-agent NSAIDs	415,984,026 (111.89)	436,182,025 (107.04)	343,249,521 (78.49)	224,498,062 (49.70)	148,025,668 (32.88)	55,058,089 (22.64)

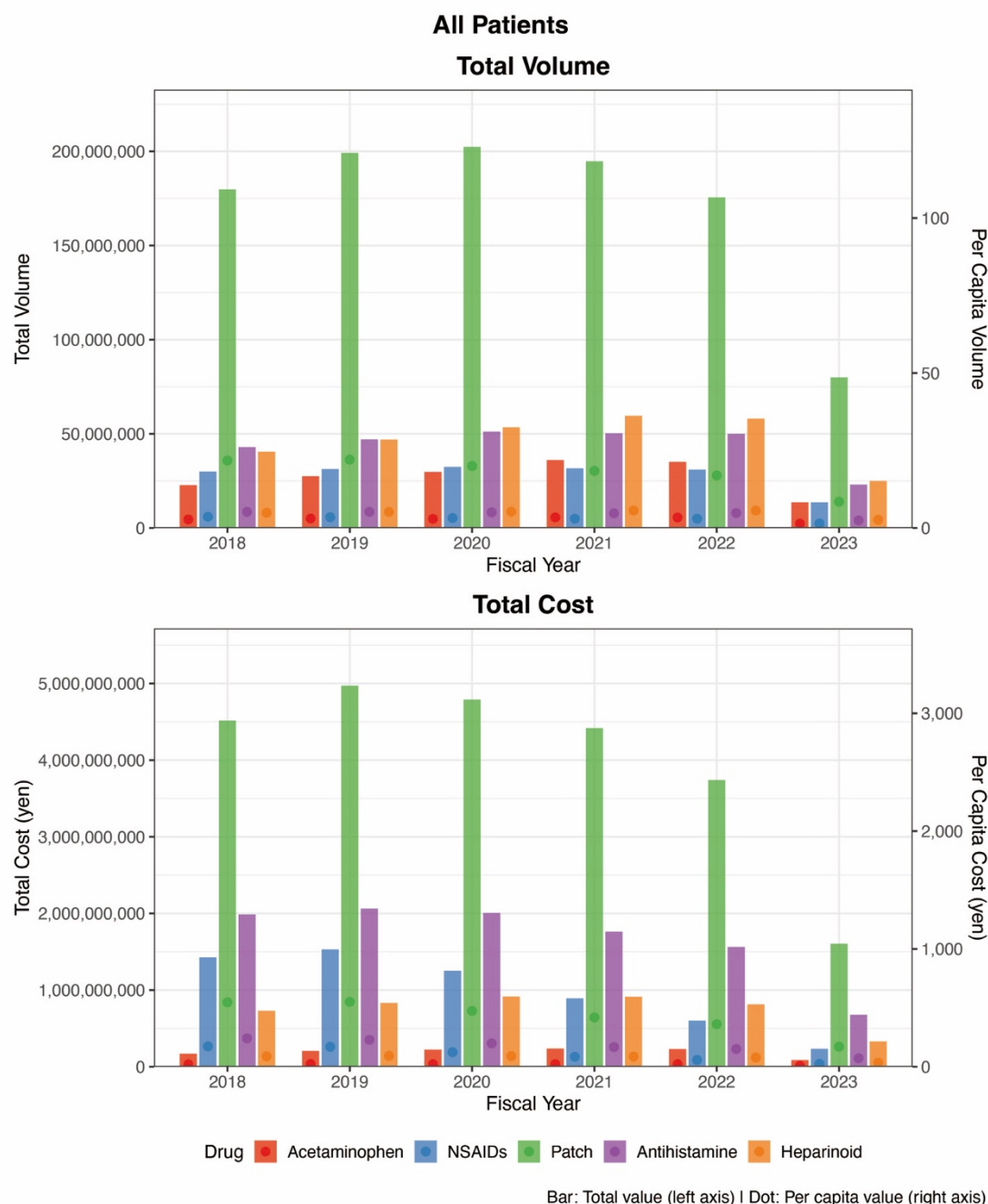
Topical anti-inflammatory patches	806,486,365 (216.93)	871,497,049 (213.87)	817,134,474 (186.85)	745,054,778 (164.93)	609,263,471 (135.34)	236,944,090 (97.43)
Second-generation antihistamines	321,268,815 (86.41)	342,776,690 (84.12)	341,594,862 (78.11)	304,929,115 (67.50)	266,320,867 (59.16)	110,460,160 (45.42)
Heparinoid-containing topical preparations	159,772,778 (42.98)	183,505,712 (45.03)	206,814,200 (47.29)	207,892,867 (46.02)	189,694,886 (42.14)	72,784,004 (29.93)
University hospitals						
Prescription volume (number) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	1,032,826 (2.12)	1,238,627 (2.29)	1,306,413 (2.29)	1,580,090 (2.72)	1,626,076 (2.76)	640,427 (2.04)
Oral single-agent NSAIDs	907,844 (1.86)	867,975 (1.61)	860,938 (1.51)	920,161 (1.59)	928,888 (1.58)	314,571 (1.00)
Topical anti-inflammatory patches	2,488,296 (5.11)	2,555,241 (4.73)	2,440,074 (4.28)	2,542,234 (4.38)	2,283,270 (3.87)	930,306 (2.96)
Second-generation antihistamines	1,337,709 (2.75)	1,442,731 (2.67)	1,447,553 (2.54)	1,565,497 (2.70)	1,550,391 (2.63)	541,847 (1.72)
Heparinoid-containing topical preparations	3,142,110 (6.45)	3,505,660 (6.49)	3,879,171 (6.81)	4,340,625 (7.48)	4,250,783 (7.21)	1,377,912 (4.38)
Prescription costs (Japanese Yen) of the study drugs						
	2018	2019	2020	2021	2022	2023
Oral single-agent acetaminophen	8,320,946 (17.09)	10,018,576 (18.54)	10,681,827 (18.76)	11,357,306 (19.58)	11,682,651 (19.81)	4,250,778 (13.51)

Oral single-agent NSAIDs	52,662,558 (108.18)	52,252,543 (96.72)	39,920,660 (70.10)	32,735,155 (56.43)	20,987,409 (35.59)	5,212,671 (16.57)
Topical anti-inflammatory patches	75,509,972 (155.11)	76,592,794 (141.77)	69,773,931 (122.53)	68,943,475 (118.84)	54,716,114 (92.79)	21,126,985 (67.16)
Second-generation antihistamines	67,385,396 (138.42)	70,424,275 (130.35)	63,814,459 (112.06)	65,419,366 (112.77)	58,020,301 (98.39)	18,711,912 (59.49)
Heparinoid-containing topical preparations	67,338,614 (138.33)	74,901,937 (138.64)	82,469,701 (144.82)	87,073,625 (150.09)	81,288,634 (137.85)	23,920,216 (76.04)

The data in parentheses represent per capita values.

OTC: over-the-counter, NSAIDs: nonsteroidal anti-inflammatory drugs

Supplementary Figure 1. Trends in the prescription volume and costs of representative OTC-like drugs in the overall population: Analysis of the DeSC database



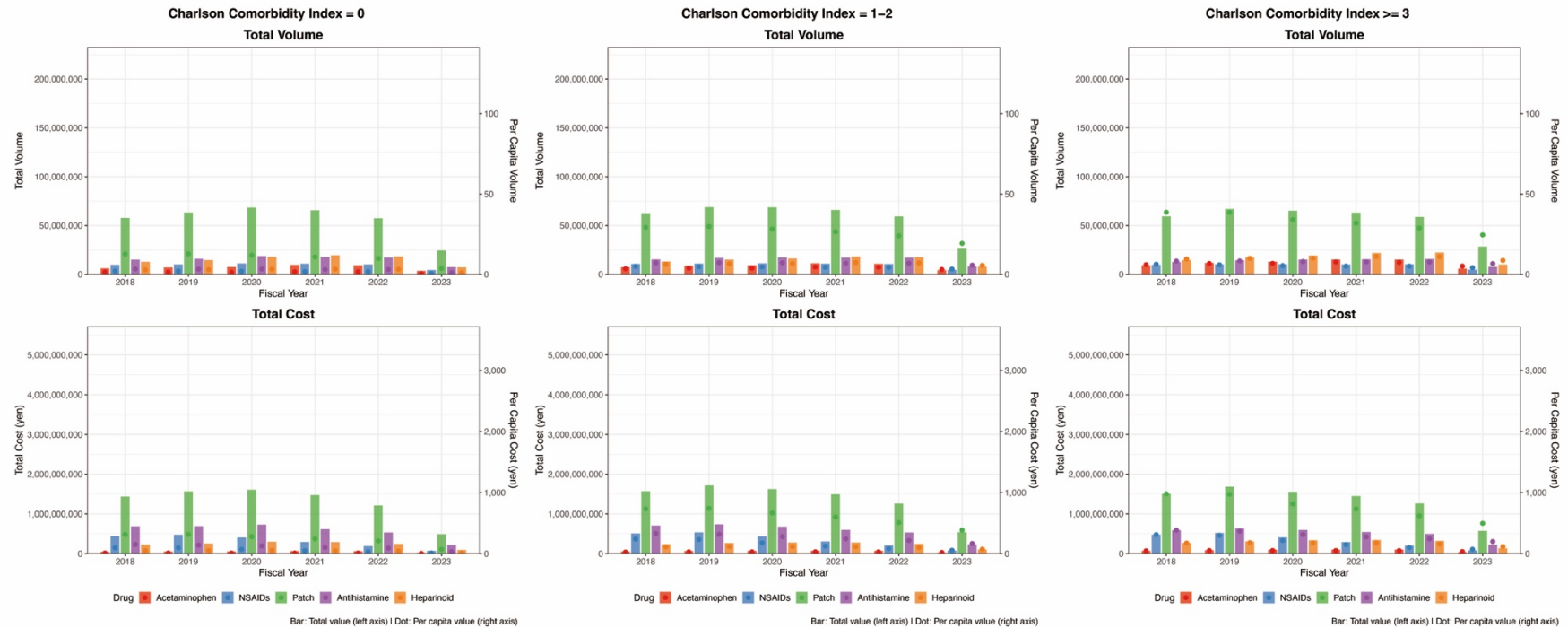
The upper panel shows the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis), and the lower panel shows the total prescription costs (bars, left y-axis) and per capita prescription costs (dots, right y-axis).

Note: Prescription volume and costs are presented for oral single-agent acetaminophen,

oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations.

OTC: over-the-counter

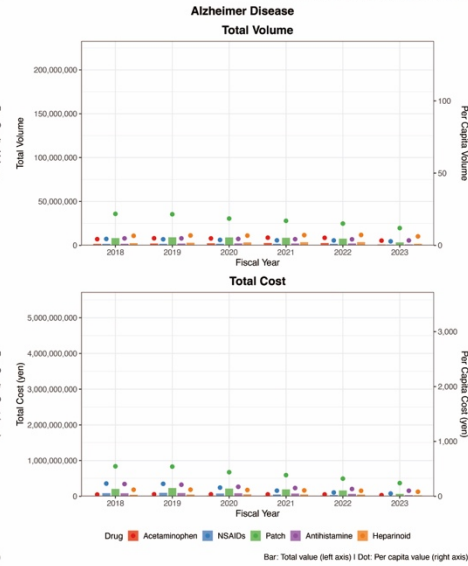
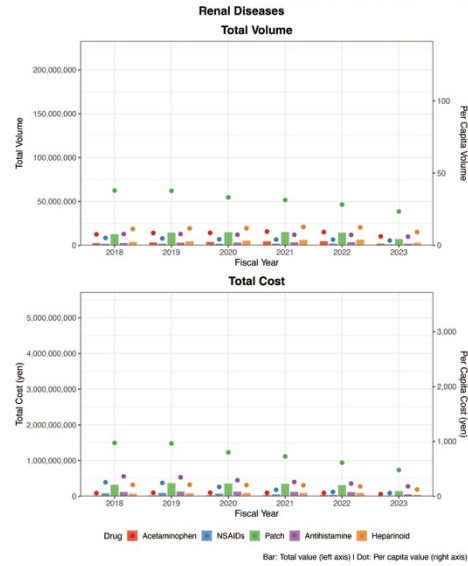
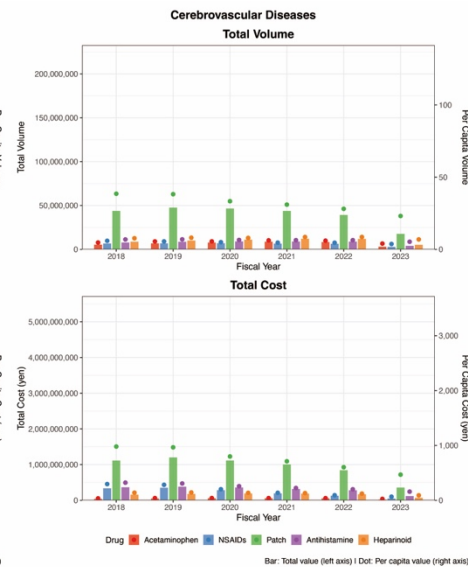
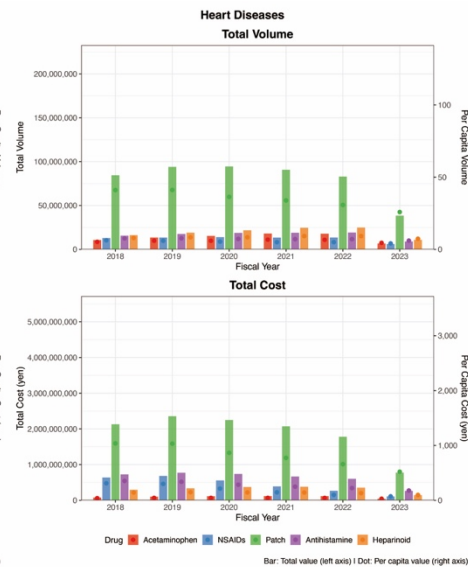
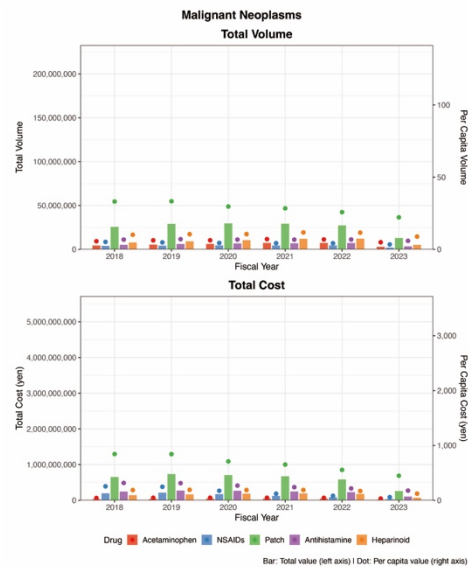
Supplementary Figure 2. CCI-specific trends in the prescription volume and costs of representative OTC-like drugs: Analysis of the DeSC database



- (A) Trends in the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals with a Charlson Comorbidity Index (CCI) of 0.
- (B) Trends in the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals with a CCI of 1–2.
- (C) Trends in the total prescription volume (bars, left y-axis) and per capita prescription volume (dots, right y-axis) among individuals with a CCI of ≥ 3 .

Note: Prescription volume and costs are presented for oral single-agent acetaminophen, oral single-agent nonsteroidal anti-inflammatory drugs (NSAIDs), topical anti-inflammatory patches, oral second-generation antihistamines, and heparinoid-containing topical preparations.
OTC: over-the-counter

**Supplementary Figure 3. Major-disease-specific trends in the prescription volume and costs of representative OTC-like drugs:
Analysis of the DeSC database**

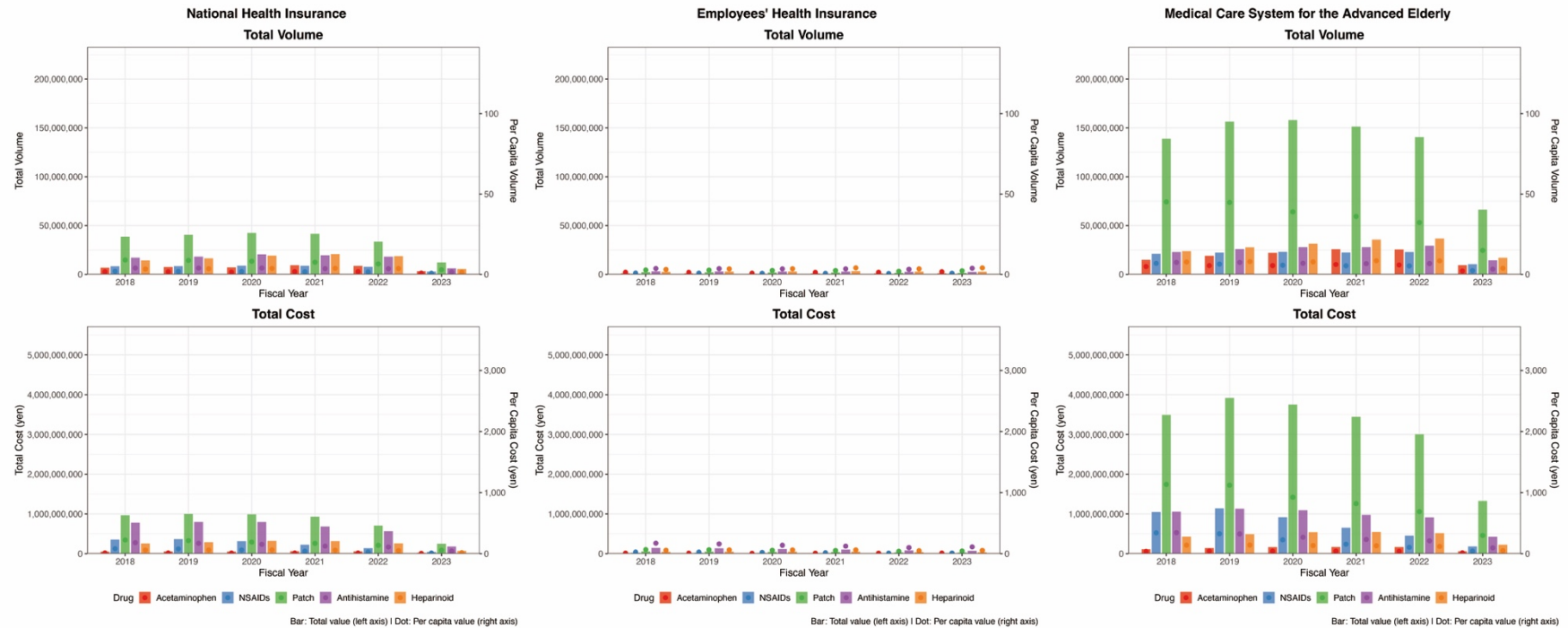


- (A) Trends in the prescription volume and costs of representative OTC-like drugs in individuals with malignant neoplasms.
- (B) Trends in the prescription volume and costs of representative OTC-like drugs in individuals with heart diseases.
- (C) Trends in the prescription volume and costs of representative OTC-like drugs in individuals with cerebrovascular diseases.
- (D) Trends in the prescription volume and costs of representative OTC-like drugs in individuals with renal diseases.
- (E) Trends in the prescription volume and costs of representative OTC-like drugs in individuals with Alzheimer's disease.

Note: The bars indicate total values (left y-axis), and dots indicate per capita values (right y-axis).

OTC: over-the-counter

Supplementary Figure 4. Health-insurance–disease-specific trends in the prescription volume and costs of representative OTC-like drugs: Analysis of the DeSC database

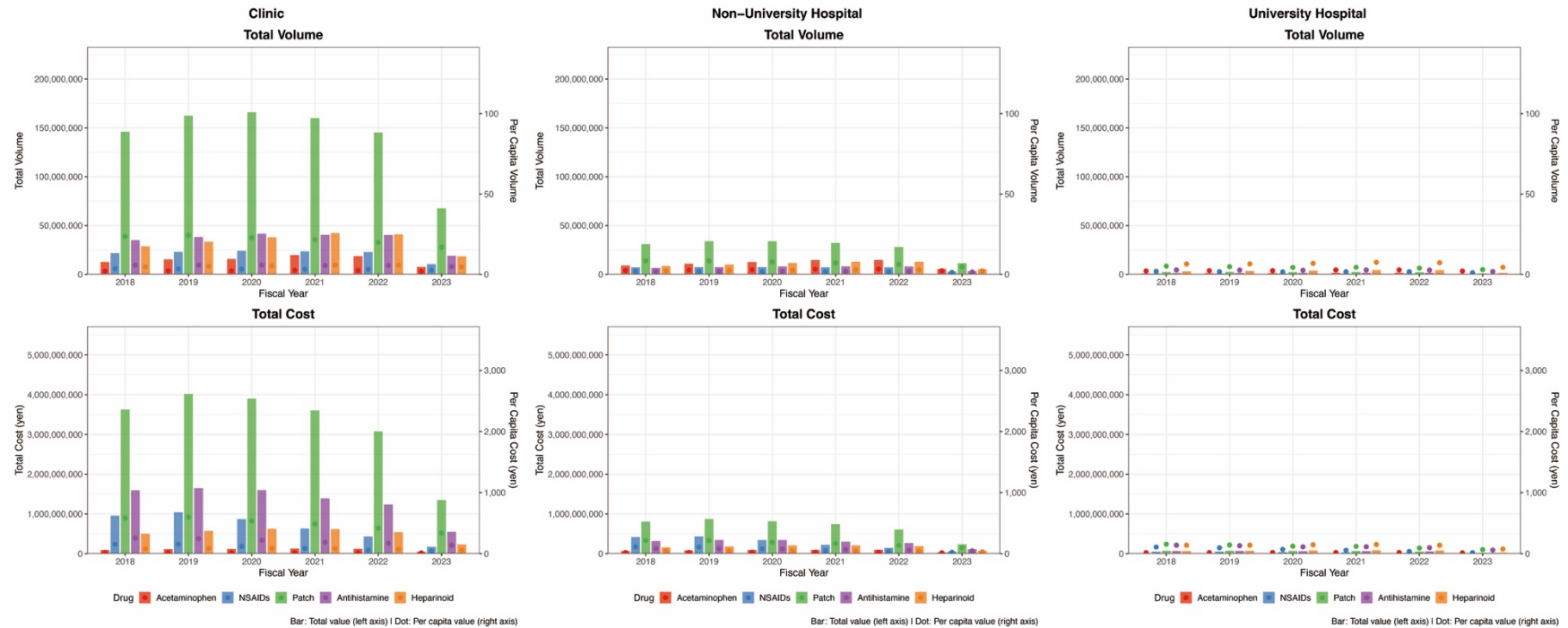


- (A) Trends in the prescription volume and costs of representative OTC-like drugs in individuals enrolled in National Health Insurance.
- (B) Trends in the prescription volume and costs of representative OTC-like drugs in individuals enrolled in Employees' Health Insurance.
- (C) Trends in the prescription volume and costs of representative OTC-like drugs in individuals enrolled in the Medical Care System for the Advanced Elderly.

Note: The bars indicate total values (left y-axis), and dots indicate per capita values (right y-axis).

OTC: over-the-counter

Supplementary Figure 5. Healthcare-facility–disease-specific trends in the prescription volume and costs of representative OTC-like drugs: Analysis of the DeSC database



(A) Trends in the prescription volume and costs of representative OTC-like drugs in individuals visiting clinics.

(B) Trends in the prescription volume and costs of representative OTC-like drugs in individuals visiting non-university hospitals.

(C) Trends in the prescription volume and costs of representative OTC-like drugs in individuals visiting university hospitals.

Note: The bars indicate total values (left y-axis), and dots indicate per capita values (right y-axis).

OTC: over-the-counter