Review began 01/22/2024 Review ended 02/03/2024 Published 02/08/2024

© Copyright 2024

Shrestha et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Nature and Trend of Pharmaceutical Payments to Japanese Board-Certified Neurologists Between 2016 and 2019: A Pre-emergence Analysis Amidst the Development of Next-Generation Alzheimer's Disease Drugs

Rajeev Shrestha¹, Hiroaki Saito², Erika Yamashita³, Sunil Shrestha⁴, Tetsuya Tanimoto⁵, Akihiko Ozaki⁶

 Palliative Care and Chronic Disease, Green Pastures Hospital, Pokhara, NPL 2. Gastroenterology, Soma Central Hospital, Soma, JPN 3. Heart Care, Medical Governance Research Institute, Tokyo, JPN 4. Pharmacy, Monash University Malaysia, Jalan, MYS 5. Internal Medicine, Navitas Clinic Shinjuku, Tokyo, JPN 6. Surgery, Graduate School of Public Health, Teikyo University, Tokyo, JPN

Corresponding author: Rajeev Shrestha, rajiv2stha@gmail.com

Abstract

Objective: There is insufficient data on the financial relationships between Japanese neurologists and pharmaceutical companies prior to the advent of new-generation Alzheimer's disease drugs. The purpose of this study is to evaluate the magnitude, prevalence, and trend of the financial relationship between Japanese neurologists and pharmaceutical companies between 2016 and 2019.

Methods: A cross-sectional study was undertaken to evaluate the financial relationships between all boardcertified neurology specialists and pharmaceutical companies in Japan from 2016 and 2019. Descriptive statistics were applied to measure the magnitude and prevalence of payments among specialists, as well as their trends during the study periods.

Results: In a four-year analysis, 77 pharmaceutical companies disbursed a total of USD 36,869,204 across 50,050 payments to 2,696 neurologists in Japan, revealing a mean payment of USD 10,809 per specialist. Notably, the Gini index of 0.997 indicated a high inequality in payment distribution, with a minority of specialists receiving a substantial proportion of payments. Trends displayed irregularities, but an overall increase in total payments from 2016 to 2019, with a significant contribution from the top 10 pharmaceutical companies accounting for 74.2% of total payments, with Takeda Pharmaceutical and Eisai Company notably increasing payments in 2019. There were notable geographical variations in neurologist and payment distribution across 47 prefectures.

Conclusion: Our analysis of neurologist payments from pharmaceutical companies in Japan showed a substantial financial relationship with overall increases, yearly varied increments, and payment inequality. Caution is warranted as financial ties may intensify with the continued development of next-generation Alzheimer's disease drugs.

Categories: Other, Neurology, Health Policy Keywords: alzheimer's drugs, neurologist, pharmaceutical payment, japan, industry payment

Introduction

Pharmaceutical payment to physicians, often referred to as "pharmaceutical marketing" or "pharmaceutical detailing," is a practice, where pharmaceutical companies provide payments, gifts, or other incentives as a part of their marketing strategies. While this practice can provide opportunities to share pharmaceutical product knowledge and develop innovative treatment approaches for patient care, it also raises concerns about conflicts of interest. These conflicts may lead clinicians to favour their products, which can be problematic and result in negative patient outcomes. This preference can manifest in the form of favoured prescribing, specific treatment guideline recommendations, and biased research [1,2]. Therefore, strict financial support or transaction monitoring between pharmaceutical companies and clinicians is imperative.

Many developed countries have formulated and implemented regulatory policies and guidelines to ensure transparency in the financial transactions between the pharmaceutical industry and physicians [3-5], namely the Physician Payment Sunshine Act and the Open Payments Database in the United States [3,4]. The Japan Pharmaceutical Manufacturers Association (JPMA), representing major pharmaceutical companies in Japan, introduced transparency guidelines in 2013 that require its members to disclose payments made to physicians [5]. Under this regulation, pharmaceutical companies affiliated with the JPMA are required to disclose their payment information on their websites, although the level of detail is less comprehensive than what is disclosed in the United States.

How to cite this article

Shrestha R, Saito H, Yamashita E, et al. (February 08, 2024) Nature and Trend of Pharmaceutical Payments to Japanese Board-Certified Neurologists Between 2016 and 2019: A Pre-emergence Analysis Amidst the Development of Next-Generation Alzheimer's Disease Drugs. Cureus 16(2): e53848. DOI 10.7759/cureus.53848

Many previous studies from Japan, Canada, and the United States demonstrated evidence of financial relationships between pharmaceutical companies and physicians of various specialties, such as oncologists, paediatrics, and haematologists, and of various authoritative positions, such as clinical guideline authors, professors, and members of society [1,6-9]. In particular, multiple studies in the United States reported the financial relationship between pharmaceutical companies and neurologists [10,11].

The burden of neurological diseases, especially dementia, is particularly acute in developed countries experiencing population aging, and Japan is no exception. As of September 15, 2022, individuals aged 65 years or older constituted 29.1% of the Japanese population, being the highest elderly population in the world [12]. Indeed, Ikeda et al. estimated an average of JPY 1,073 billion annual healthcare cost for Alzheimer's disease dementia, one of the common neurological conditions in Japan [13]. Currently, we are witnessing the emergence of next-generation Alzheimer's disease drugs, such as lecanemab, developed by the Japanese pharmaceutical company Eisai, which costs nearly three million yen per patient per year [14]. It is anticipated that associated payments will rise in the future, affecting Japan and beyond. In light of this situation, it is important to understand the trends in payments before the widespread introduction of these new therapeutic agents and prepare for the future upsurge. This study explored the pharmaceutical payment magnitudes and trends in Japan from 2016 to 2019.

Materials And Methods

Study design

This cross-sectional retrospective analysis evaluates the financial relationships between all board-certified neurology specialists in Japan and pharmaceutical companies. The study population comprises all neurology specialists certified by the Japanese Society of Neurology (JSN). JSN is the sole and largest professional medical society for neurology in Japan, which trains and certifies neurologists with extensive skills and knowledge.

Data collection

We extracted specialists' names and affiliations from the official JSN webpage on December 31, 2021. We obtained information on the prefectures of affiliated facilities associated with the data provided in this study. Additionally, we collected details of payments (speaking/lecturing, writing, consulting, etc.) made by all JPMA-member pharmaceutical companies to healthcare specialists between 2016 and 2019. This data collection was facilitated by the JPMA transparency guidance, a voluntary initiative promoting the disclosure of payments to healthcare professionals and organizations. As of December 2021, these collected data represented the latest publicly available dataset in Japan. Information on payments for speaking, writing, and consulting was available at the individual physician level. Notably, smaller and more common payment categories (meals & beverages, travel/accommodation, trial enrolment reimbursements) were not individually disclosed by companies, as previously mentioned.

Data analysis

Payment values and counts were analysed descriptively for both specialists and pharmaceutical companies. Subsequently, the Gini index, a measure of income inequality ranging from 0 to 1, was employed to assess payment concentration among specialists. Higher Gini values indicated a greater disparity in payment distribution. Furthermore, this study examined trends in physician payments from pharmaceutical companies in Japan. Payment data were analysed for companies participating in the JPMA over a four-year period. The relative percentage of the average annual increase in payments per specialist and the number of specialists receiving payments were also calculated. Payment trends were assessed for years of payments, number of recipient physicians, and individual payment values. To explore regional variations in physicianindustry relationships, we aggregated payments and specialist numbers by prefecture of the physician's affiliated facility. We then calculated and compared payment amounts and neurologist numbers per million people in each prefecture. Population data were based on the October 1, 2019, Basic Resident Register. The payment values were expressed in USD dollars using the 2019 average monthly exchange rate, JPY 109.0 per USD 1. Analyses were conducted with Microsoft Excel 16.0 (Microsoft® Corp., Redmond, WA) and Python 3.9.10.

Ethical approval

This study received ethical approval from the Medical Governance Research Institute (approval number: MG2018-04-20200605; date: June 5, 2020). Due to its reliance on publicly available data from pharmaceutical companies and the society webpage, informed consent was waived by the Ethics Committee.

Results

Overview of payments

Out of a total of 6,107 registered neurologists under the Japanese Society of Neurology, only 3,411 (55.9%) neurologists received a total of USD 36,869,204 (JPY 4,018,743,154) from 77 pharmaceutical companies with 50,050 payment counts. Among the 93 companies, 15 companies did not pay money for the physician

included in the study. The mean (standard deviation, SD) and median (interquartile range, IQR) four-year combined payment values per specialist were USD 10,809 (SD: USD 29,791) and USD 2,214 (IQR: USD 715-7,690), respectively. At maximum, one specialist received USD 502,645 personal payments over the four years. The mean and median number of counts over the four years were 15 (SD: 29) and five (IQR: 2-14) counts per specialist. The neurologists received payments from an average of 8.9 (SD: 4.3) and a median of 4.0 (IQR: 2-11) pharmaceutical companies. The maximum payment counts and pharmaceutical companies per specialist over the four years were 355 payments and 119 companies. The Gini index was reported at 0.997 for the four-year combined total payments per specialist, indicating high inequality in payment distribution among neurologists. A very low proportion of specialists are receiving a high proportion of payment (Figure 1). The most common payment category was speaking, which occupied 84.8% (USD 31,272,630) of total payments (Table 1).



FIGURE 1: Pharmaceutical payment concentration among neurologists in Japan

| Variables | Content | Value | |
|---|---------------------|-------------------|--|
| | Payment values, USD | 36,869,204 | |
| Total payments, USD | Counts, n | 50,050 | |
| | Companies, n | 77 | |
| | Payment values, USD | 10,809±29,791 | |
| Average per specialist ± SD | Counts, n | 15±29 | |
| | Companies, n | 8.9 | |
| | Payment values, USD | 2,214 (715-7,690) | |
| Median (IQR) | Counts, n | 5 (2-14) | |
| | Companies, n | 4 (2-11) | |
| | Payment values, USD | 31-502,645 | |
| Range | Counts, n | 1-355 | |
| | Companies, n | 1-119 | |
| | Any payments | 3,411 (55.9) | |
| | Payments>USD 500 | 2,950 (48.3) | |
| | Payments>USD 1000 | 2,334 (38.2) | |
| Physicians with specific payments, n (%) | Payments>USD 5000 | 1,137 (18.6) | |
| | Payments>USD 10000 | 714 (11.7) | |
| | Payments>USD 50000 | 155 (2.5) | |
| | Payments>USD 100000 | 70 (1.1) | |
| Gini index | | 0.997 | |
| | Speaking | 31,272,630 (84.8) | |
| Catagony of normanta LISD (%) | Consulting | 4,154,762 (11.3) | |
| | Writing | 1,430,748 (3.9) | |
| | Other | 10,860 (0.0) | |
| Note: SD: Standard Deviation; n: number, IQR; interquartile range | | | |

TABLE 1: Summary of personal payments from pharmaceutical companies to neurologists from2016 to 2019

Trends of payments

Table 2 presents the trend of pharmaceutical payments to neurologists from 2016 to 2019. The median payments per specialist ranged from USD 1,055 (IQR: USD 511-3,319) in 2016 and USD 1,331 (IQR: USD 520-3,772) in 2019. The annual change rate was 2.6% for all pharmaceutical companies for four years; however, it was only 1% while specifically reviewing the complete four-year pharmaceutical payment data. The Gini index is uniform in all years in the four-year complete database group, while the index increased in 2019, viewing the overall payment scale. The yearly payment increase was the highest in the specialist group receiving more than USD 100,000.

| Variables | Content | 2016 | 2017 | 2018 | 2019 | Average yearly change, % |
|------------------------------|----------|-----------|-----------|-----------|-----------|--------------------------|
| All pharmaceutical companies | s (n=77) | | | | | |
| | | 8,633,140 | 9,213,717 | 9,220,946 | 9,801,197 | |

| Total payments | USD (JPY) | (941,012,221) | (1,004,295,168) | (1,005,083,103) | (1,068,330,426) | |
|---|-------------------------|----------------------------|----------------------------|----------------------------|----------------------------|------|
| Average payments ± SD | USD | 3,962±9,439 | 4,102±9,668 | 4,107±9,140 | 4,276±9,262 | 2.6 |
| Median payments | USD | 1,055 (511- 3,319) | 1,226 (511-3,270) | 1,328 (511-3,576) | 1,331 (520-3,772) | |
| Payment range | USD | 58-110,581 | 0-134,906 | 31-138,830 | 68-144,195 | |
| Gini index | | 0.997 | 0.997 | 0.997 | 0.998 | |
| | Any payments | 2,179 (36.0) | 2,242 (37.0) | 2,245 (37.0) | 2,292 (38.0) | 1.7 |
| | Payments>USD 500 | 1,751 (29.0) | 1,863 (31.0) | 1,885 (31.0) | 1,936 (32.0) | 3.4 |
| | Payments>USD 1,000 | 1,196 (20.0) | 1,285 (21.0) | 1,344 (22.0) | 1,378 (23.0) | 4.9 |
| Physicians with specific payments, n (%) | Payments>USD 5,000 | 376 (6.2) | 410 (6.7) | 414 (6.8) | 446 (7.3) | 5.9 |
| | Payments>USD 10,000 | 188 (3.1) | 211 (3.5) | 207 (3.4) | 221 (3.6) | 5.7 |
| | Payments>USD 50,000 | 23 (0.38) | 19 (0.31) | 24 (0.39) | 19 (0.31) | -4.0 |
| | Payments>USD 100,000 | 3 (0.05) | 4 0.07 | 1 (0.02) | 2 (0.03) | 19.4 |
| Pharmaceutical companies w | vith 4-year payment | data (n=46) | | | | |
| Total payments | USD (JPY) | 8,534,024 (930,208,577) | 9,138,961 (996,146,764) | 8,737,552 (952,393,158) | 9,028,687 (984,126,840) | |
| Average payments ± SD | USD | 3,955±9,416 | 4,122±9,659 | 3,952±8,895 | 4,061±8,865 | 1.0 |
| Median payments | USD | 1,055 (511- 3,317) | 1,226 (511-3,275) | 1,276 (511-3,401) | 1,328 (520-3,631) | |
| Payment range | USD | 58-110,581 | 0-132,862 | 31-134,241 | 68-141,086 | |
| Gini index | | 0.997 | 0.997 | 0.997 | 0.997 | |
| | Any payments | 2,158 (35.0) | 2,213 (36.0) | 2,211 (36.0) | 2,223 (36.0) | 1.0 |
| Physicians with specific payments, n (%) | Payments>USD 500 | 1,730 (28.0) | 1,845 (30.0) | 1,858 (30.0) | 1,881 (31.0) | 2.9 |
| | Payments>USD 1,000 | 1,184 (19.0) | 1,279 (21.0) | 1,323 (22.0) | 1,339 (22.0) | 4.2 |
| | Payments>USD 5,000 | 373 (6.1) | 408 (6.7) | 390 (6.4) | 410 (6.7) | 3.4 |
| | Payments>USD 10,000 | 188 (3.1) | 211 (3.5) | 189 (3.1) | 196 (3.2) | 1.8 |
| | Payments>USD 50,000 | 22 (0.4) | 19 (0.3) | 21 (0.3) | 16 (0.3) | -9.0 |
| | Payments>USD 100,000 | 3 (0.0) | 4 (0.1) | 1 (0.0) | 2 (0.0) | 19.4 |

TABLE 2: Trend of personal payments from pharmaceutical companies to neurologists from 2016 to 2019

Payments by company

The payment types by the top 10 paying companies are shown in Figure 2. Among 77 paying pharmaceutical

companies, payments from the top 10 companies accounted for 74.2 % of total payments, with USD 27,355,989 between 2016 and 2019. Daiichi Sankyo was the top company providing the largest payment in all years, except in 2019. However, in recent years, two companies (Takeda Pharmaceutical and Eisai Company) have drastically increased their payments in 2019 compared to previous years, securing the highest-paying company in 2019.





Distribution of payment and specialists by prefecture

There were notable geographical differences in the distribution of neurologists and payment in Japan (Figure 3). Kyoto (111.11 per million people) and Tottori (91.73 per million people) were the top two prefectures having the highest proportion of neurology specialists' distribution, while Tottori (USD 649,999) and Tokyo (USD 579,634) had the highest payment distribution. Similarly, the lowest payment distribution was in Okinawa (USD 74,461) and Miyazaki (USD 94,236), while the lowest neurologist distribution was different, in Ehime (26.14 per million people) and Gifu (26.17 per million people). The details of payment and specialist distribution among prefectures are given in the attached supplementary file (see Appendix, Table 3).



FIGURE 3: Schematic distribution of neurologists and payment based on prefecture – (a) number of neurologists per million people and (b) payment amounts per million people in USD

Discussion

This study is the first to record the pharmaceutical payment trend to neurologists in Japan. This study found that a total of 36,869,204 US dollars was received by Japanese neurologists from 2016 to 2019, with 10,809 US dollars as an average payment per specialist from 8.9 companies. Many previously conducted pharmaceutical payment studies have also shown a huge payment trend in Japan from 2016 to 2019: \$53,547,391 to respiratory specialists [6], \$33,223,806 to dermatologists [15], \$908,900 to paediatric haematologists/oncologists [16], and \$36,291,434 to haematologists [17]. Furthermore, Ahlawat et al. [11] reported that \$6,210,414 was given to American neurologists for non-research purposes, with an average of \$891 in 2015, and Nalleballe et al. [10] reported an average of \$627 in 2013 and \$3,396 in 2018 to vascular neurologists of the United States. Although a clear picture of payment to neurologists cannot be drawn globally due to the limited studies on pharmaceutical payments to neurologists, the overall findings reported

to date showed huge investment in pharmaceutical payments to neurologists, even before the launch of the new Alzheimer's disease agents. Similarly, there is a lack of detailed documentation on payment; for example, American studies reported payments for research or non-research purposes.

Furthermore, the overall payment of neurologists increased from 2016 to 2019, with an average yearly increment of 2.6%, which is comparatively very low compared to yearly payment increase among other fields of specialities in Japan, such as respiratory specialists (7.6%) [18], head and neck surgery specialists (12.4%) [19], dermatologists (14.1%) [15], and gastroenterologists (2.4%) [20], but similar to haematologists (1.1%) [17]. Similarly, two studies on payment to vascular neurologists and neurology subspecialities in America showed an increasing payment trend. Non-research annual payments to vascular neurologists proportion increased from \$99,749 in 2013 to \$1,032,302 in 2018, while the receiving neurologist proportion increased only by 1% [10]. The overall industry payment to neurology subspecialties increased by 16% from 2014 to 2018 in the United States [21]. The higher payments observed in the US compared to Japan may be attributed to the inclusion of payments from medical device companies to neurologists in the US data, whereas our study only accounted for payments from pharmaceutical companies [22]. Actually, there is a lack of data on payment by the medical device industry in Japan. Penetration of newer medicines in the neurology market was assumed to be the influencing factor for increased payment in the United States [21] and in previous studies of Japan [23], which could also be a potential cause in our context.

One of the prominent reasons for industry payment to prescribers is to increase the market consumption of their product by prescribing by prescribers. Therefore, many studies illustrated that the sponsorship for education interactions (for example, educational training and food and beverage) and consultation fees increase prescribing [24,25]. In our study, most of the payment was given for speaking (\$31,272,630,84.8%), followed by consulting (4,154,762,11.3%), which is consistent with previous studies of Japan [6,17,19,23]. Currently, very few countries are only presenting pharmaceutical payments publicly. Limited database studies of US neurologists also showed higher payment distribution for consultation fees and lower for activities such as food and beverages, around 10-11.5% of the total payment amount [10,26]. Ahlawat et al. [26] specified that the most common payment was for food and beverages (86.5%) but covered a total of 11.5% of total payments. Therefore, further detailed exploration of activities and payment purposes needed to be explored to understand the potential impact and implication of increasing payment trends in Japan.

Similar to the previous studies of Japan, this study also showed the uneven distribution of payment to specialists, irrespective of the geography and population of the prefecture [6,17]. Half of the specialists received less than \$1,000, while only 1.1% received more than \$100,000 payments yearly. This is very similar to the payment studies among head and neck surgeons [19], dermatologists [15], gastroenterologists [20], and respiratory physicians [6], but higher compared with haematologists [17] in Japan. For example, Nalleballe et al. reported a higher distribution of payment to neuroimmunology/MS specialties in the United States [21]. The most significant reason for not being able to use detailed specialties of neurologists in our study is the failure to evaluate positions at their institutions, positions in academic societies, positions in guidelines and academic activities, etc. Past studies have shown that monetary donations are concentrated on physicians who hold important and influential positions in guidelines and academic societies in Japan [20,27,28], and it is possible that the same is true in neurology. Furthermore, the diverse payment distribution could be the result of high payment by the selected pharmaceutical companies producing specific medicines targeting specific specialists. Out of 77 paying pharmaceutical companies, only 10 cover 74.2% of total payments (\$27,355,989), where Daiichi Sankyo was the top company providing the highest payment amount in all years, except in 2019. This is the same company that provided the highest research payment to neurologists in America in 2015 [11]. Meanwhile, two companies, Takeda Pharmaceutical and Eisai Company, have drastically increased their payments in 2019 compared to Daiichi, which can change the payment distribution pattern in the coming years with the possibility of securing the highest payment position. This can be expected because they have already started launching a few medicines targeting neurologists, such as lemborexant and perampanel by Eisai company and a combination of vonoprazan aspirin by Takeda [29,30].

Limitation

This study retains some limitations with areas to explore in the future. First, the study utilized the publicly available database for four years; therefore, there could be the possibility of underreporting or not all the pharmaceutical companies disclosing their payment details. Secondly, this study has not explored the details of payment distribution patterns in neurologists and the causes for that. The detailed information on payment purposes and payments for specific groups or categories of medicines would help explore and have a comprehensive understanding of payment trends uncovered in this study due to limited access to data. Furthermore, the monetary inflation rate during the four-year period (2016-2019) in Japan was not evaluated and adjusted while calculating the payment values.

Conclusions

Our analysis of personal payments from pharmaceutical companies to neurologists in Japan from 2016 to 2019 reveals a total disbursement of USD 36,869,204 across 50,050 payment instances to 2,696 neurologists. Despite an overall increase in payments, yearly increments are highly unequal. Only a very low proportion of

specialists are receiving a high amount of payment. Geographical analysis highlighted differences in neurologist and payment distribution across prefectures. Our findings provide insights into the landscape of personal payments in neurology, emphasizing trends, disparities, and the influential role of top-paying pharmaceutical companies in this financial dynamic. Considering the anticipated increase in payments from pharmaceutical companies due to the development of novel Alzheimer's disease treatments, it is essential to understand the current financial landscape within the neurology field and prepare for this expected upsurge.

Appendices

| S.N. | Prefecture | Number of specialists per million people | Payment amount per million people |
|------|----------------------|--|-----------------------------------|
| 1 | Aichi Prefecture | 47.66949153 | 289279.1654 |
| 2 | Akita | 32.09109731 | 97107.18559 |
| 3 | Aomori Prefecture | 26.4847512 | 209676.2189 |
| 4 | Chiba Prefecture | 39.46317303 | 244916.2835 |
| 5 | Ehime Prefecture | 26.13890963 | 421497.6328 |
| 6 | Fukui Prefecture | 42.96875 | 129207.0671 |
| 7 | Fukuoka Prefecture | 50.15673981 | 262631.5949 |
| 8 | Fukushima Prefecture | 34.12784399 | 199886.4791 |
| 9 | Gifu Prefecture | 26.17010569 | 146132.268 |
| 10 | Gunma Prefecture | 33.98558187 | 172523.8239 |
| 11 | Hiroshima | 47.07560628 | 186106.0477 |
| 12 | Hokkaido | 36.38095238 | 195209.5955 |
| 13 | Hyogo Prefecture | 35.49213319 | 186255.2963 |
| 14 | Ibaraki Prefecture | 29.72027972 | 117891.602 |
| 15 | Ishikawa Prefecture | 57.11775044 | 378821.3508 |
| 16 | Iwate Prefecture | 52.97473513 | 406652.2883 |
| 17 | Kagawa Prefecture | 36.61087866 | 172930.7992 |
| 18 | Kagoshima Prefecture | 83.6454432 | 226175.3141 |
| 19 | Kanagawa Prefecture | 47.18417047 | 296697.4492 |
| 20 | Kochi Prefecture | 35.81661891 | 206781.6566 |
| 21 | Kumamoto Prefecture | 64.64530892 | 316708.957 |
| 22 | Kyoto | 111.111111 | 524038.4057 |
| 23 | Mie Prefecture | 48.28747894 | 229562.6722 |
| 24 | Miyagi Prefecture | 55.94102342 | 484496.5785 |
| 25 | Miyazaki Prefecture | 34.48275862 | 94235.93286 |
| 26 | Nagano Prefecture | 60.02928258 | 260829.2208 |
| 27 | Nagasaki Prefecture | 40.69329314 | 289935.1438 |
| 28 | Nara Prefecture | 53.38345865 | 153534.7313 |
| 29 | Niigata Prefecture | 60.27890238 | 326590.8744 |
| 30 | Oita Prefecture | 45.81497797 | 174123.9623 |
| 31 | Okayama Prefecture | 52.38095238 | 413013.6498 |
| 32 | Okinawa Prefecture | 27.52924983 | 74461.12125 |

| 33 | Osaka Prefecture | 48.0190714 | 304155.3436 |
|----|----------------------|-------------|-------------|
| 34 | Saga Prefecture | 35.58282209 | 225569.0325 |
| 35 | Saitama | 32.5170068 | 206139.8465 |
| 36 | Shiga Prefecture | 50.21216407 | 220069.813 |
| 37 | Shimane Prefecture | 86.05341246 | 421448.5204 |
| 38 | Shizuoka Prefecture | 34.8518112 | 123658.9291 |
| 39 | Tochigi Prefecture | 46.01861427 | 572870.3832 |
| 40 | Tokushima | 45.32967033 | 157042.4942 |
| 41 | Tokyo | 73.05509662 | 579634.3133 |
| 42 | Tottori Prefecture | 91.72661871 | 649998.68 |
| 43 | Toyama Prefecture | 37.35632184 | 197223.1977 |
| 44 | Wakayama Prefecture | 32.43243243 | 262027.0965 |
| 45 | Yamagata Prefecture | 36.17810761 | 135775.0847 |
| 46 | Yamaguchi Prefecture | 48.60088365 | 203510.62 |
| 47 | Yamanashi Prefecture | 43.15659679 | 181234.1542 |

TABLE 3: Details of the distribution of the number of specialists per million people and payment amount per million people in all provinces of Japan

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Rajeev Shrestha, Hiroaki Saito, Erika Yamashita, Sunil Shrestha, Tetsuya Tanimoto, Akihiko Ozaki

Drafting of the manuscript: Rajeev Shrestha

Critical review of the manuscript for important intellectual content: Rajeev Shrestha, Hiroaki Saito, Erika Yamashita, Sunil Shrestha, Tetsuya Tanimoto, Akihiko Ozaki

Acquisition, analysis, or interpretation of data: Hiroaki Saito, Erika Yamashita, Akihiko Ozaki

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Medical Governance Research Institute issued approval MG2018-04-20200605. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: Dr. Ozaki received personal fees from Medical Network Systems, Kyowa Kirin Inc.; Becton, Dickinson and Company; Pfizer, Inc.; and Taiho Pharmaceutical Co., Ltd., outside the scope of the submitted work. Hiroaki Saito received personal fees from Taiho Pharmaceutical Co. Ltd. outside the scope of the submitted work. Tetsuya Tanimoto received personal fees from Medical Network Systems and Bionics Co. Ltd., outside the scope of the submitted work. All remaining authors have nothing to disclose. Regarding non-financial conflicts of interest among the study authors, Dr. Ozaki is engaged in ongoing research examining financial and nonfinancial conflicts of interest among healthcare professionals and pharmaceutical companies in Japan and other countries. Financial relationships: Dr. Ozaki declare(s) personal fees from Tansa. This study also received support from Tansa (formerly known as the Waseda Chronicle), an independent nonprofit news organization dedicated to investigative journalism. Dr. Ozaki declare(s) a grant from Medical Governance Research Institute. This study was funded in part by the Medical Governance Research Institute. This nonprofit enterprise receives donations from a dispensing pharmacy, namely Ain Pharmacies, Inc., other organizations, and private individuals. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

We express our gratitude to Mr. Kohki Yamada for his constructive help in our analysis.

References

- Mitchell AP, Trivedi NU, Gennarelli RL, et al.: Are financial payments from the pharmaceutical industry associated with physician prescribing?: a systematic review. Ann Intern Med. 2021, 174:353-61. 10.7326/M20-5665
- Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L: Industry sponsorship and research outcome. Cochrane Database Syst Rev. 2017, 2:MR000033. 10.1002/14651858.MR000033.pub3
- Tringale KR, Marshall D, Mackey TK, Connor M, Murphy JD, Hattangadi-Gluth JA: Types and distribution of payments from industry to physicians in 2015. JAMA. 2017, 317:1774-84. 10.1001/jama.2017.3091
- Marshall DC, Jackson ME, Hattangadi-Gluth JA: Disclosure of industry payments to physicians: an epidemiologic analysis of early data from the Open Payments Program. Mayo Clin Proc. 2016, 91:84-96. 10.1016/j.mayocp.2015.10.016
- Ozaki A, Saito H, Senoo Y, et al.: Overview and transparency of non-research payments to healthcare organizations and healthcare professionals from pharmaceutical companies in Japan: analysis of payment data in 2016. Health Policy. 2020, 124:727-35. 10.1016/j.healthpol.2020.03.011
- Murayama A, Hoshi M, Saito H, et al.: Nature and trends in personal payments made to the respiratory physicians by pharmaceutical companies in Japan between 2016 and 2019. Respiration. 2022, 101:1088-98. 10.1159/000526576
- Lexchin J: Health services and policy research in Canada: an editor's reflections. Healthc Policy. 2022, 17:42-8. 10.12927/hcpol.2022.26729
- Chambliss WG, Carroll WA, Kennedy D, et al.: Role of the pharmacist in preventing distribution of counterfeit medications. J Am Pharm Assoc (2003). 2012, 52:195-9. 10.1331/JAPhA.2012.11085
- Singh A, Hyman MJ, Modi PK: Evaluation of industry payments to US advanced practice clinicians in 2021. JAMA Netw Open. 2022, 5:e2242869. 10.1001/jamanetworkopen.2022.42869
- Nalleballe K, Sheng S, Li C, et al.: Industry payment to vascular neurologists: a 6-year analysis of the Open Payments Program from 2013 through 2018. Stroke. 2020, 51:1339-43. 10.1161/STROKEAHA.119.027967
- 11. Ahlawat A, Narayanaswami P: Financial relationships between neurologists and industry: the 2015 Open Payments database. Neurology. 2019, 92:1006-13. 10.1212/WNL.00000000007640
- 12. Statistics Bureau, Ministry of Internal Affairs and Communications . (2023). Accessed: January 22, 2024: https://www.stat.go.jp/data/topics/topi1321.html.
- Ikeda S, Mimura M, Ikeda M, Wada-Isoe K, Azuma M, Inoue S, Tomita K: Economic burden of Alzheimer's disease dementia in Japan. J Alzheimers Dis. 2021, 81:309-19. 10.3233/JAD-210075
- 14. van Dyck CH, Swanson CJ, Aisen P, et al.: Lecanemab in early Alzheimer's disease . N Engl J Med. 2023, 388:9-21. 10.1056/NEJMoa2212948
- Murayama A, Kamamoto S, Saito H, Ozaki A: Pharmaceutical payments to Japanese board-certified dermatologists: a 4-year retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019. Sci Rep. 2023, 13:7425. 10.1038/s41598-023-34705-8
- Kamamoto S, Murayama A, Kusumi E, et al.: Evaluation of financial relationships between Japanese certified pediatric hematologist/oncologists and pharmaceutical companies: a cross-sectional analysis of personal payments from pharmaceutical companies between 2016 and 2019. Pediatr Blood Cancer. 2022, 69:e29891. 10.1002/pbc.29891
- Kusumi E, Murayama A, Kamamoto S, et al.: Pharmaceutical payments to Japanese certified hematologists: a retrospective analysis of personal payments from pharmaceutical companies between 2016 and 2019. Blood Cancer J. 2022, 12:54. 10.1038/s41408-022-00656-y
- Murayama A, Hoshi M, Saito H, et al.: Nature and trends of pharmaceutical payments to the board certified respiratory specialists in Japan between 2016 and 2019 [PREPRINT]. medRxiv. 2022, 10.1101/2022.01.16.22269188
- Murayama A, Shigeta H, Kamamoto S, et al.: Pharmaceutical payments to Japanese board-certified head and neck surgeons between 2016 and 2019. OTO Open. 2023, 7:e31. 10.1002/oto2.31
- Murayama A, Kamamoto S, Kawashima M, Saito H, Yamashita E, Tanimoto T, Ozaki A: Cross-sectional analysis of pharmaceutical payments to Japanese board-certified gastroenterologists between 2016 and 2019. BMJ Open. 2023, 13:e068237. 10.1136/bmjopen-2022-068237
- 21. Nalleballe K, Veerapaneni KD, Harada Y, et al.: Trends of industry payments in neurology subspecialties . Cureus. 2020, 12:e9492. 10.7759/cureus.9492
- 22. Program overview. (2022). Accessed: January 11, 2024: https://openpaymentsdata.cms.gov/about.
- Ozaki A, Saito H, Onoue Y, et al.: Pharmaceutical payments to certified oncology specialists in Japan in 2016: a retrospective observational cross-sectional analysis. BMJ Open. 2019, 9:e028805. 10.1136/bmjopen-2018-028805
- Yeh JS, Franklin JM, Avorn J, Landon J, Kesselheim AS: Association of industry payments to physicians with the prescribing of brand-name statins in Massachusetts. JAMA Intern Med. 2016, 176:763-8. 10.1001/jamainternmed.2016.1709
- Mitchell AP, Winn AN, Lund JL, Dusetzina SB: Evaluating the strength of the association between industry payments and prescribing practices in oncology. Oncologist. 2019, 24:632-9. 10.1634/theoncologist.2018-0423
- Ahlawat A, Narayanaswami P: Financial relationships between neurologists and industry: the 2015 Open Payments database. Neurology. 2018, 90:1063-70. 10.1212/WNL.000000000005657
- Murayama A, Saito H, Tanimoto T, Ozaki A: Financial conflicts of interest between pharmaceutical companies and executive board members of internal medicine subspecialty societies in Japan between 2016 and 2020. J Eval Clin Pract. 2023, 29:883-6. 10.1111/jep.13877
- 28. Murayama A, Kamamoto S, Murata N, et al.: Evaluation of financial conflicts of interest and quality of

evidence in Japanese gastroenterology clinical practice guidelines. J Gastroenterol Hepatol. 2023, 38:565-73. 10.1111/jgh.16089

- 29. Double haul of Japanese approvals for Eisai. (2020). Accessed: January 11, 2024:
- https://www.thepharmaletter.com/article/double-haul-of-japanese-approvals-for-eisai.. 30. Launch of aspirin/vonoprazan fumarate combination tablets: 'Cabpirin® combination tablets'. (2020).
- Launch of aspirin/vonoprazan rumarate combination tablets: Cabpirin® combination tablets. (2020). Accessed: January 12, 2024: https://www.otsuka.co.jp/en/company/newsreleases/2020/20200522_1.html.