

Cross-sectional analysis of financial relationships between board certified allergists and pharmaceutical industry in Japan

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Background

Financial interactions between pharmaceutical companies and physicians can lead to conflicts of interest, potentially biasing physicians' clinical practice. This study examines the extent and trends of non-research payments made by pharmaceutical companies to board-certified allergists in Japan between 2016 and 2020.

Methods:

A retrospective analysis of disclosed payment data from pharmaceutical companies affiliated with the Japanese Pharmaceutical Manufacturers Association was conducted. The study focused on non-research payments for lecturing, consulting, and manuscript drafting made to board-certified allergists from 2016

to 2020. We performed descriptive analyses on payment data. Trends were analyzed using generalized estimating equation models.

Results

Of the 3,943 board-certified allergists, 2,398 (60.8%) received non-research payments totaling \$43.4 million over five years. Lecturing fees comprised 85.7% (\$37.2 million) of the total payment amounts. For allergists who received at least one payment, the median amount per allergist was \$3,106 (interquartile range: \$966 – \$12,124), in contrast to a mean of \$18,092 (standard deviation: \$49,233) over the five-year span. The top 1% and 10% of these allergists accounted for 20.8% and 68.8% of all non-research payments, respectively. The annual payment amounts significantly increased by 7.2% annual increase (95% CI: 4.4% – 10.0%, $p < 0.001$) each year until 2019, but saw a significant decrease in 2020 amid the COVID-19 pandemic.

Conclusion

The majority of allergists received non-research payments, with a notable concentration among a small group. Payments increased annually until the pandemic’s onset, which coincided with a substantial decrease. Further research is needed to explore the implications of these financial interactions on clinical practice and patient care in Japan.

List of abbreviations

95% CI: 95% confidence interval; GEE: generalized estimating equation; IQR: interquartile range; JPM: Japanese Pharmaceutical Manufacturers Association

Main body of the manuscript

Introduction

Pharmaceutical companies frequently provide payments to physicians for both research and non-research activities[1,2]. Such financial interactions, while often instrumental in fostering healthcare innovation and enhancing patient care, may also engender potential conflicts of interest[3]. In Japan, pharmaceutical companies have been reported to make substantial non-research payments totaling \$1.8 billion, with \$1.1 billion allocated for the sponsorship of conferences and lectures geared toward drug promotion, and \$236.0 million distributed for lecture and consulting services[4]. The majority of these lecture and consulting payments were directly made to individual physicians. Previous studies suggest that the incidence of non-research payments among Japanese physicians[5-12] surpasses that in other developed countries such as the United States, Australia, and France[1,13-19].

The discipline of allergy and clinical immunology has been marked by the introduction of numerous novel biologics for the treatment of allergic diseases, including asthma, atopic dermatitis, and allergic rhinitis. Concurrently, the last decade in Japan has witnessed the approval of new therapeutic agents for allergic rhinitis, such as antihistamines (e.g., rupatadine, desloratadine, and bilastine) and sublingual immunotherapy products.

The introduction of these novel drugs has expanded the therapeutic choices available to physicians and patients, yet the absence of comparative clinical trials assessing these drugs has resulted in increased promotional activities by pharmaceutical companies. Prior research indicates a yearly 7.2% increase in marketing payments to allergists in the United States, rising from \$13.1 million in 2014 to \$19.2 million in 2019[20]. Additionally, these payments were associated with the prescribing patterns of new biologics for moderate and severe asthma among allergists in the United States[21]. The scrutiny of the financial relationships between allergists and pharmaceutical companies is therefore of particular importance. However, data on these relationships in Japan remain sparse. This study aims to assess the financial interactions between allergists and pharmaceutical companies in Japan using publicly disclosed payment data.

Methods

Study design setting, and participants

We conducted a retrospective analysis of payment data publicly disclosed by major pharmaceutical companies in Japan. The aim was to examine the extent and trends of personal payments made to all board-certified allergists in the country. The analysis included all allergists certified by the Japanese Society of Allergology as of February 2022. The Society, established in 1952, is the preeminent professional organization for medical researchers and physicians specializing in allergy in Japan and is the sole credentialing body for allergists in the nation. As of the specified date, 3,943 allergists were recognized as board-certified by the Society[22].

Payment data disclosed by pharmaceutical companies.

To improve transparency in financial relationships between pharmaceutical companies and healthcare professionals, the Japanese Pharmaceutical Manufacturers Association (JPMA), representing over 80 leading pharmaceutical companies, mandates its members to disclose payments for lecturing, consulting, and manuscript drafting made to physicians, including the recipients' names and affiliations on their websites, as previously explained[4,23,24]. However, according to the JPMA guidance, payment categories, such as meals, travel and accommodations, and other gifts, are disclosed in aggregated amounts and could not be analyzed at individual physician level. Additionally, payments for lecturing, consulting, and drafting are generally paid directly to physicians from pharmaceutical companies and in larger amounts than payments for other categories[13,25-27].

Data collection and coding

We retrieved the names and affiliated hospitals of all board-certified allergists from the Japanese Society of Allergology's website. Following this, we compiled the non-research payments made for lecturing, consulting, and drafting services to these allergists by JPMA-affiliated companies from 2016 to 2020, in line with methodologies used in prior studies[28-30]. Instances of allergists with identical names were resolved by manual searches via Google and verification through official hospital and organizational websites, as previously described.[30,31] We excluded payments to individuals who could not be verified as board-certified allergists or were confirmed as ineligible physicians through our search process from our study samples.

Statistical analyses

We calculated mean and median payments per allergist and proportion of allergists receiving payments. We assessed the concentration of payments among allergists using the Gini index, a measure traditionally applied to analyze income inequality in economics[32,33]. The index ranges from 0 (indicating uniform payment distribution) to 1 (where a single allergist receives all payments), with higher values signaling greater disparity. We also analyzed payment data by category and the pharmaceutical companies making these payments. Trends in the number of allergists receiving payments and the payment amounts from 2016 to 2020 were evaluated using generalized estimating equation (GEE) models. Due to the non-normal distribution of payments, the analyses were conducted using a log-linked GEE model with a Poisson distribution and a negative binomial GEE model[6-8,29]. The study period was bifurcated into two intervals (2016-2019 and 2020) to determine the impact of the COVID-19 pandemic on payments, as indicated by a notable reduction in payments to physicians in the United States in 2020[15,20,34-36]. A sensitivity analysis was also conducted for companies that consistently made payments over the five-year span. For trend analysis, we adjusted for inflation, converting all payment values to their 2020-Japanese yen equivalent. Statistical significance was set at a p-value of less than 0.05.

Ethical clearance

As all data used in this study were publicly available and met the definition of non-human subjects research, no institutional review board approval was required.

Results

Summary of non-research payments to board-certified allergists

Between 2016 and 2020, 2,398 of the 3,943 board-certified allergists (60.8%) received at least one non-research payment for lecturing, consulting, and drafting from pharmaceutical companies, as detailed in Table 1. The total number of payments amounted to 30,849, with an aggregate value of \$43,385,284, distributed by 84 different pharmaceutical entities over the five years. Lecturing payments constituted the majority of this sum, exceeding \$37.2 million (85.7% of the total payment amounts), followed by consulting at \$4.3 million (9.9%) and drafting at \$1.9 million (4.3%). There was large gap between mean and median payment amounts. For allergists who received at least one payment, the median amount per allergist was \$3,106 (interquartile range [IQR]: \$966 – \$12,124), in contrast to a mean of \$18,092 (standard deviation [SD]: \$49,233) over the five-year span. The Gini index, used to measure payment distribution among allergists, was 0.874, suggesting that a small proportion of allergists received the majority of non-research payments over the five years. Specifically, the top 1%, 5%, and 10% of these allergists accounted for 20.8%, 52.8%, and 68.8% of all non-research payments, respectively (Figure 1).

Payments by company

Table 2 presents the distribution of payments and amounts by the top 10 companies. Of the 84 companies contributing payments, the foremost 10 and 20 companies, by total payment magnitude, were responsible for 64.6% (\$28.0 million) and 83.8% (\$36.4 million) of all payments within the 2016 to 2020 timeframe. AstraZeneca made the largest total payments amounting to 14.0% of all payments (\$6.1 million) in monetary value, followed by Boehringer Ingelheim Japan (\$4.1 million, 9.4%), Novartis Pharma (\$3.2 million, 7.4%), Kyorin Pharmaceutical (\$2.6 million, 6.0%), and Mitsubishi Tanabe Pharma (\$2.4 million, 5.6%). Regarding the number of allergists receiving payments, Kyorin Pharmaceutical was at the forefront, providing payments to 994 allergists (25.2% of all allergists), with AstraZeneca following closely at 884 allergists (22.4%), and Novartis Pharma at 799 allergists (20.3%), over the span of five years.

Trends in non-research payments to allergists between 2016 and 2020

The aggregate sum of non-research payments to allergists showed an upward trend from \$7.8 million in 2016 to \$10.0 million in 2019 but experienced a downturn to \$8.4 million in 2020 (Table 3). During the period of 2016 to 2019, between 40.3% and 42.2% of all allergists received non-research payments from pharmaceutical companies, whereas this proportion contracted to 36.0% (comprising 1418 allergists) in 2020. The median annual payments to those allergists who received payments increased from \$1,332 in 2016 to \$1,526 in 2019. The payments per allergist each year significantly increased by 7.7% (95% CI: 5.0 – 10.6, $p < 0.001$) from 2016 to 2019. There was no significant trend in the number of allergists receiving payments during the same span. Contrarily, there was a significant reduction of 14.8% (95% CI: -17.9% to -11.5%, $p < 0.001$) in the number of allergists receiving payments and a 21.2% decrease (95% CI: -25.4% to -16.8%, $p < 0.001$) in payments per allergist in 2020 when compared to the preceding years.

In sensitivity analyses that only included data from the 54 companies making consistent payments over the five-year period, there was a 7.2% annual increase (95% CI: 4.4% – 10.0%, $p < 0.001$) in payments per allergist from 2016 to 2019. Yet, in 2020, both the number of allergists receiving payments and the amount of payments per allergist diminished significantly by 14.8% (95% CI: -17.4% to -10.7%, $p < 0.001$) and 20.4% (95% CI: -24.6% to -15.9%, $p < 0.001$), respectively.

Discussion

Summary of principal findings

This comprehensive longitudinal cross-sectional study scrutinized the financial relationships between pharmaceutical companies and all allergists certified by the Japanese Society of Allergology for non-research activities from 2016 to 2020. To the best of our knowledge, this research is the first study to assess the scale and trends of non-research reimbursements to physicians from pharmaceutical companies for services such as lecturing, consulting, and manuscript drafting in the Japanese discipline of allergology and clinical immunology. The analysis revealed that 60.8% of all allergists received non-research payments totaling \$43.4 million (over 4.6 billion yen) across the five-year span. Notably, these payments escalated annually by more

than 7% in the pre-pandemic era, with the largest contributions stemming from companies that manufacture and distribute medications for allergic conditions including allergic rhinitis, asthma, and atopic dermatitis within Japan.

Comparison with previous studies

This investigation discerned that approximately 40% of allergists received annual non-research payments, with over 60% compensated across a five-year period for activities such as lecturing, consulting, and drafting. These percentages are consistent with prior research conducted within Japan. The lowest annual proportions of physicians receiving such payments were reported among otolaryngologists (24.3% to 26.0%) and the highest among rheumatologists (49.8% to 52.5%) across 10 clinical specialties previously documented[6-10,12,28,29,31,37]. Concurrently, the annual median payments received by allergists (\$1,332 to \$1,526) fell within the range reported for other internal medicine subspecialties. For example, gastroenterologists received \$829 to \$946[8], pulmonologists \$1085 to \$1428[10], hematologists \$1241 to \$1629[31], infectious disease specialists \$1430 to \$1737[9], and rheumatologists \$1544 to \$1635 annually[6]. Thus, the financial engagements between the pharmaceutical industry and board-certified allergists do not appear to be markedly distinct when compared to other medical fields.

The analysis revealed that annual non-research payments to allergists ranged from \$7.8 million to \$10.0 million. In comparison, the United States recorded annual payments between \$10.6 million and \$18.8 million for similar non-research activities among allergists and clinical immunologists[20,21]. Considering the healthcare expenditure of approximately \$4.3 trillion in the United States against Japan's \$403.4 billion, the non-research payments to Japanese allergists for activities such as lecturing, consulting, and drafting appear relatively substantial. This disparity may be attributed to the high prevalence of allergic diseases in Japan, estimated at 49.2% for allergic rhinitis[38], compared to 15%-30% in the United States [39-41].

Additionally, the period between 2014 and 2018 saw the approval of several novel drugs for allergic rhinitis in Japan. For instance, Kyorin Pharmaceutical, ranking fourth among the top payers, released desloratadine (Desalex) in 2016. Additionally, four out of the top ten payers introduced new second-generation antihistamines—rupatadine fumarate (Rupafin by Mitsubishi Tanabe Pharma, approved in 2017), bilastine (Bilanoa by Taiho Pharmaceutical, approved in 2016), and fexofenadine hydrochloride/pseudoephedrine hydrochloride (Dellegra by Sanofi, approved in 2012). The first sublingual immunotherapy product for cedar pollen allergy, Cedartolen by Torii Pharmaceutical, received approval in 2014 for patients aged 12 years and older. Following suit, Miticure, another product by Torii Pharmaceutical for dust mite allergy, was initially approved in 2015 for patients over 12 years and later extended for younger patients in 2018[42]. The introduction of these novel drugs and the expansion of treatment options for allergic rhinitis likely contributed to the high volume of payments and the ascending trend observed from 2016 to 2019.

The investigation also revealed that a disproportionate amount of non-research payments was concentrated among the small number of allergists. This finding is also consistent with previous research across specialties[1,6-9,16,20,29]. Pharmaceutical companies often engage and make payments to physicians who are well-recognized for their clinical expertise and research contributions to deliver lectures to their peers. These leading physicians, often referred to as key opinion leaders, received substantial amounts of non-research payments as reimbursements of giving lectures, consultations, and drafting manuscripts and pamphlets[43-45]. While the collaboration between leading physicians and pharmaceutical companies can be instrumental in advancing drug and medical product development, such significant financial ties may pose conflict of interest concerns. This is particularly true for physicians holding positions that demand high ethical standards, such as board members of professional medical societies[5,8,18,46], editors of medical journals[47-49], authors of clinical guidelines[11,33,50-54], and members of governmental advisory boards[55-59]. Conflicts of interest in these influential roles may introduce bias in decision-making, potentially compromising the quality of patient care[60,61]. Future research should aim to scrutinize the characteristics of the allergists receiving the most considerable payments and examine how these financial associations influence their clinical and policy decisions.

The study identified a notable reduction in non-research payments to allergists in Japan in 2020, coinciding with the onset of the COVID-19 pandemic. Payments to allergists declined by over 20% in terms of amounts per allergist during this year. Comparative studies in the United States documented a significant drop in non-research payments across various specialties[13-15,25-27,34,36,62-65], while research payments remained unaffected during the pandemic[13,25-27,36,66-69]. Notably, to mitigate the spread of COVID-19, numerous academic conferences were either canceled or deferred, and the activities of pharmaceutical representatives were considerably curtailed within healthcare facilities in Japan. To our knowledge, this investigation is the inaugural study to demonstrate the pandemic's impact on the financial dynamics between physicians and the pharmaceutical industry in Japan, supported by a substantial dataset. Nonetheless, the implications of this significant decline in financial payments on the influence of the industry over physicians' clinical decisions remain unclear. Previous studies have indicated associations between payments to allergists and their prescribing behaviors[69-75], particularly for new asthma biologics in the United States[69]. It is imperative for future research to delve into the relationship between physician payments and clinical practice, as well as to assess how the pandemic has affected the pharmaceutical industry's influence on clinical practice in Japan.

This study has several limitations. Firstly, the analysis was confined to payment data from JPMa-affiliated pharmaceutical companies, potentially overlooking financial relationships between allergists and non-member companies. However, it is important to note that JPMa-affiliated companies represent over 80% of the market share for drugs and medical products in Japan[76]. Additionally, non-member companies do not publicly disclose payment information to allergists. Consequently, the impact of undisclosed financial relationships with non-member companies is likely minimal. Secondly, the payment data are self-reported by the companies in compliance with JPMa guidelines, which do not impose penalties for non-adherence, raising concerns about the accuracy of the disclosed data. Thirdly, the Japanese Society of Allergology publishes only the most recent list of board-certified allergists; therefore, the study may include some allergists who were not board-certified during the payment period.

Conclusion

In conclusion, this investigation revealed that over 60% of allergists certified by the Japanese Society of Allergology received non-research payments related to lecturing, consulting, and manuscript drafting from pharmaceutical companies between 2016 and 2020. These payments were predominantly distributed to a limited number of allergists. Notably, there was a significant annual increase in payment amounts exceeding seven percent prior to the pandemic. In contrast, a marked decline in both the number of allergists receiving payments and the total payment amounts was observed in 2020, concurrent with the onset of the COVID-19 pandemic in Japan.

Declarations

Ethics approval and consent to participate:

As all data used in this study were publicly available and met the definition of non-human subjects research, no institutional review board approval was required.

Consent for publication:

Not applicable.

Availability of data and materials

All data were collected from publicly accessible databases. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

We declare that there are no conflicts of interest for this study.

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Authors' contributions

Anju Murayama: conceptualization; methodology; resource; software; formal analysis; investigation; writing - original draft; writing - review & editing; visualization; study administration

Yuki Senoo: conceptualization; methodology; writing - original draft; writing - review & editing

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Table 1. Summary of non-research payments to board-certified allergists

Variables	Value
Total amounts of payments	
Payment values, \$	43,385,284
Number of payments, No.	30,849

Variables	Value
Number of companies making payments, No.	84
Payments per allergist	
Mean (standard deviation) ^a	
Payment values, \$	18,092 (49,233)
Number of payments, No.	12.9 (17.7)
Median (interquartile range) ^a	
Payment values, \$	3,106 (966 – 12,124)
Number of payments, No.	6.0 (2.0 – 16.0)
Maximum ^a	
Payment values, \$	611,190
Number of payments, No.	161.0
Gini index	0.874
Allergists with specific amount of payments (N=3943), n (%)	
No payment	1545 (39.2)
\$1-\$1,000	615 (15.6)
\$1,001-\$5,000	802 (20.3)
\$5,001-\$10,000	297 (7.5)
\$10,001-\$50,000	485 (12.3)
\$50,001-\$100,000	100 (2.5)
\$100,001-\$200,000	57 (1.5)
\$200,001-	42 (1.1)

Legends: ^a Payments per allergist were calculated among allergists who received one or more payments, as 39.2% of allergists did not receive any payments over the five years.

Table 2. Payments by top 10 companies making the largest payments to allergists between 2016 and 2020.

Ranking	Company name	Amounts of payments (%), \$	Number of payments (%), No.	Number of allergi
1st	AstraZeneca	6,056,278 (14.0)	2839 (9.2)	884 (22.4)
2nd	Boehringer Ingelheim Japan	4,071,844 (9.4)	2139 (6.9)	717 (18.2)
3rd	Novartis Pharma	3,205,803 (7.4)	1919 (6.2)	799 (20.3)
4th	Kyorin Pharmaceutical	2,585,524 (6.0)	2241 (7.3)	994 (25.2)
5th	Mitsubishi Tanabe Pharma	2,434,910 (5.6)	1354(4.4)	589 (14.9)
6th	Taiho Pharmaceutical	2,044,290 (4.7)	1491 (4.8)	623 (15.8)
7th	Sanofi	2,038,459 (4.7)	1292 (4.2)	599 (15.2)
8th	GlaxoSmithKline	2,026,210 (4.7)	1012 (3.3)	516 (13.1)
9th	Torii Pharmaceutical	1,841,077 (4.2)	1222 (4.0)	500 (12.7)
10th	Maruho	1,706,618 (3.9)	1037 (3.4)	409 (10.4)

Legend: The ranking was based on the monetary amounts of non-research payments between 2016 and 2020.

Table 3. Trend in personal payments from pharmaceutical companies to board-certified allergists between 2016 and 2020.

Variables	2016	2017	2018	2019	2020	Average relative yearly change between 2016 and 2019 (95% CI), %	Relative change rate between 2016-2019 and 2020 (95% CI), %
All phar- maceutical companies							
Total payments , \$	7,821,861	8,274,237	8,953,824	9,981,069	8,354,293	—	—
Payments per allergist							
Mean (standard deviation), \$	4,819 (11,395)	5,204 (12,305)	5,517 (12,200)	6,002 (13,243)	5,892 (13,200)	7.7 (5.0 – 10.6)*	-21.2 (-25.4 to -16.8)***
Median (in- terquartile range), \$	1,332 (521 – 3,898)	1,435 (521 – 3,974)	1,526 (521 – 4,521)	1,535 (539 – 5,021)	1,518 (539 – 4,674)		
Maximum, \$	167,946	155,035	125,560	154,826	131,500		
Physicians with payments (%), n	1623 (41.2)	1590 (40.3)	1623 (41.2)	1663 (42.2)	1418 (36.0)	0.9 (-0.1 to 2.1)	-14.8 (-17.9 to -11.5)***
Gini index	0.888	0.890	0.888	0.885	0.904	—	—
Pharmaceutical companies making payments through- out five years							
Total payments , \$	7,645,832	8,192,889	8,710,193	9,653,679	8,144,163	—	—
Payments per allergist							
Mean (standard deviation), \$	4,782 (11,289)	5,208 (12,254)	5,468 (12,085)	6,015 (13,280)	5,919 (13,171)	7.2 (4.4 – 10.0)*	-20.4 (-24.6 to -15.9)*
Median (in- terquartile range), \$	1,317 (521 – 3,873)	1448 (521 – 3,990)	1,526 (521 – 4,495)	1,564 (547 –4,931)	1,526 (539 – 4,666)		
Maximum, \$	166,980	155,035	125,560	154,826	130,757		
Physicians with payments (%), n	1599 (40.6)	1573 (39.9)	1593 (40.4)	1605 (40.7)	1376 (34.9)	0.2 (-0.9 to 1.3)	-14.8 (-17.4 to -10.7)*

Variables	2016	2017	2018	2019	2020	Average relative yearly change between 2016 and 2019 (95% CI), %	Relative change rate between 2016-2019 and 2020 (95% CI), %
Gini index	0.889	0.891	0.889	0.889	0.906	—	—

Abbreviations: standard deviation (SD); interquartile range (IQR),95% confidence interval (95% CI)

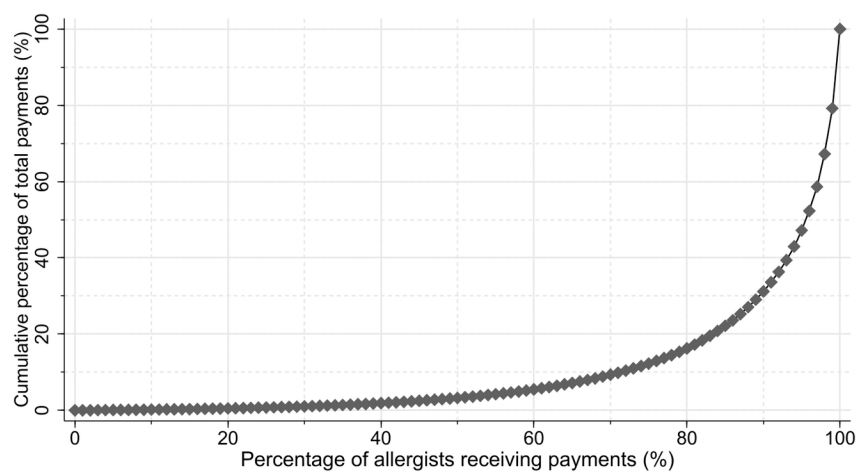


Figure 1. Concentration of non-research payments to allergists between 2016 and 2020.