Pharmaceutical Payments to Japanese Certificated Hematologists: A Retrospective Analysis of Personal Payments from Pharmaceutical Companies between 2016 and 2019

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Abstract

Background: A growing and significant financial relationship exist between physicians and pharmaceutical companies. However, little is known about the characteristics and trends of personal payments from pharmaceutical companies to hematologists. This study was aimed to evaluate the financial relationship between hematology specialists and pharmaceutical companies in Japan between 2016 and 2019.

Methods: Descriptive analyses were performed to evaluate personal payments from 92 major pharmaceutical companies to all board-certificated hematologists in Japan. Furthermore, trend of payments over four years were evaluated by generalized estimating equations.

Results: Among the 4,183 hematology specialists, 2,706 (64.7%) received a total of US$36,291,434 (¥3,955,766,292). The personal payments were worth $13,411 (standard deviation: $34,856) on average, with a median of $2,471 (Interquartile range: $851–$9,677) over the four-year period, respectively. Only the top 10% of specialists accounted for 76.8% of the total payments. The average payment values constantly increased from $4,259 to $5,574 between 2016 and 2019, with a significant mean
annual increase rate of 11.2% (95%CI: 9.1%–13.4%). The proportion of hematology specialists with payments also slightly increased by 1.8% (95%CI: 0.6%–3.0%) per year.

Conclusions: Most Japanese board-certified hematology specialists received substantial personal payments. These payments are becoming increasingly more prevalent and greater among hematology specialists.
Main text

Introduction

Although collaboration between healthcare professionals, patients, and pharmaceutical companies has played a significant role in the development of novel drugs and a better understanding of diseases (ref.[1, 2]), proper management of conflicts of interest (COIs) is currently one of the most fundamental concerns of all healthcare professionals (ref.[3]), as financial COIs between healthcare sectors and pharmaceutical companies could jeopardize patient-centered care. Indeed, the financial relationship between the healthcare sector and pharmaceutical companies might affect physician prescribing patterns (ref.[4-6]), recommendations in clinical guidelines (ref.[7-11]), and conducting and reporting of clinical research (ref.[12, 13]). These concerns and motivation to increase transparency in financial COIs has led to the creation of transparency initiatives worldwide (ref.[14, 15]), including in Japan. The Japan Pharmaceutical Manufacturers Association (JPMA), the largest pharmaceutical trade organization in Japan, requires all JPMA member companies from 2013 onwards to voluntarily publish all payments made to healthcare professionals and healthcare organizations (ref.[16]).
In the field of hematology, a wide variety of therapeutic strategies and novel therapies (ref.[17-19]), including chemotherapy, targeted therapy, and hematopoietic stem cell transplantation for the treatment of hematological cancers, have brought significant therapeutic benefits to patients and attracted considerable attention from pharmaceutical companies, resulting in intense marketing by pharmaceutical companies. The financial relationships of hematologists and oncologists with pharmaceutical companies as compared to other specialists have increased in recent years (ref.[20-22]). In addition, Japanese hematology guideline authors receive an average of $25,471 to $49,693 in personal payments from pharmaceutical companies (ref.[23]), one of the largest average payments among guideline authors in several specialties (ref.[11, 24, 25]). Considering the current pharmaceutical marketing strategy and the sizable evidence indicating that pharmaceutical marketing could influence physician prescription patterns (ref.[5, 26, 27]), the elucidation and proper management of the financial relationships between pharmaceutical companies and hematologists are important.
This study aims to elucidate the prevalence of board-certified hematologists receiving payments from pharmaceutical companies, the magnitude of the payments, and the payment trend in recent years.

Methods

Participants

This study considered all hematologists certified by the Japanese Society of Hematology, as of October 10, 2021, as hematology specialists. The Japanese Society of Hematology was established in 1937 and is the most prestigious and largest medical professional society in hematology in Japan, with 7,744 members as of October 8, 2021. The Japanese Society of Hematology is the sole professional medical society authorized to certify hematology specialists in Japan. The list of names of the hematology specialists is publicly available on the society’s webpage and was last updated on July 7, 2021 (http://www.jshem.or.jp/modules/senmoni/).
Certification of hematologists by the Japanese Society of Hematology

The Japanese Society of Hematology is the sole society in Japan authorized to certify hematology specialists. As of October 2021, to be certificated as a hematology specialist, physicians are required to meet all of the following six requirements: (1) submission of clinical records for 15 inpatients as an attending physician, including at least three cases of erythrocyte disease, three cases of leukocyte disease, two cases of thrombosis and hemostasis, and one case of immunology and blood transfusion; (2) must be listed as the first author of at least two academic articles or conference presentations; (3) must have completed at least six years of clinical practice training after having acquired a medical license and at least three years of specialized training in hematology at an institution accredited by the Japanese Society of Hematology; (4) must have a board certification in internal medicine issued by the Japanese Society of Internal Medicine or in pediatrics issued by the Japan Pediatric Society; (5) must be a registered member of the Japanese Society of Hematology for at least three years; and (6) must clear the written examination for the hematology specialists conducted by the Japanese Society of Hematology.
Data collection

The names, affiliations, and addresses of all hematology specialists were disclosed and collected from the Japanese Society of Hematology webpage on October 10, 2021.

Payment data of all healthcare professionals and healthcare organizations regarding lecturing, writing, and consulting were collected for the period 2016-2019 from 92 pharmaceutical companies belonging to the JPMA. After collecting the payment data, a single unified database was developed, as described previously (ref.[24, 28]). JPMA requires the member companies to disclose only the payment concerning lecturing, writing, and consulting, along with the individuals’ names and affiliations; therefore, these payment categories could be analyzed on an individual specialist basis. Personal payments, such as those for lecturing, writing, and consulting, are directly and widely paid to specialists by pharmaceutical companies. (ref.[6, 28-31]) Considering the nature of payments, only the personal payments concerning lecturing, writing, and consulting were included in this study.
We scanned for specialist names in the payment database and extracted the payment data from the payment database of hematology specialists. The extracted data included the recipient names, affiliations, monetary amount, number of payment cases, payment category, and names of the respective pharmaceutical companies. To remove payment data of different persons with similar names in the database, we checked and compared the affiliations, affiliation addresses, and recipient specialties between the data from the Japanese Society of Hematology and the pharmaceutical companies. For payments to specialists whose affiliations reported by the pharmaceutical company differed from those reported by the society, we manually searched the name of the specialists on the internet and collated other data from official institutional webpages and other sources to verify their identity. We also excluded payments that could not be verified from the analysis. The detailed procedure has been previously described (ref.[24, 28]).

Furthermore, the lists of drugs newly approved for hematological diseases between 2015 and 2020 were collected from the webpage of the Pharmaceuticals and Medical Devices Agency, which is the official agency for reviewing drugs in Japan.
Analysis

Descriptive analyses of payment values and the number of cases were performed per specialist and per pharmaceutical company. Average and median payments, cases, and number of companies making payments per specialist were calculated based only on the number of specialists receiving payments each year, as in other studies. (ref.[20, 29, 30, 32]) As several companies such as Shire Japan and Baxalta did not disclose the number of payment cases, the payments from these companies were excluded from the analysis of the number of cases, while the payment values were included in the analysis. To examine the concentration of payments to individual specialists, the Gini index and shares of the value of payments held by the top 1%, 5%, 10%, and 25% of specialists were calculated. The Gini index ranges from 0 to 1, and the greater the Gini index, the greater the disparity in the distribution of payments on a specialist basis, as mentioned previously. (ref.[24, 25]) Payment distribution was also examined geographically.

Further, to examine the trend of payments from pharmaceutical companies to specialists from 2016 to 2019, the population-averaged generalized estimating equation negative
binomial regression model for the trend of payment value and the linear generalized estimating equation model log linked with binomial distribution for the trend of numbers of specialists with payments were used. The relative ratios of the average annual increase in payments per specialist to the number of specialists with payments were used to report the results.

The year of payments was set as an independent variable, and the proportion of physicians receiving payments, number of payments, and payment values were set as dependent variables. (ref.[20, 33, 34]) As several pharmaceutical companies disaffiliated from the JPMA and newly joined the JPMA, among all 92 companies, there were 18 companies without payment data over the four years. Thus, the average and median payments for each year and the trend of payments were calculated based on payments from all 92 companies and 74 companies with payment data for the four years between 2016 and 2019.

To adjust for inflation and to make the payment value comparable, Japanese yen (¥) was converted into US dollars ($) using the 2019 average monthly exchange rate of ¥109.0
per $1. All analyses were conducted using Microsoft Excel (version 16.0; Microsoft
Corp.) and Stata (version 15; StataCorp).

Ethical approval

This study was approved by the Ethics Committee of the Medical Governance Research
Institute. As this study is a retrospective analysis of publicly available information,
informed consent was waived and direct contact with the society was allowed by the
Ethics Committee of the Medical Governance Research Institute.

Results

Overview of payments

We identified 4,183 hematology specialists certified by the Japanese Society of
Hematology as of October 10, 2021. Our payment database recorded 1,474,653
payment cases and $996,291,009 (¥108,595,720,027) in total monetary value from 92
pharmaceutical companies between 2016 and 2019.
Of the 4,183 specialists, 2,706 (64.7%) received a total of US$36,291,434 (¥3,955,766,292) corresponding to 47,863 cases from 71 (77.2%) pharmaceutical companies between 2016 and 2019 (Table 1). The payment cases and values to the hematology specialists occupied 3.2% and 3.6% of total cases and values, respectively.

A total of 82.5% ($29,951,526) of the total payments were for lecturing, followed by 13.5% from consulting ($4,890,255), 3.9% from writing ($1,398,729), and 0.1% from others ($50,924). The average monetary value per case was $758, ranging from $736 for lecturing to $922 for consulting.

Payments per specialists

The hematology specialists received personal payments worth $13,411 (Standard deviation (SD): $34,856) on average and a median of $2,471 (Interquartile range (IQR): $851–$9,677) over the four-year period. The average and median number of cases over the four years was 17.7 (SD: 35.9) and 5.0 (IQR: 2.0–17.0) cases per specialist, respectively. The average number of companies making payments per specialist was 5.5 (SD: 5.2; median: 4.0; IQR: 2.0–8.0; and range: 1.0–32.0) (Table 1).
For the concentration of payments, 4.2% and 1.9% of hematology specialists received more than $50,000 and $100,000, respectively. The Gini index for the four-year cumulative payments per specialist was 0.856, indicating that the distribution of the total payments per specialist was highly skewed. Top 1%, 5%, 10% and 25% of specialists occupied 26.0% (95% confidence interval (CI): 23.1%–28.9%), 61.0% (95%CI: 58.2%–63.7%), 76.8% (95%CI: 74.8%–78.8%), and 93.3% (95%CI: 92.6%–94.0%) of total payments, respectively (Figure 1).

Payment trend between 2016 and 2019

Regarding the payment trend of all 71 companies through the four years, annual total payments increased from $7,700,346 (839,337,686) in 2016 to $10,279,218 (¥1,120,434,752) in 2019. In addition, payments per specialist and the number of specialists with payments increased from $4,259 (SD: $9,291) and 1,808 (43.2%) in 2016 to $5,574 (SD: $11,688) and 1,844 (44.1%) in 2019, respectively. The relative annual increase rates were 1.112 (95%CI: 1.091–1.134; p < 0.001) in payments per specialist and 1.018 (95%CI: 1.006–1.030; p =0.003) for specialists with payments,
indicating that the payment values and number of specialists increased by 11.2% 
(95%CI: 9.1%–13.4%) and 1.8% (95%CI: 0.6%–3.0%) each year (Table 2).

Of 74 companies collecting payments data over four years, there were 64 companies 
with the four-years payment data. Limiting to the payments from the 64 companies, 
both the average and median payment values also constantly increased from $4,259 
(SD: $9,291) and $1,241 (IQR: $511–$3,442) to $5,536 (SD: $11,557) and $1,633 
(IQR: $613–$4,760) between 2016 and 2019, respectively. The relative annual change 
rate for payments per specialist and number of specialists with payments also 
significantly increased by 11.2% (95%CI: 9.1%–13.4%) and 1.8% (95%CI: 
0.6%–3.0%), respectively, each year.

Furthermore, the annual change rate was higher among those with greater four-year 
cumulative payments, such as those receiving $1,000–$10,000 at 12.8% (95%CI: 
9.5%–16.1%; p < 0.001), $10,000–$50,000 at 13.7% (95%CI: 10.4%–17.1%; p < 
0.001), and $50,000–$100,000 at 13.8% (95%CI: 8.1%–19.8%; p < 0.001), while those 
with payments of more than $100,000 had a lower annual increase rate of 8.1% 
(95%CI: 4.2%–11.1%; p < 0.001).
Among 71 pharmaceutical companies making payments to specialists, payments from the top 10 companies accounted for 70.8% of the total payments ($25,236,750) between 2016 and 2019 (Figure 2). The payment types for each of the top 10 paying companies are shown in Figure 3. Four among the 10 companies, namely, Takeda Pharmaceutical, Chugai Pharmaceutical, Janssen Pharmaceutical, and Novartis Pharma, increased their payments to hematology specialists. A total of 673 drugs were newly approved and introduced between 2015 and 2020 in Japan. Among these indicators, 211 (31.4%) were from the top 10 companies, and of these, 52 drugs (24.6%) were for hematological diseases (Supplemental Material 1).

Geographical differences were observed in the distribution of the number of hematology specialists. Based on the prefecture, payments from pharmaceutical companies (Supplemental Material 2A) to hematology specialists per one million of the population
ranged from 18.2 in Aomori Prefecture to 64.4 in Kyoto (Supplemental Material 2B).

The average payment values per specialist were the highest in Tochigi Prefecture ($15,806) and lowest in Kumamoto Prefecture ($3,178) (Supplemental Material 2D).

Discussion

This study demonstrated that 3.6% ($36,291,434) of total personal payments concerning lecturing, consulting, and writing from all major pharmaceutical companies to healthcare professionals were distributed to board certified hematology specialists, who accounted for 1.3% (4,183 out of 327,210) of total physicians in Japan, according to the latest survey by the Japanese Ministry of Health, Labor and Welfare in 2018 (ref.[35]). Among all Japanese board-certified hematology specialists, 64.7% received an average of $13,411 in personal payments between 2016 and 2019, with an annual average increase rate of 11.2%. To the best of our knowledge, this is the first study to assess the distribution and the trend of financial relationships between board-certified hematologists and pharmaceutical companies. Although our study could have limitations such as underreported payments due to the limited category of personal
payments in Japan, there were important similarities and differences between our
findings and those of the previous studies.

Previous studies in the United States demonstrated that 80.2% of hematologists and
oncologists received general payments averaging $6,166 ($2,055 in one year) between
2015 and 2017. (ref.[31]) Another study by Marshall et al. reported that 63.0% of
medical oncologists, including pediatric hematologists/oncologists and
hematologist/oncologists, received $7,750 in average general payment in 2014 (ref.[22]),
and, in the six years between 2014 and 2019, 84.6% (13,190 out of 15,585) of medical
oncologists received $38,601 (6,434 in one year) in average general payment per
physician (ref.[20]). Another study by Ozaki et al. evaluated pharmaceutical payments
among Japanese board-certified oncologists, and they found that 70.6% of certified
oncologists received an average of $4,982 in annual personal payments. (ref.[28]) Our
study showed that the average personal payments ranged from $4,259 to $5,574 and the
proportion of (mention specialist type) specialists with payments ranging from 40.2% to
45.3% in a single year were fewer than those in the United States and less than the
average proportion of Japanese hematologists and oncologists.

Meanwhile, in other specialties, the average total payments per physician, such as general, research, and ownership payments, were $907 among pediatricians in 2014 (ref.[36]); $4,183 ($2,091 per year) among psychiatrists between 2016 and 2017 (ref.[37]); $3,433 ($1,144 in one year) in general payments among obstetricians and gynecologists between 2013 and 2015 (ref.[38]); from $1,795 in 2014 to $2,227 in 2017 among board certificated nephrologists (ref.[39]); $3,260 among orthopedic surgeons in 2013 (ref.[40]); $4,177 among dermatologists in 2014 (ref.[30]); $25,960 ($5,191 per year) among ophthalmologists between 2013 and 2017 (ref.[41]); $16,914 ($5,638 per year) among cardiologists between 2014 and 2016 (ref.[42]); $38,664 ($6,444 per year) among rheumatologists between 2014 and 2019 (ref.[43]); and $7,263 among neurologists in 2015. (ref.[44]) Comparing these findings, the Japanese board certificated hematologists might have similar or greater financial relationships with pharmaceutical companies than other specialists in the United States and Japan.
This study showed that only a very small proportion of hematology specialists received the majority of personal payments from pharmaceutical companies. As previous studies have found (ref.[25, 30, 41-43]), pharmaceutical companies have concentrated their payments on a small number of physicians with extensive clinical and research experience. These specialists, or “key opinion leaders,” (ref.[45]) who had substantial financial relationships with pharmaceutical companies, played a significant role in delivering information about newer drugs, novel findings from clinical trials, and drug related risks, to healthcare professionals at conferences for continuing medical education sponsored by pharmaceutical companies (ref.[46]). We should note that while the financial relationships of specialists with pharmaceutical companies might help to rapidly unroll novel drugs with greater benefits (ref.[26, 46]), it could also increase healthcare costs when the specialists prescribe brand name drugs (ref.[4, 47]) or drugs whose benefits are unproven (ref.[48, 49]).

Further, regarding the trend of payments, we found that total and average payments increased significantly every year, with an 11.2% yearly increase in average payments.

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This trend of increasing payments to physicians was also observed among oncologists in the United States. Marshall et al. found that since the launch of the US Open Payment Database, the total and annual average payment value per physician declined by -1.7% and -0.6%, respectively (ref.[34]). However, pharmaceutical companies increasingly prioritized the payments to hematologists and oncologists, with a 4.9% and 1.7% annual increase in total value and average payments (ref.[20]). Furthermore, although the disclosure of personal payments from pharmaceutical companies to healthcare professionals and healthcare organizations was intended to improve transparency rather than curb the financial relationships, our findings indicate that disclosure itself did not sufficiently decrease the financial relationships between pharmaceutical companies and hematology specialists in Japan, as corroborated by previous studies in the United States.

Companies’ payment trends would provide further understanding of the increase in the average payments and proportion of specialists with payments among Japanese hematology specialists. The top 10 companies expanded their indications in the field of hematology, ranging from one to 11 new indications per company. While the payment
from Celgene, the largest paying company, remained stable, four companies, namely, Takeda Pharmaceutical, Chugai Pharmaceutical, Janssen Pharmaceutical, and Novartis Pharma, remarkably increased their payments to the hematology specialists between 2016 and 2019. As a drug target, multiple myeloma accounted for the largest proportion (17 out of 52 indications), which may explain the recent trend of increasing payments. In fact, all the companies mentioned above, except Chugai Pharmaceutical, have developed newly approved drugs for multiple myeloma. In addition to multiple myeloma, Novartis made the largest total payments of $1,323,027 in 2019, when the chimeric antigen receptor T cells, tisagenlecleucel (KYMRIAH), was granted approval for the treatment of B-cell precursor acute lymphoblastic leukemia and large B-cell lymphoma and was priced at about 32 million JPY (equal to about 300,000 USD), covered by the Japanese public health insurance. Regarding Chugai Pharmaceutical, emicizumab (HEMLIBRA, approved in 2018 for congenital blood coagulation factor 8 deficiency) may account for the increased payment.

This study has several limitations. First, our payment database was constructed by
manually collecting payment data from 92 pharmaceutical companies and repeatedly

crosschecking it for any errors by two or more persons. Despite careful and repeated

checks, the inclusion of errors by our study team and pharmaceutical companies

reporting data could not be ruled out. However, the publicly disclosed payment database

(https://db.tansajp.org/en) welcomed inquiries from the recipients of payments and

pharmaceutical companies reporting any errors in the data, and the payment database

was checked and revised for each inquiry. These procedures minimized the inclusion of

errors in this study. In addition, payment data concerning meals, education, travel, and

accommodations were not disclosed with the individual names of recipients by

pharmaceutical companies in Japan (ref.[16]). Thus, these payment data are not

analyzable. Considering that such payment categories like meals were the most

prevalent among physicians (ref.[30, 42, 48]), this study underreports the prevalence

and magnitude of financial relationships between hematology specialists and

pharmaceutical companies in Japan. However, this study highlights the magnitude and

prevalence of financial relationships between pharmaceutical companies and Japanese

hematologists.
In conclusion, this study found that between 2016 and 2019, 64.7% of Japanese board-certified hematology specialists received an average of $13,411 in personal payments as the reimbursement for lecturing, consulting, and writing. Only a small proportion of hematology specialists received the vast majority of payments from pharmaceutical companies. Furthermore, these personal payments from pharmaceutical companies were increasingly more prevalent and greater among Japanese hematology specialists.

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For the financial conflicts of interest, Dr. Kusumi received personal fees from Otsuka Pharmaceutical Co. Ltd outside the scope of the submitted work. Dr. Saito received personal fees from TAIHO Pharmaceutical Co. Ltd outside the scope of the submitted work. Drs. Ozaki and Tanimoto received personal fees from Medical Network Systems outside the scope of the submitted work. Dr. Tanimoto also received personal fees from Bionics Co. Ltd, outside the scope of the submitted work. Regarding non-financial conflicts of interest among the study authors, all are engaged in ongoing research
examining financial and non-financial conflicts of interest among healthcare professionals and pharmaceutical companies in Japan. Individually, Anju Murayama, Hiroaki Saito, Toyoaki Sawano, Tetsuya Tanimoto, and Akihiko Ozaki have contributed to several published studies assessing conflicts of interest and quality of evidence among clinical practice guideline authors in Japan and the United States. Among their previous articles, the authors have self-cited several articles in this study to gain deeper insights and explain the context of financial conflicts of interest among healthcare professionals in Japan. Dr. Kusumi was a hematology specialist board certificated by the Japanese Society of Hematology. The other authors have no example conflicts of interest to disclose.

Author Contributions:

EK was responsible for study concept, data collection, statistical analysis, and drafting and reviewing of the manuscript. AM was responsible for study concept and design, data collection, statistical analysis, and drafting and reviewing of the manuscript. SK was responsible for study concept and design, data collection, statistical analysis, and
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drafting of the manuscript. MY contributed to study concept, data collection, and
drafting of the manuscript. HS contributed to study concept and design, drafting of the
manuscript, and critically reviewing of the manuscript. TS contributed to study concept
and design, drafting of the manuscript, and critically reviewing of the manuscript. EY
contributed to study concept and design, and critically reviewing of the manuscript.

TT conducted to study concept and design, drafting of the manuscript, and study
supervision. AO conducted study concept and design, statistical analysis, drafting of the
manuscript, and study supervision. All authors had full access to all the data in the study
and take responsibility for the integrity of the data and the accuracy of the data analysis.
Competing interests:

For the financial conflicts of interest, Dr. Kusumi received personal fees from Otsuka Pharmaceutical Co., Ltd outside the scope of the submitted work. Dr. Saito received personal fees from TAIHO Pharmaceutical Co. Ltd outside the scope of the submitted work. Drs. Ozaki and Tanimoto received personal fees from Medical Network Systems outside the scope of the submitted work. Dr. Tanimoto also received personal fees from Bionics Co. Ltd, outside the scope of the submitted work. Regarding non-financial conflicts of interest among the study authors, all are engaged in ongoing research examining financial and non-financial conflicts of interest among healthcare professionals and pharmaceutical companies in Japan. Individually, Anju Murayama, Hiroaki Saito, Toyoaki Sawano, Tetsuya Tanimoto, and Akihiko Ozaki have contributed to several published studies assessing conflicts of interest and quality of evidence among clinical practice guideline authors in Japan and the United States. Among their previous articles, the authors have self-cited several articles in this study to gain deeper insights and explain the context of financial conflicts of interest among healthcare professionals in Japan. Dr. Kusumi was a hematology specialist board certificated by
the Japanese Society of Hematology. The other authors have no example conflicts of interest to disclose.
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Table 1. Summary of personal payments from pharmaceutical companies to hematology specialists certified by the Japanese Society of Hematology between 2016 and 2019

| Variables                      | Total                                      | Average per specialist (SD) | Median per specialist (IQR) |
|--------------------------------|--------------------------------------------|----------------------------|-----------------------------|
|                                |                                            |                            |                             |
| Payment values, US$ (%)        | 36,291,434 (3.6)                           | 13,411 (34,856)            | 2,471 (851 - 9,677)         |
| Cases, n (%)                   | 47,863 (3.2)                               | 17.7 (35.9)                | 5 (2 - 17)                  |
| Companies, n (%)               | 71 (77.2)                                  | 5.5 (5.2)                  |                             |

All data is presented in US dollars (US$).
| Companies, n | 4 (2-8) |
|-------------|---------|
| **Range**   |         |
| Payment values, US$ | 46,528,038 |
| Cases, n  | 0-487 |
| Companies, n | 0-32 |
| **Physicians with specific payments, n (%)** |         |
| Any payments | 2,706 (64.7) |
| Payments >US$500 | 2,392 (57.2) |
| Payments >US$1,000 | 1,947 (46.6) |
| Payments >US$5,000 | 980 (23.4) |
| Payments >US$10,000 | 666 (15.9) |
| Payments >US$50,000 | 175 (4.2) |
| Payments >US$100,000 | 78 (1.9) |
| **Gini index** | 0.856 |
| **Category of payments** |         |
| **Lecturing** |         |
| Payment value, US$ (%) | 29,951,526 (82.5) |
| Category     | Cases, n (%) | Payment value, US$ (%) |
|--------------|--------------|------------------------|
| Consulting   | 40,686 (85.0)| 4,890,255 (13.5)       |
| Writing      | 5,302 (11.1)| 1,398,729 (3.9)        |
| Other        | 59 (0.1)     | 50,924 (0.1)           |
Table 2. Trend of personal payments from pharmaceutical companies to the hematology specialists board certified by the Japanese Society of Hematology between 2016 and 2019

| Variables                      | 2016          | 2017          | 2018          | 2019          | Relative yearly change ratio (95% CI) | P value | Four-years combined total |
|-------------------------------|---------------|---------------|---------------|---------------|-------------------------------------|---------|--------------------------|
| All pharmaceutical companies |               |               |               |               |                                     |         |                          |
| Total payments , US$ (¥)      | 7,700,346     | 8,266,798     | 10,045,073    | 10,279,218    |                                     |         | 35,949,597               |
| US$ (¥)                       | (839,337,686) | (901,080,935) | (1,094,912,919) | (1,120,434,752) |                                     |         | (3,955,766,292)          |
| Average payments (SD), US$    | 4,259 (9,291) | 4,918 (10,677)| 5,306 (11,403)| 5,574 (11,688)| 1.112 (1.091–1.134)                 | <0.001  | 13,411 (34,856)          |
| Median payments               | 1,241 (511–3,442) | 1,343 (525–4,087) | 1,504 (525–4,628) | 1,629 (613–4,839) |                                     |         | 2,471 (851–9,677)       |
(IQR), US$

| Payment range, US$ | 46[106, 834] | 46[167, 828] | 46[148, 942] | 52[140, 947] | □ | □ | 46[528, 038] |
|-------------------|--------------|--------------|--------------|--------------|----|----|--------------|

Physicians with specific payments, n (%)

| Payments          | 1,808 (43.2) | 1,681 (40.2) | 1,893 (45.3) | 1,844 (44.1) | 1.018 (1.006-1.030) | 0.003 | 2,706 (64.7) |
|-------------------|--------------|--------------|--------------|--------------|-------------------|-------|--------------|
| Payments >US$500  | 1,444 (34.5) | 1,373 (32.8) | 1,577 (37.7) | 1,570 (37.5) | 1.040 (1.027-1.054) | <0.001 | 2,374 (56.8) |
| Payments >US$1,000| 1,024 (24.5) | 998 (23.9)   | 1,178 (28.2) | 1,159 (27.7) | 1.055 (1.039-1.071) | <0.001 | 1,945 (46.5) |
| Payments >US$5,000| 331 (7.9)    | 360 (8.6)    | 454 (10.9)   | 446 (10.7)   | 1.117 (1.088-1.146) | <0.001 | 975 (23.3)   |
| Payments >US$10,000| 187 (4.5)    | 208 (5.0)    | 239 (5.7)    | 253 (6.0)    | 1.109 (1.071-1.149) | <0.001 | 660 (15.8)   |
### Pharmaceutical companies with 4-years payment data

| Payments | >US$50,000 | >US$100,000 |
|----------|------------|-------------|
| Gini index | 0.876 | 0.885 | 0.870 | 0.872 | □ | □ | 0.856 |

| Total payments, US$ (¥) | 7,700,346 | 8,266,798 | 10,045,073 | 10,142,157 | □ | □ | 35,972,679 |
|-------------------------|------------|------------|------------|------------|----|----|------------|
|                         | (838,940,102) | (884,814,326) | (1,091,772,525) | (11,05,495,102) | □ | □ | (3,921,022,055) |

| Average payments, (SD), US$ | 4,259 (9,291) | 4,918 (10,677) | 5,306 (11,403) | 5,536 (11,557) | 1.112 (1.091) | 1.134 | 1.12 (1.091) | <0.001 | 13,333 (34,685) |

| Median payments, (IQR), US$ | 1,241 (511,4,442) | 1,343 (525,4,087) | 1,504 (523,4,628) | 1,633 (613,4,760) | 2,470 (851,9,500) |

| Payment range, US$ | 46,106,834 | 46,167,828 | 0,148,942 | 0,137,882 | □ | □ | 46,528,038 |
| Payments | Any payments | Payments >US$500 | Payments >US$1,000 | Payments >US$5,000 | Payments >US$10,000 | Payments >US$50,000 | Payments >US$100,000 |
|----------|--------------|-----------------|-------------------|-------------------|-------------------|-------------------|-------------------|
|          | n (%)        | n (%)           | n (%)             | n (%)             | n (%)             | n (%)             | n (%)             |
| Any payments | 1,808 (43.2) | 1,681 (40.2)    | 1,893 (45.3)      | 1,844 (44.1)      | 1,018 (1.006)     | 1,030 (1.030)     | 0.003             | 2,698 (64.5)      |
| Payments >US$500 | 1,444 (34.5) | 1,373 (32.8)    | 1,577 (37.7)      | 1,570 (37.5)      | 1,040 (1.027)     | 1.054 (1.054)     | <0.001            | 2,383 (57.0)      |
| Payments >US$1,000 | 1,024 (24.5) | 998 (23.9)      | 1,178 (28.2)      | 1,159 (27.7)      | 1,055 (1.039)     | 1.071 (1.071)     | <0.001            | 1,938 (46.3)      |
| Payments >US$5,000 | 331 (7.9)    | 360 (8.6)       | 454 (10.9)        | 446 (10.7)        | 1,117 (1.088)     | 1.146 (1.146)     | <0.001            | 973 (23.3)        |
| Payments >US$10,000 | 187 (4.5)    | 208 (4.8)       | 239 (5.7)         | 253 (6.0)         | 1,109 (1.071)     | 1.149 (1.149)     | <0.001            | 659 (15.8)        |
| Payments >US$50,000 | 15 (0.36)    | 20 (0.48)       | 26 (0.62)         | 24 (0.57)         | 1,169 (1.033)     | 1.323 (1.323)     | <0.001            | 174 (4.2)         |
| Payments >US$100,000 | 2 (0.048)    | 2 (0.048)       | 4 (0.096)         | 5 (0.12)          | 1.420 (0.940)     | 2.147 (2.147)     | 0.096             | 77 (1.8)          |
| Gini index | 0.876 | 0.885 | 0.870 | 0.872 | □ | □ | 0.857 |

Abbreviations: standard deviation (SD); interquartile range (IQR); and the United States (US); and 95% confidence interval (95%CI)

7 pharmaceutical companies were excluded because the companies did not disclose or we could not collect the four-years payment data between 2016 and 2019.
Figure 1. Concentration of payment to individual hematology specialists
Figure 2. Total payments from top 10 largest paying pharmaceutical companies between 2016 and 2019.
Figure 3. Category and distribution of payments by top 10 largest paying pharmaceutical companies.
