Association between pharmaceutical industry payments to physicians and prescription of PARP inhibitors in the United States

Anju Murayama (ange21tera@gmail.com)
Tohoku University https://orcid.org/0000-0002-4279-4748

Research Article

Keywords: Breast cancer, ovarian cancer, industry payments, Open Payments Database, Sunshine Act, poly ADP-ribose polymerase inhibitor

Posted Date: August 22nd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3280055/v1

License: ☺️ Ⓞ This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Purpose

To evaluate the association between industry payments to physicians related to poly (ADP-ribose) polymerase inhibitors (PARPis) and physicians’ prescribing behaviors for PARPis.

Methods

This cross-sectional study used the publicly accessible Open Payments Database and Medicare Part D database between 2017 and 2021. All physicians who reported more than 10 claims for either olaparib, rucaparib, or niraparib were included in this study. Non-research payments for the PARPis to the physicians from the PARPi manufacturers were extracted from the Open Payments Database. Associations between the physicians’ receipt of payments and likelihood of prescribing PARPis were assessed with logistic generalized estimating equations (GEEs). Dose-response associations between the number of payments and prescription volumes and Medicare expenditures were evaluated with linear GEEs.

Results

Of the 1,706 eligible physician prescribers, 68.1% received one or more non-research payments related to any of the three PARPis from the manufacturers between 2017 and 2021. Median annual payments per physician were $55 for olaparib, $40 for rucaparib, and $60 for niraparib. Receipt of payments for each PARPi was associated with higher odds of prescribing olaparib (odds ratio [OR]: 1.33 [95% CI: 1.17-1.52], p<0.001), rucaparib (OR: 2.25 [95% CI: 1.72-2.95], p<0.001), and niraparib (OR: 1.45 [95% CI: 1.20-1.76], p<0.001). Dose-response effects were observed between the number of annual payments and the number of prescriptions and/or Medicare expenditures for olaparib and rucaparib.

Conclusion

Non-research payments to physician prescribers of PARP inhibitors from the manufacturers were significantly associated with increased prescriptions and Medicare expenditures for olaparib and rucaparib in the United States.

Highlights

This study evaluated associations between payments to physicians from PARP inhibitor manufacturers and the physicians’ prescribing patterns for PARP inhibitors in the United States.

Physicians who received payments from the manufacturers were more likely to prescribe the sponsored PARP inhibitors than those who did not.

Increased industry-sponsored gift payments were significantly associated with higher prescription volumes and Medicare expenditures for olaparib and rucaparib.

Introduction

Since the initial accelerated approval of olaparib in 2014, four poly (ADP-ribose) polymerase inhibitors (PARPis) have obtained full approval for the treatment of BRCA-associated cancers, including breast and ovarian cancer, in the United States (US). The elevated efficacy of PARPis compared to the current standard of care has provided a new therapeutic pathway for patients (1–4). However, the financial implications of these drugs are considerable, surpassing the willingness-to-pay thresholds, as demonstrated in several studies (5, 6).

In the US, the financial relationships between healthcare professionals and the healthcare industry are widespread both for research and non-research purposes (7–11). "Unfortunately, while not all, several of these financial relationships have at times posed challenges for patient-centered care, potentially leading to biased clinical trials, improper drug prescriptions, and biased guideline recommendations (12–14). Consequently, the Physician Payments Sunshine Act, also known as section 6002 of the Affordable Care Act, was enacted in response to the increasing public demand for transparency in physician-industry relationships in the US in 2010 (15). This regulation mandates that pharmaceutical and medical device companies must disclose all financial transfers with greater
than $100 in annual aggregates or $10 per payment made to physicians, nurse practitioners, and teaching hospitals. The reported payments have been disclosed under a federal transparency database, namely the Open Payments Database, since 2013. Using the Open Payments Database, previous studies showed that payments from the healthcare industry to physicians are associated with increased physician prescribing and healthcare costs in the US (13, 16, 17).

Using the Centers for Medicare and Medicaid Services (CMS) Medicare Part D database and the Open Payments Database, this study aims to evaluate the association between industry payments to physicians related to PARPis and physicians’ prescribing behaviors of PARPis.

Methods

Study design, setting, and the Open Payments Database

This cross-sectional analysis linked four publicly accessible databases: the CMS Medicare Part D files, the Open Payments Database, the National Plan and Provider Enumeration System (NPPES), and the Physician Compare database between 2017 and 2021. The Open Payments Database covers three financial transfers to physicians: 1) general payments (non-research payments), 2) research payments, and 3) stock and investment interests (amounts of ownership interest held by physicians in the year disclosed) (7–9, 18).

The Open Payments Database only covers financial transfers to physicians and does not include detailed information regarding the contents of payments.

Publicly accessible Medicare Part D database

Among the four PARPis approved by the US Food and Drug Administration, this study focused on drugs prescribed more than 10 claims by 20 or more physicians using the Medicare Part D during the study period. Consequently, three PARPis (olaparib, rucaparib, and niraparib) were included. The publicly accessible Medicare Part D database contains physician names reporting more than 10 claims of a drug in a single year to protect patients’ privacy. To cover physicians who could prescribe PARPis, the number of claims (30-day standardized, including refills) and Medicare spending associated with each PARPi for only physicians who prescribed more than 10 claims of any of the three PARPis were extracted at individual physician level from the Medicare Part D database between 2017 and 2021 (17, 19). As the Open Payments Database covers payments to physicians, physician prescribers were included in this study.

Demographic data

Demographic characteristics of physician prescribers were collected from the Physician Compare as previously conducted (17, 19). The physicians' medical school graduations were categorized into three groups based on the 2023 U.S. News & World Report rankings, which list the research ranking of US medical schools: ranked 1 to 20, 21 to 50, and other schools, including all unranked and foreign schools, as done in previous studies (19, 20). Physician specialties were categorized into four groups: general obstetrics and gynecology; gynecologic oncology; oncology including medical oncology, hematology/oncology, and hematology; and other specialties.

The Open Payments Database

As previous studies showed that majority of physicians accepted payments for non-research purposes from the healthcare industry (7–9, 18, 21, 22), this study extracted all general payments provided to the physician prescribers from the Open Payments Database between 2017 and 2021. The Open Payments Database contains up to five product names and National Drug Code (NDC) numbers associated with each general and research payment. Then, the general payments related to olaparib, rucaparib, and niraparib were identified from the extracted general payments using string NDC number (“0310-0657-58” [brand name: Lynparza, generic name: olaparib], “69660-201-91” [brand name: Rubraca, generic name: rucaparib], and “69656-103-90” [brand name: Zejula, generic name: niraparib]).

Statistical analyses

The prescription and payment data were descriptively analyzed. Associations between payments for each drug and the prescriptions of that drug were evaluated using multivariable population-averaged logistic generalized estimating equations (GEEs), adjusting for covariates such as gender, practice region, years in practice, medical school graduation, specialty, and payment year. Furthermore, multivariable linear GEEs were employed to assess associations between the number of payments and the number of claims (30-day...
standardized, including refills) and Medicare spending. General payments were further categorized as gifts (meal and education payments) and compensations (consulting, speaking compensation, honoraria, and travel payments), and the associations were also analyzed based on payment categories. Additionally, this study performed subgroup analysis of the associations between the payments to physicians and physicians’ PARPi prescription patterns by physician gender and specialty, as previous studies suggested that female physicians received less industry payments(9, 23) and consequently might be less influenced by these payments(24). All payment values and healthcare costs were adjusted to 2021-US dollar values using U.S. Bureau of Labor Statistics Consumer Price Index calculator. All statistical analyses were performed using Python 3.9.12 (Python Software Foundation, Beaverton, OR, USA), Microsoft Excel, version 16.0 (Microsoft Corp., Redmond, WA, USA), and Stata version 17.0 (StataCorp, College Station, TX, USA). This study considered p values less than 0.05 as statistical significance.

**Ethical clearance**

As all data used in this study were freely available public data and met the definition of non-human subjects research, no institutional board review and approval were required for this study. Also, informed consent from study participants was not required.

**Results**

**Demographic characteristics**

Table 1 describes the demographic characteristics of physicians prescribing PARP inhibitors (PARPi). In total, 1706 physicians reported more than 10 claims for any of the three PARPis between 2017 and 2021. Among them, 1144 (67.1%) were oncologists, 344 (20.2%) were gynecologic oncologists, and 1093 (64.1%) were male. The mean number of years since graduation from medical school is 27.2 (standard deviation: 10.2), with 10.8% of physicians having graduated from a top-twenty medical school.
Table 1
Demographic characteristics of physicians who prescribed more than 10 claims of olaparib, rucaparib, and niraparib between 2017 and 2021.

<table>
<thead>
<tr>
<th>Variables (N = 1706)</th>
<th>Number of physicians (%), n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty</td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>1144 (67.1)</td>
</tr>
<tr>
<td>Gynecological oncology</td>
<td>344 (20.2)</td>
</tr>
<tr>
<td>General obstetrics and gynecology</td>
<td>116 (6.8)</td>
</tr>
<tr>
<td>Other specialties a</td>
<td>102 (6.0)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1093 (64.1)</td>
</tr>
<tr>
<td>Female</td>
<td>613 (35.9)</td>
</tr>
<tr>
<td>Year since graduation from medical school b</td>
<td></td>
</tr>
<tr>
<td>Mean (standard deviation), yr</td>
<td>27.2 (10.2)</td>
</tr>
<tr>
<td>Medical school ranking</td>
<td></td>
</tr>
<tr>
<td>Top 1–20</td>
<td>184 (10.8)</td>
</tr>
<tr>
<td>Top 21–50</td>
<td>290 (17.0)</td>
</tr>
<tr>
<td>Other medical schools</td>
<td>1232 (72.2)</td>
</tr>
<tr>
<td>Practice region</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>348 (20.4)</td>
</tr>
<tr>
<td>South</td>
<td>597 (35.0)</td>
</tr>
<tr>
<td>Midwest</td>
<td>322 (18.9)</td>
</tr>
<tr>
<td>West</td>
<td>427 (25.0)</td>
</tr>
<tr>
<td>US territories</td>
<td>12 (0.7)</td>
</tr>
</tbody>
</table>

Legends: a Other specialties include internal medicine, urology, general practice, hematopoietic cell transplantation and cellular therapy, dermatology, neurology, surgical oncology, and hospice and palliative care. b Year since graduation from medical school was based on data disclosed on the Centers for Medicare and Medicaid Services Physician Compare database last updated on July 20, 2023.

Payments and prescriptions for PARPis between 2017 and 2021

Among all 1706 physician prescribers, 1162 (68.1%) received one or more general payments related to any of the three PARPis between 2017 and 2021 (Table 2), while 1652 (96.8%) received general payments from any healthcare companies, including companies that do not manufacture PARPis. The proportion of physician prescribers receiving general payments ranged from 43.0% for rucaparib to 51.8% for olaparib. The total five-year combined amounts of general payments were $4.8 million for olaparib, $2.7 million for rucaparib, and $5.7 million for niraparib in inflation-adjusted values. Meanwhile, the number of general payments was 10,602 for olaparib, 5,637 for rucaparib, and 10,393 for niraparib. The median annual general payments per physician were $55 (interquartile range [IQR]: $20–$143) for olaparib, $40 (IQR: $18–$129) for rucaparib, and $60 (IQR: $24–$158) for niraparib.
Table 2
Summary of payments to prescribers and prescription for olaparib, rucaparib, and niraparib between 2017 and 2021.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Olaparib</th>
<th>Rucaparib</th>
<th>Niraparib</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of physicians receiving payments, No. (%)</td>
<td>884 (51.8)</td>
<td>734 (43.0)</td>
<td>853 (50.0)</td>
<td>1162 (68.1)</td>
</tr>
<tr>
<td>Total payment amounts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monetary amounts, $</td>
<td>4,814,014</td>
<td>2,687,861</td>
<td>5,660,866</td>
<td>13,162,741</td>
</tr>
<tr>
<td>Number of payments, No.</td>
<td>10,602</td>
<td>5,637</td>
<td>10,393</td>
<td>26,632</td>
</tr>
<tr>
<td>Median annual payments (interquartile range) a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monetary amounts, $</td>
<td>55 (20–143)</td>
<td>40 (18–129)</td>
<td>60 (24–158)</td>
<td>–</td>
</tr>
<tr>
<td>Number of payments, No.</td>
<td>3 (1–5)</td>
<td>2 (1–3)</td>
<td>2 (1–4)</td>
<td>–</td>
</tr>
<tr>
<td>Prescription amounts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of physicians prescribing each drug, No. (%)</td>
<td>1309 (76.7)</td>
<td>220 (12.9)</td>
<td>477 (28.0)</td>
<td>1706 (100)</td>
</tr>
<tr>
<td>Total number of 30-day standardized claims including refills, No.</td>
<td>36,274</td>
<td>5,146</td>
<td>12,723</td>
<td>52,213</td>
</tr>
<tr>
<td>Total Medicare spending, $</td>
<td>480,860,685</td>
<td>72,306,615</td>
<td>162,040,219</td>
<td>664,830,742</td>
</tr>
<tr>
<td>Likelihood of prescribing each drug, odds ratio (95% confidence interval)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receipt of any general payments</td>
<td>1.33 (1.17–1.52)***</td>
<td>2.24 (1.71–2.94)***</td>
<td>1.45 (1.20–1.76)***</td>
<td>–</td>
</tr>
<tr>
<td>Receipt of any gift payments b</td>
<td>1.28 (1.12–1.47)***</td>
<td>2.28 (1.73–2.99)***</td>
<td>1.44 (1.19–1.75)***</td>
<td>–</td>
</tr>
<tr>
<td>Receipt of any compensation payments c</td>
<td>1.81 (1.38–2.38)***</td>
<td>2.61 (1.57–4.35)***</td>
<td>1.70 (1.19–2.44)**</td>
<td>–</td>
</tr>
</tbody>
</table>

Legend: *p < 0.05. **p < 0.01. ***p < 0.001. a Per-physician annual payment amount and number were calculated among physicians receiving payments, as majority of physicians did not receive any payments for each PARPi. b Gift payments included general payments for food and beverage and education. c Compensation payments included general payments for consulting fees, speaking compensation fees, honoraria, and travel and lodging fees.

Regarding prescription data, the proportion of physician prescribers was 76.7% for olaparib, 12.9% for rucaparib, and 28.0% for niraparib, respectively (Table 2). The total amounts of claims and healthcare expenditures were the largest for olaparib at 36,274 and $480.9 million, and the lowest for rucaparib at 5,146 and $72.3 million, respectively. Receipt of any type of general payment for each PARPi was associated with higher odds of prescribing olaparib (odds ratio [OR]: 1.33 [95% CI: 1.17–1.52], p < 0.001), rucaparib (OR: 2.25 [95% CI: 1.72–2.95], p < 0.001), and niraparib (OR: 1.45 [95% CI: 1.20–1.76], p < 0.001). Additionally, the prescriptions of each PARPi were associated with the receipt of both gift and compensation payments by the physician prescribers (Table 2).

Among the three PARPis, dose-response effects were observed between the number of annual general payments and the number of annual prescriptions and/or Medicare expenditures for olaparib and rucaparib (Table 3). There was, however, no dose-response effect for niraparib. Notably, one increase in the annual number of gift payments to physicians was significantly associated with an increase in annual Medicare spending of $2,701.0 (95% CI: $1,101.6 – $4,300.5, p = 0.001) for olaparib and $2,669.4 (95% CI: $1,173.7 – $4,165.1, p < 0.001) for rucaparib. Meanwhile, weakly significant associations were found between an increase in compensation payments and higher annual numbers of claims and Medicare spending for olaparib. There were no associations between the number of compensation payments and physicians' prescription amounts for rucaparib and niraparib.
Table 3
Associations between one increase in annual general payments to prescribers and change in annual number of claims and Medicare spending costs for olaparib, rucaparib, and niraparib between 2017 and 2021.

<table>
<thead>
<tr>
<th>One payment increase</th>
<th>Change in annual number of claims (95% confidence interval), No.</th>
<th>Change in annual Medicare Part D spending (95% confidence interval), $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Olaparib</td>
<td>Rucaparib</td>
</tr>
<tr>
<td>General payments</td>
<td>0.13 (0.03–0.23)*</td>
<td>0.05 (-0.001 to 0.10)</td>
</tr>
<tr>
<td>Gift payments&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.17 (0.05–0.29)**</td>
<td>0.17 (0.07–0.27)**</td>
</tr>
<tr>
<td>Compensation payments&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.21 (0.03–0.40)*</td>
<td>0.01 (-0.05 to 0.08)</td>
</tr>
</tbody>
</table>

Legend: *p < 0.05. **p < 0.01. ***p < 0.001. <sup>a</sup>Gift payments included general payments for food and beverage and education. <sup>b</sup>Compensation payments included general payments for consulting fees, speaking compensation fees, honoraria, and travel and lodging fees.

Payments and prescriptions for PARPis by gender and specialty

Although there were no gender differences in the proportion of physicians prescribing olaparib, rucaparib, and niraparib, male physicians were more likely to receive general payments for olaparib (56.3% vs 43.9%, p < 0.001 in chi-square test) rucaparib (45.8% vs 38.2%, p < 0.001 in chi-square test), and niraparib (51.3% vs 47.6%, p = 0.001 in chi-square test) (Supplemental Material 1).

Table 4 showed that associations between the industry payments and physicians’ PARPis prescribing amounts and Medicare expenditures. While there were strongly significant associations between the receipt of general payments and higher odds ratio of prescribing all three PARPis among male physicians, there were weakly significant associations between receipt of industry payments and odds ratios of prescribing olaparib and rucaparib among female physicians. Additionally, there were no significant associations between the number of general payments and annual claim numbers and annual Medicare expenditures for all PARPis among the female physicians.
Table 4
Associations between industry payments to physicians and physicians’ prescribing patterns for PARP inhibitors by gender.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Olaparib</th>
<th>Rucaparib</th>
<th>Niraparib</th>
<th>Olaparib</th>
<th>Rucaparib</th>
<th>Niraparib</th>
<th>Olaparib</th>
<th>Rucaparib</th>
<th>Niraparib</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Likelihood of prescribing each drug, odds ratio (95% confidence interval)</td>
<td>Change in annual number of claims (95% confidence interval), No.</td>
<td>Change in annual Medicare Part D spending (95% confidence interval), $</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General payments</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.32 (1.13–1.54)***</td>
<td>2.17 (1.55–3.02)***</td>
<td>1.46 (1.16–1.84)***</td>
<td>0.14 (0.03–0.27)*</td>
<td>0.04 (-0.01 to 0.09)</td>
<td>-0.01 (-0.04 to 0.03)</td>
<td>2,316.3 (698.9–3,933.8)***</td>
<td>639.9 (-92.0 to 1,371.7)</td>
<td>-45.5 (-505.0 to 414.1)</td>
</tr>
<tr>
<td>Female</td>
<td>1.36 (1.06–1.75)*</td>
<td>2.53 (1.56–4.11)***</td>
<td>1.38 (0.97–1.97)</td>
<td>0.05 (-0.07 to 0.2)</td>
<td>0.07 (-0.03 to 0.17)</td>
<td>0.006 (-0.07 to 0.08)</td>
<td>690.5 (-933.2 to 2,314.2)</td>
<td>1,404.9 (-196.6 to 3,006.4)</td>
<td>271.6 (-751.9 to 1,295.1)</td>
</tr>
<tr>
<td>Gift paymentsa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.29 (1.11–1.51)**</td>
<td>2.14 (1.53–2.99)***</td>
<td>1.45 (1.15–1.83)***</td>
<td>0.20 (0.05–0.34)**</td>
<td>0.16 (0.04–0.29)*</td>
<td>0.01 (-0.08 to 0.10)</td>
<td>3,159.8 (1,216.3–5,103.2)***</td>
<td>2,445.7 (697.5–4,193.9)***</td>
<td>172.2 (-939.9 to 1,274.4)</td>
</tr>
<tr>
<td>Female</td>
<td>1.28 (0.98–1.67)***</td>
<td>2.77 (1.69–4.52)***</td>
<td>1.40 (0.97–2.01)</td>
<td>0.09 (-0.09 to 0.27)</td>
<td>0.18 (0.02–0.34)*</td>
<td>-0.03 (-0.15 to 0.09)</td>
<td>1,406.5 (884.6–2,697.6)</td>
<td>3,229.6 (584.4–5,874.8)*</td>
<td>-29.8 (-1,467.8 to 1,408.3)</td>
</tr>
<tr>
<td>Compensation paymentsb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.01 (1.44–2.80)***</td>
<td>2.86 (1.61–5.10)***</td>
<td>1.75 (1.14–2.68)*</td>
<td>0.24 (0.03–0.45)*</td>
<td>0.01 (-0.06 to 0.08)</td>
<td>-0.01 (-0.07 to 0.05)</td>
<td>3,670.4 (672.7–6,668.0)*</td>
<td>228.8 (-723.2 to 1,180.8)</td>
<td>-181.9 (-880.6 to 516.7)</td>
</tr>
<tr>
<td>Female</td>
<td>1.48 (0.95–2.29)***</td>
<td>1.44 (0.53–3.90)***</td>
<td>1.58 (0.78–3.20)</td>
<td>0.01 (-0.15 to 0.17)</td>
<td>-0.04 (-0.19 to 0.012)</td>
<td>0.05 (-0.10 to 0.19)</td>
<td>105.7 (2,634.3 to 2,845.6)</td>
<td>-415.3 (-2,652.7 to 1,822.2)</td>
<td>885.7 (-1,350.8 to 3,122.2)</td>
</tr>
</tbody>
</table>

Legend: *p < 0.05. **p < 0.01. ***p < 0.001. a Gift payments included general payments for food and beverage and education. b Compensation payments included general payments for consulting fees, speaking compensation fees, honoraria, and travel and lodging fees.

Supplemental Material 2 represents the differences in the payments and prescription amounts by physicians’ clinical specialties. Olaparib was prescribed by more than 70% of physicians in each specialty, while rucaparib and niraparib were more likely to be prescribed by gynecological oncologists and obstetrician/gynecologists than oncologists and other specialists. Of four specialties, gynecological oncologists had the highest proportions of physicians receiving general payments from pharmaceutical companies for all three drugs (57.3% for olaparib, 63.7% for rucaparib, and 71.2% for niraparib).

Among the four specialties, the receipt of general payments was significantly associated with higher odds of prescribing all three PARPi among oncologists, and also with higher odds of prescribing olaparib and rucaparib, but not niraparib, among gynecologic oncologists (Supplemental Material 3). There were weakly significant associations between the payment receipt and higher odds ratio of prescribing rucaparib among obstetrician/gynecologists (OR: 2.65 [95% CI: 1.07–6.59], p = 0.04) and other specialists (OR: 3.20 [95% CI: 1.16–8.81], p = 0.02). The receipts of gift payments were also associated with higher odds of prescribing all three PARPi among oncologists, and olaparib and rucaparib among gynecological oncologists.

Discussion
This study demonstrated that 68.1% of PARPi prescribers received non-research payments related to the three PARPi from the manufacturers in the United States. Significant associations were found between non-research payments from the manufacturers to
PARPi physician prescribers and the likelihood of prescribing industry-sponsored PARPis in the US. Furthermore, the industry-sponsored gift payments were significantly associated with increased prescription volumes and Medicare spending for olaparib and rucaparib. Subgroup analyses by physician demographics showed that female physician prescribers were less likely to receive payments from the industry, and the payments to female physicians were less associated with their prescribing patterns for PARPis than those to male physicians. Not surprisingly, oncologists and gynecological oncologists were more targeted by the pharmaceutical industry manufacturing PARPis than other physicians. However, their prescription patterns were more associated with the receipt of payments than those of general obstetricians/gynecologists and other specialists. This study could provide important insights into the financial relationships between obstetricians/gynecologists and the healthcare industry in the US.

First, as this study is a cross-sectional analysis, the observed associations do not indicate causality. Additionally, industry sponsorship for the sole purpose of meals, travel fees, and gifts associated with increasing prescriptions is not allowed in the US. Thus, reported gift payments likely primarily reflect participation in company-sponsored lectures and events where the company explains the PARPis, rather than the provision of funds that did not involve a formal company activity. It should also be noted that payments from the healthcare industry to physicians do not necessarily indicate unethical or problematic financial relationships, nor do they necessarily lead to conflicts of interest or biased prescriptions by physicians. Indeed, these PARPis show a significant safety and efficacy profile (1, 2, 25, 26) and are increasingly considered as alternative and combination treatments to cytotoxic chemotherapy and other biologics for ovarian cancers and beyond (25, 27). For example, PARPis such as olaparib, niraparib, and rucaparib are currently recommended for maintenance treatment for newly diagnosed and recurrent ovarian cancer in the US (4, 26). The industry-sponsored meal payments, as well as the industry-sponsored educational events and activities for PARPi prescribers, might be contributing to the sufficient distribution of effective PARPis to patients in the US, as the majority of physicians consider the information provided by pharmaceutical companies to be helpful and beneficial for their clinical practice (28).

Meanwhile, this study found that more than 95% of physicians prescribing PARPis received general payments from healthcare companies, and 68.1% received PARPi-related payments from the PARPi manufacturers. These fractions of physicians receiving payments were higher than those of obstetricians/gynecologists, oncologists, and other previously documented specialists. Using the Open Payments Database, Muffy et al. reported that less than half (49.7%) of all practicing obstetrician/gynecologists received one or more general payments from any healthcare companies between 2013 and 2015 (29). Marshall et al. found that 45.0–52.2% of all physicians received the payments each year (30). Furthermore, Tarras et al. reported that 57.2–67.4% of practicing oncologists received general payments from any healthcare industry each year between 2014 and 2019 (22). More than 84.6% of oncologists received at least one general payment over the six years (22). In other medical specialists evaluated with similar methodology, 76.7% of cardiology (31), 81.5% of infectious disease physicians (32), 85.1% of allergists and clinical immunologists (21), 87% of nephrologists (9), 88.7% of pulmonologists (8), and 91.3% of rheumatologists (11, 33) received at least one general payments since the Open Payments Database inception in 2014. Compared to these previous findings and the high drug costs of PARPis, PARPi prescribers might be more targeted by the healthcare industry than other physicians.

A significant question remains as to whether the industry-sponsored meals and lectures are the best way to sufficiently distribute the drugs to physicians and patients from an ethical and economic perspective. A recent systematic review by Mitchell et al. found that industry-sponsored lectures and meals were significantly associated with increased prescriptions and healthcare costs in the US (16). The healthcare industry is more likely to market drugs with inadequate evidence and other competing drugs than those with adequate safety and efficacy profiles (16). Presentation materials and manuscripts are sometimes prepared by the healthcare industry and presented by influential physicians who received speaking compensations, called key opinion leaders (34, 35). In many cases, the speaking physicians and industry representatives are not permitted to mention competing drugs manufactured by other companies in their speeches. As a result, the industry-sponsored events and lectures are sometimes biased. The COVID-19 pandemic, however, has shifted the healthcare industry’s marketing approach to physicians from offline representative visits and free meals to online speaking events, because many industry representatives were not allowed to visit physicians to prevent COVID-19 infection and also because some companies consider online marketing strategies to be more cost-effective than offline visits and free meals (11, 21, 31, 32, 36). Therefore, even though this study found that there were significant associations between industry-sponsored meals to prescribers and their prescriptions between 2017 and 2021, the future trends of these associations are unclear.

In addition, their high costs and uncertain cost-effectiveness remain significant concerns, with the potential for escalating healthcare costs in the US healthcare system (5). The total PARPi costs per patient were $12,422 (6), w and while the majority of the costs are covered by the financial assistance program from the manufacturers, the government, and other foundations (37), some researchers
stated that the financial assistance program is not sustainable and hides problems such as the high drug costs increased by the manufacturers and the increased number of patients who might not need the drugs and can be managed with more affordable alternatives (38). These significant associations between industry gift payments to the physicians and the physicians’ prescription amounts and Medicare expenditures might suggest that industry-sponsored meals, as well as educational materials and lectures provided to the PARPi prescribers, could be a driving factor contributing to increased PARPi prescriptions in the US.

Apart from the pros and cons of the associations between the industry payments to the physicians and the physicians’ prescribing patterns, physicians need to be transparent in their financial relationships with the healthcare industry and their clinical practice, not only in the field of obstetrics and gynecology but also across the whole medical community. Additionally, many patients wish to know about the physician-industry relationship and the influence of payment on their treatment (39–41). However, fewer than 10% of patients were aware of the public disclosure of industry payments to physicians in the US (40–42). Together with an increase in awareness of physician-industry financial relationships and their influence on physicians’ clinical practice, further discussion with the public, patients, physicians, and policymakers is necessary for managing appropriate physician-industry relationships and constructing trustworthy healthcare in the US.

Several limitations should be acknowledged. First, there could be potential errors in databases including Medicare Part D files, Physician Compare Database, and the Open Payments Database. Second, as this study only included Medicare beneficiaries, the study findings might not be generalized to non-Medicare beneficiaries. Third, due to the protection of patient privacy, prescription data with fewer than 11 claims were suppressed, leading to underestimation of the prescription amounts and Medicare expenditures (17). Fourth, there would be unmeasured confounding factors such as patient numbers, targeted diseases, and detailed information on payment content and reasons, as well as the prescribing physicians’ beliefs, motivations, and preferences toward the prescriptions, because the information were not available from the publicly available databases. Finally, as the author discussed in the discussion section, industry sponsorship for the sole purpose of meals associated with increasing prescriptions is not allowed in the US. Thus, the increased PARPi prescriptions and Medicare expenditures could be attributed not only to industry payments and meals, but also to the information and lectures provided by the manufacturers.

Conclusion

In conclusion, this study found that the majority of physicians who prescribed PARP inhibitors received non-research payments from the manufacturers between 2017 and 2021 in the United States. The receipts of gift payments including meals and educational materials from the manufacturers were significantly associated with higher likelihood of prescribing olaparib, rucaparib and niraparib. In addition, these gift payments were also significantly associated with increased prescription volumes and higher Medicare expenditures of the PARP inhibitors such olaparib and rucaparib.

Abbreviations

95% CI: 95% confidence interval; CMS: Centers for Medicare & Medicaid Services; GEE: generalized estimating equation; IQR: interquartile range; NPPES: National Plan and Provider Enumeration System; PARP: poly ADP-ribose polymerase inhibitors; US: United States

Declarations

Conflicts of interest:

The author declared no conflict of interest.

Funding

The author did not receive any financial support for this study.

Author contribution:

Anju Murayama: Conceptualization; methodology; software; formal analysis; investigation; resources; writing - original draft; writing - review & editing; visualization; study administration
Acknowledgments

I would like to thank Ms. Megumi Aizawa for her dedicated support of my research project. The author declares no conflict of interest and did not receive any funding for this study.

References


Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementalmaterials13.docx