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Industry payments to US physicians for cancer therapeutics: An analysis of the 2016–2018 open payments datasets

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ABSTRACT

Background: Many oncologists who lead guidelines and clinical trials have financial conflicts of interest (fCOI) with industry. However, the extent to which fCOI reaches all cancer care providers is not known. Here we describe industry payments across all cancer care specialties by specific drug.

Methods: This observational, retrospective cohort study used Open Payments to describe general payments (i.e. consulting fees, meals, travel) to all US physicians for any cancer medicine during 2016–2018. Endpoints included number and value of payments by specialty, drug, and year.

Results: During 2016–2018, industry made general payments to 52 441 physicians for 137 unique cancer drugs. Annual number of payments (465 655 in 2018) and total value (\$98.5 million in 2018) increased over the study period (20 % and 31 % increase since 2016). Medical/hematologic oncologists, surgical oncologists and radiologists received the highest total value of payments, accounting for \$65.7 million (67 % of total), \$13.4 million (14 % of total) and \$10.8 million (11 % of total) in 2018. In 2018, 5 % of physicians (n = 1660) received >\$10 000 in annual payments and 0.6 % (n = 209) received >\$100 000. Pembrolizumab and Nivolumab, were associated with the highest total payment in each year, accounting for 12 % and 6 % (2018) of total value, respectively.

Conclusions: While prior work has identified fCOIs among oncology leaders, these data suggest that payments extend across the cancer system.

Policy summary: Pre-existing data suggest a strong relationship between industry payments and physician prescribing. The current study demonstrates that fCOIs among oncology prescribers are pervasive. The oncology community must consider the extent to which these relationships influence clinical practice and regulatory policies.

1. Introduction

Financial relationships between physicians and the pharmaceutical industry are widespread [1–3]. Although industry collaboration is a necessary part of the research enterprise, the receipt of travel, meal, consultancies, honoraria and other personal payments creates financial conflicts of interest (fCOI) that are relevant to patient care. In oncology, fCOI are problematic as they may lead to physician-driven promotion of therapeutics that are costly, toxic, and are associated with uncertain or

modest improvements in outcome [4–9].

Studies of fCOI in the US have been made possible by the advent of the Open Payments (OP) database. OP, implemented in 2013 under the Affordable Care Act, is a centralized repository of industry payments made to US physicians and teaching hospitals [10]. Data generated from OP have demonstrated that fCOI are pervasive throughout medicine [11]. Oncology may be particularly vulnerable to industry influence, as spending on cancer drugs has more than doubled in the US since 2013 – now exceeding more than \$56 billion annually, with the median annual

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cost of therapy of nearly \$150 000 [12,13].

Prior work has illustrated that fCOI are common across leaders of the cancer system including authors of randomized controlled trials (RCTs) [14], clinical practice guidelines [15,16], and high-profile editorials [17]. Moreover, fCOI may alter how physicians discuss therapeutics on social media [18]. fCOI have also been linked to prescribing patterns in oncology [9]. However, the extent to which fCOI exists within the broader community of oncology physicians is not known, and there are also no published data that link industry payments to specific cancer drugs.

Prior studies have used data from the OP program to evaluate fCOI for a pre-selected population of oncologists (i.e. authors of clinical practice guidelines, clinical trialists, or those with active social media accounts). To understand the broader context of physician payments and cancer care, we describe the scope of general payments to all practicing physicians (regardless of specialty) for all cancer medicines across three years (2016–2018). While prior research has examined conflicts among a set of physicians, here we examine payments for a set of drugs. This novel approach allows for the evaluation of an entire population, and mitigates bias that may be associated with a pre-defined cohort. We sought to address three objectives: 1) how are industry payments for cancer therapeutics distributed to physicians across medical specialties; 2) what is the prevalence of “significant” payments (>\$10 000 USD) to physicians; and 3) which cancer therapeutics are associated with the highest total payments.

2. Methods

2.1. Study population

In this observational study, we used OP datasets from 2016 to 2018 [<https://openpaymentsdata.cms.gov/about>] to identify all physicians who received general payments specifically linked to a cancer therapeutic. As defined by OP, general payments include consulting fees, honoraria, speaking fees, travel expenses and meals. Research and ownership/investment interests, the other two broad classifications of payments, were not considered in our dataset. Specific definitions used by OP to classify payment types can be found at <https://www.cms.gov/OpenPayments/About/Natures-of-Payment>.

Only osteopathic and allopathic physicians were considered; payments to other medical professions, and academic institutions were excluded. To ensure our final dataset was restricted to therapeutics with an oncology-based indication, we excluded all payments made for devices or medical supplies, and only included payments that fell under a product category containing the word “oncology”.

2.2. Drug and physician categorization

In order to ensure specificity of our analysis to cancer therapeutics, a summative list of all drugs/biologics was created for the 2016–2018 reporting years. This list was reviewed and all agents without a direct anti-cancer indication (i.e. anti-emetics, hematologic growth factors) and/or drugs with both anti-cancer and other indications (i.e. Rituximab, Everolimus) were excluded (Supplementary Tables 1 & 2). Twenty percent of payments were associated with more than one drug; only the primary agent listed for each payment was considered. Group classification of physician specialties and drugs was initially performed by one investigator (D.E.M) and subsequently reviewed by two practicing oncologists (C.M.B. and V.P.); discrepancies were resolved by consensus agreement.

The OP dataset lists a designated specialty area of practice for each physician-payment entry. All listed physician specialties were reviewed and subsequently categorized into one of ten broader groups: Medical/Hematologic Oncology (MO), Surgical Oncology (SO), Radiation Oncology (RO), Internal Medicine (IM), Laboratory Medicine (LM), Imaging (DI), Pediatrics (PED), Dermatology (DERM), General Practice/

Primary Care (GP), and Other (Supplementary Table 3). Payments to physicians in which multiple associated specialties were listed were resolved as follows: any payments to physicians with both IM and MO were classified as MO; all others were classified as the specialty in which they were categorized most frequently during the study period.

2.3. Payment data

Our final dataset included general payments made by the pharmaceutical industry to US-based physicians for cancer therapeutics between 2016–2018. Data were analyzed separately for each reporting year. Payment endpoints included: annual total number and value of payments according to both physician specialty and specific drug, the proportion of total number and value of payments made for each payment category (i.e. consulting fees, travel, meals), and annual per-physician payment characteristics by specialty. Finally, we classified the proportion of physicians who received annual general payments with a total value of \$0–\$1000, \$1000–\$10 000, \$10 000–\$100 000, or greater than \$100 000. A cut-off of \$10 000 is defined by the US Department of Health and Human Services as being “significant” [19], whilst \$100 000 was used as a predefined endpoint of interest.

2.4. Statistical analyses

Data from OP (2013–2018) is available for download as a .csv file-type, among others, but due to the expansive nature of each dataset, an Application Programming Interface (API) is also provided. This Socrata API provides Socrata Query Language (SoSQL), which has a syntax similar to traditional SQL, for querying the data prior to download. Due to differences in the data structure prior to 2016, we used the Socrata API combined with SoQL and a developer’s app token to download data for 2016, 2017, and 2018. Data are presented descriptively, with no *a priori* iterative statistical analyses planned. All data analyses were performed using R v3.6.2.

3. Results

3.1. Physicians, therapeutics, and overall payments

We examined payments for 137 unique drugs between 2016 and 2018. Summary measures of the study cohort, including physicians, payments and therapeutics are seen in Table 1. During the study period, 52 441 unique physicians received industry payments for cancer therapeutics, corresponding to 31 188 (2016), 30 648 (2017), and 32 918 (2018) unique physicians in each of the three years studied. Through the study period, MO, SO and IM were the most-represented physician specialties. In 2018, they accounted for 32 % (n = 10 620), 30 % (n = 9 741) and 11 % (n = 3 618) of physicians, respectively.

The number (389 696, 413 790, 465 655) and total value (\$75 499 005, \$84 956 046, \$98 519 198) of general payments increased substantially from 2016 to 2018 (20 % and 31 % increases, respectively). The number of unique therapeutics peaked at 120 in the 2018 reporting year, up from 98 in 2016. In 2018 the most common classes were small molecule inhibitors (45 %, 54/120), cytotoxic drugs (23 %, 28/120), and monoclonal antibodies (15 %, 18/120).

3.2. Payments by specialty

Industry payments by specialty are shown in Table 2. In all three reporting years, MO and SO were the top two specialties in both total number, and value of payments. In 2018, MO received 337 550 payments (73 % of total payments) valued at \$65.7 million (67 % of total value) and SO received 83 487 payments (18 % of total), valued at \$13.4 million (14 % of total). DI was the third highest specialty for total value of payments across all three reporting years, with \$10.8 million (2% of total payments, 11 % of total value) received in 2018.

Table 1
General payments from the pharmaceutical industry to US physicians for cancer therapeutics during 2016–2018.

	Year of Payment		
	2016	2017	2018
Physicians			
# Physicians	31 188	30 648	32 918
# Per Specialty (% Total)			
Medical/Hematologic Oncology (MO)	9 950 (32)	10 085 (33)	10 620 (32)
Surgical (SO)	9 566 (31)	8 946 (29)	9 741 (30)
Radiation Oncology (RO)	1 576 (5)	1 614 (5)	1 670 (5)
Internal Medicine (IM)	3 299 (11)	3 177 (10)	3 618 (11)
Dermatology (DERM)	2 026 (6)	2 041 (7)	2 220 (7)
General Practice/Primary Care (GP)	1 176 (4)	1 216 (4)	1 391 (4)
Imaging (DI)	1 228 (4)	1 158 (4)	1 304 (4)
Laboratory Medicine (LM)	1 111 (4)	1 243 (4)	1 004 (3)
Pediatrics (PED)	741 (2)	701 (2)	866 (3)
Other	515 (2)	467 (2)	484 (1)
Payments			
# of Payments	389 696	413 790	465 655
Total Value (\$)	75 499 005	84 956 046	98 519 187
Median Payment Value (IQR)	16 (12–24)	16 (12–23)	16 (12–23)
Median Per-Physician Value (IQR)	98 (27–310)	99 (26–337)	109 (29–355)
Therapeutics			
# of Therapeutics	98	108	120
Therapeutic Class (%Total)			
Small-molecule inhibitor	38 (39)	47 (44)	54 (45)
Cytotoxic	26 (27)	26 (24)	28 (23)
Monoclonal antibody	15 (15)	16 (15)	18 (15)
Immunotherapy	9 (9)	9 (8)	9 (8)
Hormonal	4 (4)	3 (3)	6 (5)
Other	6 (6)	8 (7)	7 (6)

*All monetary values expressed as USD. †Complete classification can be found in Supplementary Table 3.

In general, the distribution of payment categories amongst specialty groupings was similar for both the number and total value of payments (Fig. 1). Meals comprised the majority of the total number of payments, while the total value of payments was more evenly distributed between consulting fees, speaking engagements, and travel fees. However, more than half of the payments to DI in 2018 were for consulting fees, which accounted for 98 % (\$10.6 million) of the total value of payments to that specialty. In comparison, MO had 6 628 payments for consulting totaling \$17.1 million and SO had 948 for consulting totaling \$2.4 million.

3.3. Payments per physician

The per-physician distribution of payments from 2018 are shown in Fig. 2. The median per-physician total value of payments ranged between \$98 (IQR 27–310) in 2016 and \$109 (IQR 29–355) in 2018. Although in 2018 85 % of physicians received less than \$1000 in total payments, 1 660 physicians (5 % of the total) received greater than \$10 000 in general payments, with 209 of these physicians (0.6 % of the total) receiving >\$100 000 (Supplemental Fig. 1). More than 90 % of physicians with >\$10 000 in general payments were MO (n = 1 202, 72 %), SO (n = 196, 12 %) or DI (n = 96, 6 %). The designated specialty of the physician with the highest net total of general payments in each year was: RO (\$476 612) in 2016; MO (\$595 227) in 2017; and DI (\$891 528) in 2018.

3.4. Payments by drug

Payment characteristics for the top 10 therapeutics, according to annual general payment value, are seen in Table 3. Across all three years the top 10 accounted for ~40 % of the total number of payments (range 42 %–43 %), and ~45 % of the total value (range 43 %–51 %). The

Table 2
Specialty-level characteristics of payments to US physicians for cancer therapeutics during 2016–2018.

	Year of Payment		
	2016	2017	2018
Medical/Hematologic Oncology (MO)			
<i>Summary Data</i>			
# of Payments	293 412	317 909	337 550
Total Value	54 399 618	59 027 245	65 721 011
Median Value (IQR)	16 (12–23)	15 (12–22)	16 (12–23)
<i>Per-Physician Data</i>			
Median Value (IQR)	431 (116–1644)	458 (115–1827)	457 (111–1991)
Minimum	3	1	1
Maximum	355 375	595 227	543 894
Surgical (SO)			
<i>Summary Data</i>			
# of Payments	56 978	56 248	83 487
Total Value	8 914 842	10 287 338	13 399 902
Median Value (IQR)	17 (13–25)	17 (13–25)	16 (13–23)
<i>Per-Physician Data</i>			
Median Value (IQR)	81 (27–170)	80 (25–175)	110 (39–230)
Minimum	3	1	2
Maximum	243 994	285 648	299 598
Radiation Oncology (RO)			
<i>Summary Data</i>			
# of Payments	10 932	10 776	12 309
Total Value	1 527 628	1 394 287	1 329 570
Median Value (IQR)	15 (12–21)	16 (13–21)	16 (13–21)
<i>Per-Physician Data</i>			
Median Value (IQR)	87 (26–200)	76 (26–188)	85 (26–220)
Minimum	7	10	10
Maximum	476 412	118 686	136 595
Internal Medicine (IM)			
<i>Summary Data</i>			
# of Payments	8 478	8 038	9 299
Total Value	2 333 483	2 547 879	3 149 722
Median Value (IQR)	19 (14–47)	21 (14–88)	20 (15–95)
<i>Per-Physician Data</i>			
Median Value (IQR)	38 (17–110)	34 (17–111)	38 (18–117)
Minimum	1	1	1
Maximum	392 000	222 151	296 400
Dermatology (DERM)			
<i>Summary Data</i>			
# of Payments	4 861	4 886	5 495
Total Value (\$)	1 210 492	1 172 489	1 476 092
Median Value (IQR)	16 (13–24)	15 (13–21)	17 (14–32)
<i>Per-Physician Data</i>			
Median Value (IQR)	31 (16–67)	33 (17–69)	33 (16–79)
Minimum	1	6	4
Maximum	364 500	467 236	192 750
General Practice/Primary Care (GP)			
<i>Summary Data</i>			
# of Payments	2 648	2 320	2 896
Total Value	259 378	194 517	532 138
Median Value (IQR)	18 (13–36)	18 (14–40)	19 (14–56)
<i>Per-Physician Data</i>			
Median Value (IQR)	38 (17–98)	29 (16–92)	33 (17–103)
Minimum	1	1	2
Maximum	42 672	20 250	152 519
Imaging (DI)			
<i>Summary Data</i>			
# of Payments	4 878	5 675	7 024
Total Value	4 841 940	8 169 554	10 773 948
Median Value (IQR)	21 (15–314)	63 (17–1275)	113 (17–1260)
<i>Per-Physician Data</i>			
Median Value (IQR)	36 (17–112)	39 (18–124)	39 (17–119)
Minimum	10	7	11
Maximum	314 790	528 643	891 528
Laboratory Medicine (LM)			
<i>Summary Data</i>			
# of Payments	3 826	4 246	3 632
Total Value	746 957	989 798	689 347
Median Value (IQR)	19 (14–63)	19 (14–76)	17 (14–26)
<i>Per-Physician Data</i>			
Median Value (IQR)	65 (19–120)	57 (19–117)	53 (19–125)
Minimum	9	10	11
Maximum	63 721	142 896	68 800

(continued on next page)

Table 2 (continued)

	Year of Payment		
	2016	2017	2018
Pediatrics (PED)			
<i>Summary Data</i>			
# of Payments	2 458	2 651	2 883
Total Value	859 029	1 016 109	1 341 147
Median Value (IQR)	23 (15–115)	25 (15–123)	25 (15–122)
<i>Per-Physician Data</i>			
Median Value (IQR)	63 (21–125)	56 (20–128)	80 (23–125)
Minimum	3	5	8
Maximum	131 871	119 755	332 520
Other			
<i>Summary Data</i>			
# of Payments	1 225	1 041	1 080
Total Value	405 640	156 830	106 310
Median Value (IQR)	19 (14–83)	17 (13–47)	18 (14–26)
<i>Per-Physician Data</i>			
Median Value (IQR)	42 (18–111)	35 (17–115)	38 (18–113)
Minimum	7	8	4
Maximum	96 250	13 539	23 250

*All monetary values expressed as USD, ^Complete classification can be found in Supplementary Table 3.

cancer therapeutics accounting for the highest value of annual payments during the study period were pembrolizumab (range \$7.4 million–\$11.7 million) and nivolumab (range \$4.6 million–\$6.9 million). In 2018, 29 313 payments were made in association with pembrolizumab (6 % of all 2018 payments), totaling \$11.7 million (12 % of all 2018 payment value); comparable data for nivolumab are 29 274 payments (6 %) and \$4.6 million (5 %). Enzalutamide was also consistently among the top 10 cancer therapeutics, with the number of payments ranging from 30 447 to 46 106 (7 % to 10 % of all payments) and total valuing between \$3.4 million to \$4.0 million (4 %–5 % of all payments). The median value of payments across all drugs, and years, was ~ \$15–\$25.

The distribution of drug-specific payments across specialties during

2018 are shown in Supplemental Fig. 2. For most specialties the majority of both the total number and net value of payments were accounted for by therapeutics not in the top 10 during 2018. Exceptions to this include SO where the majority of payments were made for apalutamide (18 314, 22 % of total payments to SO) or enzalutamide (34 434, 41 % of total payments to SO), which together accounted for 40 % of the total value of payments [\$5.4 million (\$3.4 million for apalutamide, \$2.0 million for enzalutamide)]. Furthermore, DI received 2 973 payments for pembrolizumab (42 % total of payments to DI), with a value of \$7.5 million. These payments to DI accounted for 10 % of the total number and 64 % of the total value of all payments for Pembrolizumab during 2018.

4. Discussion

In this study we describe general payments from the pharmaceutical industry to all US physicians for cancer therapeutics. Several important findings have emerged. First, this is a common phenomenon (>30 000 physicians/year). As per the ASCO 2018 Practice Census Survey, there are approximately 12,423 medical/hematologic oncologists in the US; based on this estimate, our data suggest that ~85 % of US medical/hematologic oncologists receive general payments for cancer therapeutics from industry [20]. Second, these payments represent a substantial financial investment (approaching \$100 million/year). Third, temporal trends suggest that both number of payments and total value of payments are increasing (20 % and 31 % respectively over a 3 year period). Fourth, although medical/hematologic oncologists receive ~70 % of both the number, and total value, of payments for cancer therapeutics other specialists such as surgeons (~\$13 million, ~14 % total) and radiologists (~\$11 million, ~11 % total) also receive a substantial volume of payments. Fifth, although the annual median per-physician total value of payments was modest (~\$100), and 85 % of physicians received <\$1 000 in total payments during 2018, ~5 % of physicians (n = 1 660) received greater than \$10 000 in annual payments, and 0.6 % (n = 209) received greater than \$100 000. Finally, across the study

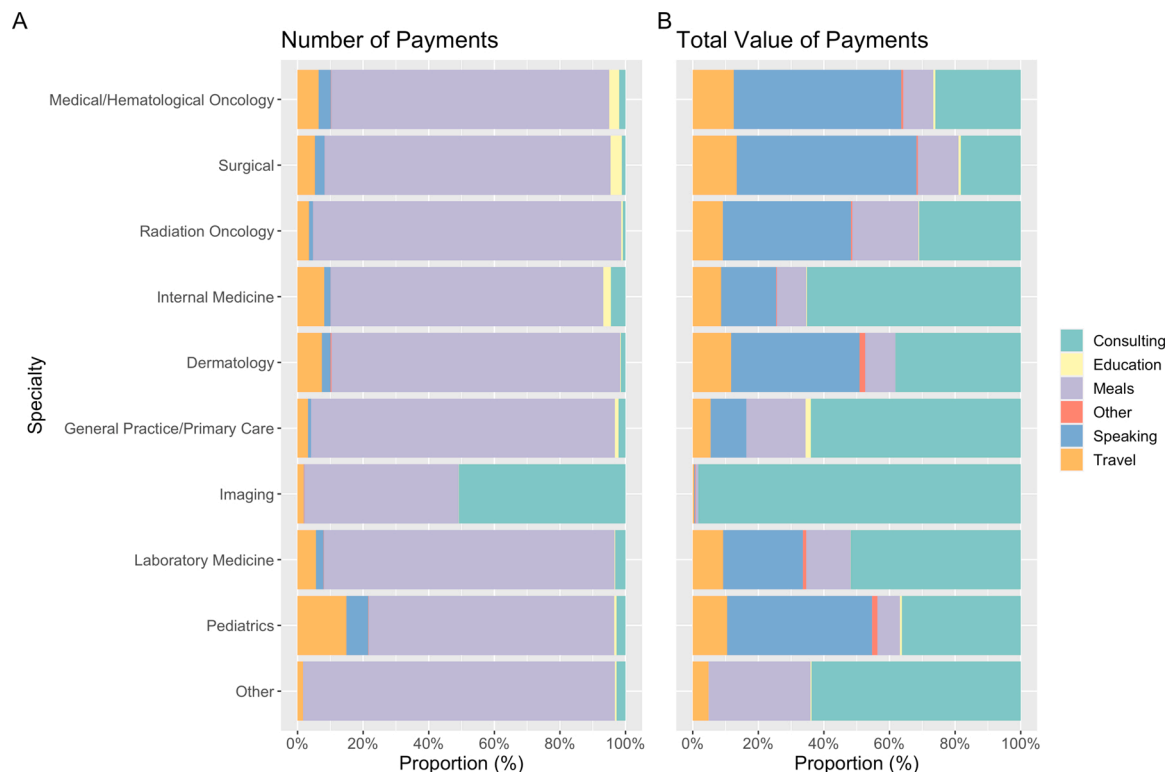


Fig. 1. The distribution of general payments for cancer therapeutics to US physicians in 2018, according to specialty. A) Number of payments. B) Total value of payments.

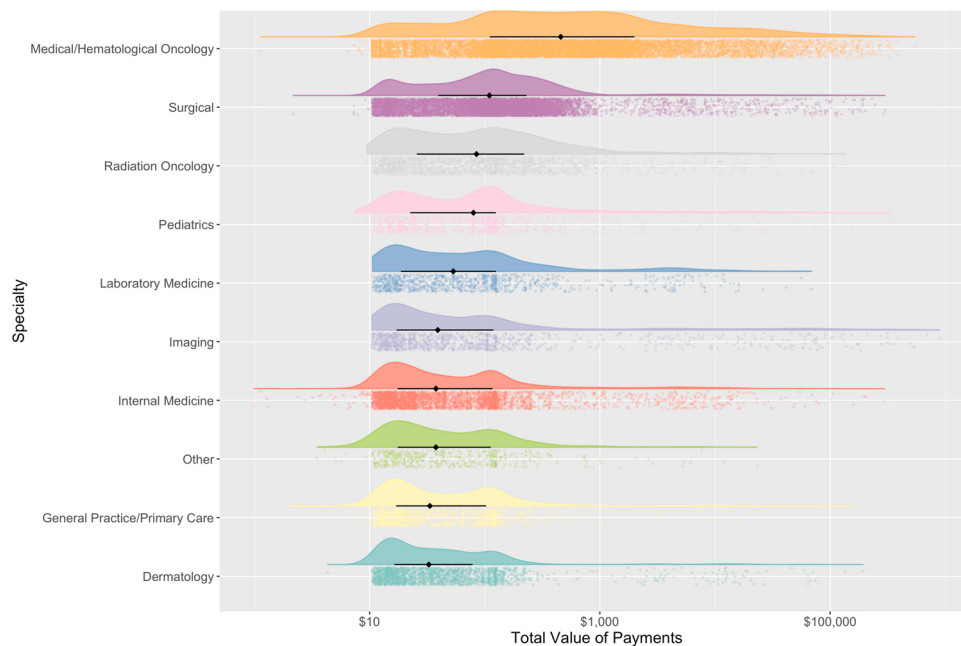


Fig. 2. Distribution and rainfall plot of the per-US physician total general payment value for cancer therapeutics during 2018, according to specialty. Diamond = median per-physician payment value, bars = 1 st and 3rd quartile. Data are presented on a logarithmic scale.

Table 3
Payment characteristics to US physicians for cancer therapeutics by specific drug. Top 10 in total value shown per year.

Drug	# of Payments	Total Value (\$)	Median Value (IQR)
2016			
Pembrolizumab	12 266	7 395 009	20 (13–150)
Nivolumab	34 533	5 086 315	15 (12–21)
Ixazomib	9 155	4 372 007	22 (15–120)
Enzalutamide	33 859	3 949 965	16 (13–22)
Bevacizumab	20 682	3 853 791	14 (11–21)
Ruxolitinib	9 815	3 590 020	16 (12–49)
Elotuzumab	13 293	2 600 596	17 (12–22)
Paclitaxel	10 095	2 344 599	20 (14–99)
Ibrutinib	14 612	2 286 290	17 (13–36)
Cabozantinib	6 057	2 093 348	16 (12–48)
2017			
Pembrolizumab	23 727	11 063 086	17 (13–100)
Nivolumab	41 482	6 928 944	14 (11–20)
Lenalidomide	11 907	3 827 775	20 (15–106)
Ixazomib	7 872	3 620 394	21 (14–103)
Enzalutamide	30 447	3 422 093	16 (12–21)
Daratumumab	9 160	3 107 655	18 (12–62)
Bevacizumab	15 727	3 005 718	15 (11–20)
Ruxolitinib	9 464	2 955 754	17 (13–49)
Ibrutinib	16 225	2 536 352	17 (13–34)
Osimertinib	10 282	2 523 589	18 (14–71)
2018			
Pembrolizumab	29 313	11 654 747	16 (13–70)
Nivolumab	29 274	4 616 903	14 (11–19)
Apalutamide	25 985	4 511 592	15 (12–22)
Enzalutamide	46 106	3 769 791	15 (12–19)
Ixazomib	8 516	3 474 591	20 (14–86)
Lenalidomide	10 099	3 165 345	21 (15–100)
Ibrutinib	19 218	2 962 556	17 (13–27)
Cabozantinib	7 867	2 692 600	18 (13–67)
Niraparib	8 969	2 637 722	26 (17–106)
Durvalumab	9 367	2 617 386	19 (14–106)

*All monetary values expressed as USD.

period, the top 10 therapeutics in terms of total annual payments accounted for ~40 % of all payments made to US physicians. Two immune checkpoint inhibitors, Pembrolizumab and Nivolumab, were associated with the highest total value of payments in all three years,

and together accounting for ~15 % of all industry payments made in 2018.

Previous literature has demonstrated that fCOI are common and substantial within the field of oncology [21]. Industry-physician relationships permeate most areas of evidence generation/appraisal; from clinical trial reporting [14], to authorship of key guidelines [16] and editorials [17]. Our novel approach looked at payments for oncology drugs in the OP dataset instead of payments to particular individuals. This work therefore provides the first comprehensive analysis of physician-industry relationships as they pertain to general payments for cancer therapeutics.

We also analyzed the distribution of general payments by payment type. Consistent with prior work by Marshall and colleagues [21], we found that the large majority of general payments were made for meals, but these payments accounted for <20 % of the total value of payments. Although some studies in the fCOI space exclude general payments for food and beverage [14], we included these as there is evidence to suggest even the provision of a single meal to a physician on behalf of a pharmaceutical company can influence prescribing patterns [22].

Our data also show that the majority of US physicians receiving payments earn modest sums with the median ~\$100. However, a small subset (~5 %) receive payments greater than \$10 000 in value. Notably, 0.6 % of physicians receiving general payments for anti-cancer therapeutics earned more than \$100 000 USD in 2018. We also found that ~90 % of US physicians receiving >\$10 000 in general payments for cancer therapeutics were medical/hematologic oncologists, surgical oncologists or radiologists. Our estimate of median annual per-physician value of general payments for medical/hematologic oncologists (~\$450) was less than previously described (~\$650) [21], however this may relate to our exclusion of any drugs without a direct anti-cancer indication (i.e. anti-emetics).

Although it is known that payments from industry may be substantial [23], this is the first study to quantify the number of physicians receiving “significant” (i.e. > \$10 000) annual payments. The identification of a small subset of radiologists receiving >\$10 000 in annual general payments is difficult to explain as they do not prescribe anti-cancer medicines; this may represent miscoding of research payments for interpreting imaging for clinical trial participants.

It is notable that there has been a major investment in payments

related to immune checkpoint inhibitors. Pembrolizumab had the highest value of payments each year; 2018 payments (~\$12 million) was more than double the next highest therapeutic (Nivolumab, ~\$5 million). This finding is unsurprising, given the rapid uptake of ICIs; an estimated 230 000 Americans are now potentially eligible to receive ICIs [12]. The increasing patient eligibility has translated into exponential revenue growth, with Pembrolizumab earning more than \$11 billion in 2019 (up 55 % from 2018) [24]. Many of the therapeutics we identified as being in the top 10 highest total value payments in 2018 were also in the top 10 highest earning drugs of 2018, with revenues exceeding \$5 billion in these cases [25]. As such, the payments to physicians for these therapeutics represent a very small fraction (<1 %) of their annual revenue. Future work examining the association between the value and timing of physician payments, with prescribing patterns, and annual revenue would be of interest.

As the rate of oncology drug development and approval increase [26], so does the potential for profits for large pharmaceutical companies. Although the development of a novel cancer drug is expensive [27], data suggests that expected revenues are far in excess of what is spent on research and development [28]. Moreover, a recent landmark study by Mitchell and colleagues suggests that not only is there a correlation between industry payments and physician prescribing, but that this relationship is seemingly causal [29]. As physicians are intimately involved in generating evidence through clinical trials, approving therapeutics as part of regulatory bodies, recommending treatment strategies in clinical guidelines, and prescribing medicine in routine care, the oncology community needs to consider how these fCOI may influence policy and practice [30].

The current study is the most comprehensive analysis of industry-physician financial relationships within oncology. However, results should be interpreted in light of potential methodologic limitations; several of which may lead to an under-estimate of the true extent of industry payment. First, we only considered drug with a direct anti-cancer indication, and did not consider drugs that may be used for the care of cancer patients from a supportive-care setting. Second, to keep our study population as homogenous as possible we excluded therapeutics with multiple indications (both within and without oncology) such as Everolimus and Rituximab. Finally, we only considered payments with a direct link to a cancer therapeutic - payments with no listed therapeutic were omitted. Further, a subset of physicians in the OP dataset were identified as belonging to multiple medical specialties. Although we developed a logical strategy to account for this as outlined in the Methods section, we cannot be certain that every physician was assigned to their true specialty of practice. However, the similarity of our estimates of the number of oncologists receiving payments to those previously reported [21] is reassuring.

In summary, industry payments to US physicians for cancer therapeutics are costly and growing in magnitude. These payments are being made to physicians across the spectrum of medical specialties, indicating that fCOI in oncology are not limited to medical/hematologic oncologists. Despite most physicians receiving only modest payments from industry, ~5 % of physicians received >\$10 000 in payments. While prior work has identified fCOIs among oncology leaders, these data suggest that payments are pervasive across the cancer system. It is important to consider the extent to which these payments may impact clinical practice and policy.

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Appendix A. Supplementary data

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