

Career success is associated with financial conflict of interest among biomedical authors of high-impact oncology publications

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Career success is associated with financial conflict of interest among biomedical

authors of high-impact oncology publications: A cross-sectional study

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Abstract

Background

Prior research has investigated the frequency of financial conflict of interest from the biopharmaceutical industry among physicians, their link to research outcomes and prescribing patterns, but to our knowledge no investigation has linked personal payments to career metrics, such as the rate of academic publication.

Methods

We assembled a set of US based physicians who had authored a first or last author paper on hematologic or oncologic topic in a high impact factor journal in 2015. We ascertained their publication history from Scopus, and personal and research payments from CMS Open Payments (2013-2015).

Results

We examined 435 physicians, who had authored a median of 140 publications, earning a median h-index of 36 and 5639 citations. The median total of general payments from 2013-2015 was \$3282 (Range 0-3.4 million dollars). The median amount of research payments from 2013-2015 was \$3500, (Range 0 to 23 million).

General payments were associated with contemporary publications with an increase of 1.99 papers (95% CI 1.1 to 2.9) per \$10,000 in payments. This persisted in multivariate analysis, adjusting for number of prior publications, seniority, and research payments (0.84 papers (95% CI 0.15 to 1.5) per \$10,000 in payments).

Conclusion

There is a positive association between personal payments and publications, and this persists after adjustment for prior publications, years since medical school and research payments.

Career success is associated with financial conflict of interest among biomedical authors of high-impact oncology publications

Introduction

Receiving payments and other valuable or desired items from the pharmaceutical industry is considered a financial conflict of interest among health care providers¹, has been found to be widespread²⁻⁷, and has been linked to provider behavior. Receipt of a meal where a specific drug is promoted has been linked to increased prescribing of that drug⁸. Acceptance of payments from the biopharmaceutical industry has been associated with increased brand name prescribing^{9,10}.

Conflict may be even more apparent with respect to the results of research and their interpretation. A Cochrane review of 48 papers showed consistently that Industry sponsored studies have more favorable efficacy results and conclusions, while minimizing harms¹¹. Others have shown industry sponsored cost-effectiveness analyses are more likely to reach favorable conclusions¹². Recently, researchers have shown that a principal investigators personal financial ties to drug makers are linked to positive study conclusions¹³.

Despite the abundant research on financial conflict of interest regarding provider behavior and the interpretation and results of research, little is known about the relationship between these conflicts in academia and the trajectory of one's academic career. Specifically, among academics, is the presence of financial ties to drug makers associated with research productivity? Moreover, do such associations persist after also accounting for seniority, and prior scholarship? We sought to answer whether there is an association between financial ties to the biopharmaceutical industry and publications, using a cross-sectional study design.

Methods:

Building our set of hematologist oncologists

We sought to create a set of clinician researchers based in the United States who are first or last author on a cancer paper in a top cancer journal in 2015. Authors had to be based in the United States, since the Affordable Care Act's Sunshine Act provides disclosures only for these persons. Authors had to be clinicians (not PhDs only), as the disclosure clause only applies to practicing doctors.

We began by searching the three highest impact factor general medical journals (the *New England Journal of Medicine*, the *Journal of the American Medical Association* and the *Lancet*) and the three highest impact factor oncology journals that publish original science (the *Lancet Oncology*, the *Journal of Clinical Oncology* and the *Journal of the National Cancer Institute*) for all original articles on a hematologic or oncologic topic appearing in 2015. We extracted the title, the first or last author, and whether the author was based in the United States or abroad. We then removed all authors without an M.D. degree, who are based outside of the United States (based on primary affiliation), or who work for the biopharmaceutical industry. Biopharmaceutical

employees were removed, as we were interested in the relationship between financial conflicts and career productivity among academic oncologists.

Identifying Financial Conflicts from Biopharmaceutical Companies

We searched the Centers for Medicare and Medicaid Services' Open Payments website (https://www.cms.gov/openpayments/) for payments from biopharmaceutical companies with at least 1 product on the US market. Companies that do not yet have a product on the US market are not included in the Affordable Care Act's sunshine provisions. General and research payments were recorded for the years 2013-2015. Other years are not included in the Sunshine act's disclosures. General payments are those typically made directly to the physician, often for consulting or honoraria, while research payments are typical paid to an institution.

Documenting publication records

For each author in our dataset, we searched Scopus (https://www.scopus.com), using "Author Search," and recorded their total publications, total citations and h-index. We then exported their publications to Excel, and sorted by year of publication. We ascertained the number of papers they published before the year 2013, and the number of papers published from 2013 to 2016.

Years since medical school

For each author, we searched Google to identify a website that listed the number of years a physician has been in practice since they completed medical school. Where

medical school graduation year was found, we subtracted this number from 2016 to calculate the years from graduation.

Statistical analysis

We summarized descriptive statistics of our dataset, after removing outliers by leverage and Cook's distance for our principal regression analysis. We performed simple linear regression analysis to ascertain the strength of association between general (or personal) financial payments from 2013-2015 and publications from 2013 to 2016. We then expanded this regression to a multivariate model adjusting for years since medical school, research payments and publications prior to 2013. Our multivariate regression asked the question: adjusting for career productivity, seniority, and research funding, is there a persistent association between general payments to physicians and scholarly output. Our analysis was performed using STATA V.13.0 (College Station, Tx). Since our study only utilized information that is publicly available, it did not require Institutional Board Review approval. Our study was conducted between Oct 1 2016 and Dec 31 2016.

Results:

We identified 435 physician authors who were first or last author on a hematology oncology paper in a high impact general or oncology journal (*The New England Journal of Medicine*, the *Journal of the American Medical Association*, the *Lancet*, the *Journal of Clinical Oncology*, *The Journal of the National Cancer Institute*, and the *Lancet Oncology*). The characteristics of these doctors are shown in **Table 1**. Notably the

median number of years since medical school among these authors was 24. These authors had authored a median of 140 publications, earning a median h-index of 36 and 5639 citations. The median total of general payments from 2013-2015 was \$3282, though the range was wide (0-3.4 million dollars). The median amount of research payments from 2013-2015 was \$3500, ranging from 0 to over 23 million dollars. A waterfall plot of general and research payments, where each bar corresponds to one physician, is shown in **Figure 1 and 2**, and demonstrates the distribution of payments to this group.

We performed simple linear regression to examine the correlation between papers published prior to 2013 and those published between 2013-2016, which is shown in **Figure 3**. We find a statistically significant correlation (Beta= 0.19, p = <0.001, 95% confidence interval 0.17 to 0.20). We then performed our primary analysis of interest (Figure 2), examining to what degree general payments were associated with publications (**Figure 4**). Again, we note a significant relationship, with a beta coefficient of 1.99 meaning an increase in 1.99 papers per every 10,000 dollar increase in general payments. Full details of the analysis are in **Table 2**.

We then performed a multivariate analysis, asking whether the relationship between personal payments persists after adjustment for prior publications, years since graduating medical school, and total research payments. The results of this analysis are in Table 2, and confirm a persistent positive association between personal payments and publications with a smaller magnitude of effect, 0.84 (p=0.017, 95% CI 0.15 to 1.5) papers per every 10,000 dollars in payment.

Discussion

Prior studies have explored the relationship between payments to investigators and the outcomes of research¹⁴⁻²⁰, the relationship between payments or gifts and prescriber behavior^{9,10}, and the even editorial attitudes towards drug products^{21,22}. However, to our knowledge, ours is the first study to examine the association between financial ties to drug makers and publications, a metric of academic success. In fact, we found that personal payments to physicians were positively associated with publication, and this relationship persist even after adjustment for years since graduating medical school (a measure of seniority) prior publications, and research funding. Our findings suggest that career productivity is positively affected by personal payments.

Some are concerned that current policies against conflict of interest, which largely are confined to forms of disclosure, may be used to cast aspersions upon conflicted biomedical researchers²³. Major journal editors have been critical of policies that restrict review or editorial articles to authors free of financial conflicts²⁴. Our results provide a reassuring note. The acceptance of industry payments is not associated with fewer publications; thus prohibitions against financial conflict of interest are not presently so daunting they hinder researchers' careers. Further prohibitions may be considered.

What drives our observation? There are two distinct possibilities underlying the association we report. First, the biopharmaceutical industry preferentially seeks and compensates the advice of physicians who are likely to have higher scholarly outputs. Alternatively, the acceptance of personal payments drive scholarly output—perhaps due to greater financial security, novel ideas for scholarship, or even ghost author publications²⁵⁻²⁷. In other words, although our paper highlights an association, we are unable to show directionality. We are unable to demonstrate which came first, the increased publications or the increased funding. Because the affordable care act's sunshine clause is not retroactive, we are unable to perform a longitudinal analysis on this question. This limitation however provides additional support for the importance of public disclosure, which permits these types of investigations. In the future, decades of public disclosure of financial conflict will facilitate important analyses of the implications of conflict.

Finally, our paper shows that the acceptance of personal payments is not used to marginalize or hinder conflicted researchers—contradicting speculation that current conflict of interest's policies are excessively restrictive²³-- as these authors have greater not fewer publications.

Limitations

As with most observational studies, our study can only highlight an association and not causation. We are unable to conclude whether accepting money from the drug industry improves a researcher's scholarly output. Yet, experts have postulated that financial

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ties with the drug industry may increase cross-pollination and ideas, driving scholarly work²⁸.

The next limitation is that although we were able to demonstrate that this association persists after examining prior publications, years since graduating medical school, and research payments, we did not examine more covariates. We were limited to publicly available covariates. Yet, we did consider total citation count and h-indices, measures of research impact; however, these were highly correlated with publication by Pearson correlation, and would introduce collinearity to models rather than refined prediction. We encourage others to explore this relationship in different cohorts of researchers.

Our findings suggest that an academic deciding to decline personal payments from drug companies may deprive them both of the benefit of that revenue, and perhaps also the benefit of increased career publications. This finding should be further explored, and if validated, may lead to consideration of policies to provide alternative incentives to physicians who decline industry payments.

Conclusion

Among US based physicians who had a first or last authored hematology oncology paper in a high impact journal, we found the acceptance of personal payments from the biopharmaceutical industry were associated with increased publications, and this relationship persisted after adjustment for seniority, prior scholarship and research funding. Although we only find an increase of about two papers per \$10,000, given that

the median number of papers in our follow-up period is 40, this is a 5% increase in

publication output. These findings suggest the careers of conflicted physicians are

boosted, not hindered by personal financial ties to the industry.

Table 1:

Characteristics of physicians with a first or last author paper on a hematologic or oncologic topic in a high impact journal

Characteristic

Median (Low; 25th Percentile; 75th Percentile; High)

Frequency as corresponding author	1 (0;0;1;3)
Years since med school	24 (1;17;33;61)
Number of publications	140 (1; 52; 253; 1,906)
Number of citations	5,639 (0; 1,452; 13,448; 116,544)
H-Index	36 (0; 18; 56; 172)
Number of papers before 2013	86 (0; 24; 175; 1486)
2013-2016 papers	40 (0; 22; 68; 423)
Total General Payments	3,282 (0; 0; 32,578; 3,369,193)
Total Research Payments	3,500 (0; 0; 691,797; 23,132,162)
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Table 2:

Simple and multivariate regression examining the association between general payments 2013-2015, research payments 2013-2015, years from medical school and prior publications on future publications between 2013-2016

Simple Linear Regression

	Beta - coefficient	P value	95% CI
General Payments from 2013-2015 (\$10,000)	1.99	< 0.001	1.07 to 2.90
Multivariate Regression			
	Beta - coefficient	P value	95% CI
General Payments from 2013-2015	0.836	0.017	0.15 to 1.52
Papers published prior to 2013	0.236	< 0.001	.213 to .260
Years since graduating medical school	-1.39	<0.001	-1.77 to -1.02
Total Research Payments (10000s)	0.0255	0.001	0.019 to 0.040

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Webpage for Jeffrey Flier Paper below:

https://hms.harvard.edu/sites/default/files/assets/About_Us/Deans_Rep/files/white_pap er_flier.pdf

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Figure 1:



Figure 1: The correlation between publications prior to 2013 and those 2013-16 among physicians publishing in top hematology oncology journals





Figure 2: The correlation between personal (general) payments from the biopharmaceutical industry to physicians 2013-15 and number of published papers 2013-16.

Figure 3:



Figure 3: Waterfall plot showing the distribution of general payments. General payments are made personally to a physician. Each individual physician is 1 vertical bar in the figure, and the baseline is set to the median general payment.



Figure 4: Waterfall plot showing the distribution of research payments. Each individual physician is 1 vertical bar in the figure, and the baseline is set to the median research payment.

STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Location in study
Title and abstract	1	(a) Indicate the study's design with a commonly used term	Title
		in the title or the abstract	
		(b) Provide in the abstract an informative and balanced	Abstract
		summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the	Abstract
6		investigation being reported	
Objectives	3	State specific objectives, including any prespecified	Introduction
	-	hypotheses	
Methods			
Study design	4	Present key elements of study design early in the paper	Last paragraph
Study design		resent key clements of study design early in the paper	Introduction
Setting	5	Describe the setting, locations, and relevant dates, including	Methods
	-	periods of recruitment exposure follow-up and data	
		collection	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the	Methods
F		sources and methods of selection of participants. Describe	
		methods of follow-up	
		<i>Case-control study</i> —Give the eligibility criteria and the	
		sources and methods of case ascertainment and control	
		selection. Give the rationale for the choice of cases and	
		controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria and the	
		sources and methods of selection of participants	
		(b) Cohort study—For matched studies give matching	N/A
		(b) Conort study—For matched studies, give matching	1N/ T A
		Case-control study—For matched studies, give matching	
		criteria and the number of controls per case	
Variables	7	Clearly define all outcomes exposures predictors potential	Methods and Results
v arrables	/	confounders, and effect modifiers. Give diagnostic criteria	(Limitations)
		if annlicable	(Emilations)
Data sources/	Q *	For each variable of interest, give sources of data and	Methods
massurament	0	details of methods of assessment (measurement). Describe	Wethous
measurement		comparability of assessment methods if there is more than	
		one group	
Bias	9	Describe any efforts to address notential sources of hias	Methods controls
Bias Study size	9	Describe any efforts to address potential sources of bias	Methods, controls
Bias Study size	9 10 11	Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the	Methods, controls N/A Methods
Bias Study size Quantitative variables	9 10 11	Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were	Methods, controls N/A Methods
Bias Study size Quantitative variables	9 10 11	Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods, controls N/A Methods
Bias Study size Quantitative variables Statistical methods	9 10 11	Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to	Methods, controls N/A Methods
Bias Study size Quantitative variables Statistical methods	9 10 11 12	Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (<i>a</i>) Describe all statistical methods, including those used to control for confounding	Methods, controls N/A Methods Methods (Statistical

		interactions	
		(c) Explain how missing data were addressed	Methods
		(d) Cohort study—If applicable, explain how loss to follow-	Methods
		up was addressed	
		Case-control study-If applicable, explain how matching of	
		cases and controls was addressed	
		Cross-sectional study—If applicable, describe analytical	
		methods taking account of sampling strategy	
		(<u>e</u>) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study-eg	Results
		numbers potentially eligible, examined for eligibility,	
		confirmed eligible, included in the study, completing follow-	
		up, and analysed	
		(b) Give reasons for non-participation at each stage	Methods/Results
		(c) Consider use of a flow diagram	
Descriptive	14*	(a) Give characteristics of study participants (eq	Methods/Results
data	11	demographic clinical social) and information on exposures	ivietilous, results
uutu		and notential confounders	
		(b) Indicate number of participants with missing data for	N/A
		each variable of interest	1.0/1.1
		(c) Cohort study_Summarise follow-up time (eg. average	
		and total amount)	
Outcome data	15*	Cohort study—Report numbers of outcome events or	
		summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure	
		category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events	N/A
		or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-	Results
	10	adjusted estimates and their precision (eg. 95% confidence	
		interval) Make clear which confounders were adjusted for	
		and why they were included	
		(b) Report category boundaries when continuous variables	N/A
		were categorized	1.0/1.1
		(c) If relevant, consider translating estimates of relative risk	N/A
		into absolute risk for a meaningful time period	IV/A
Other analyses	17	Report other analyses done—eq analyses of subgroups and	N/A
Other analyses	17	interactions, and sensitivity analyses	
		interactions, and sensitivity analyses	
Discussion	10		
Key results	18	Summarise key results with reference to study objectives	Discussion
Limitations	19	Discuss limitations of the study, taking into account sources of	Discussion: Limitation
		potential bias or imprecision. Discuss both direction and	
		magnitude of any potential bias	
Intomastation	20	Give a cautious overall interpretation of results considering	Discussion
Interpretation			

		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study	Conclusion
		results	
Other informatio	n		
Funding	22	Give the source of funding and the role of the funders for the	N/A
		present study and, if applicable, for the original study on which	
		the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.