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Industry marketing payments to physicians and prescription patterns for sacubitril/valsartan in the USA

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ABSTRACT

Objectives Although financial interactions between physicians and pharmaceutical and medical device companies could be potential conflicts of interest, in certain instances, industry promotion targeted at physicians may facilitate the early adoption of effective, novel care for patients such as sacubitril/valsartan in the USA. This study aims to evaluate associations between industry-sponsored meal payments to physicians and their prescribing patterns for sacubitril/valsartan in the USA.

Methods Using the publicly accessible Centers for Medicare and Medicaid Services Medicare Part D database and the Open Payments Database, this study assessed associations between industry-sponsored meal payments to physician prescribers and total amounts of Medicare claims and spending for sacubitril/valsartan between 2015 and 2021.

Results Among 220 147 eligible physician prescribers, 60 568 (27.5%) received at least one meal payment related to sacubitril/valsartan from the manufacturer, totaling US\$13.9 million. The receipt of meal payments was significantly associated with a higher proportion of sacubitril/valsartan prescriptions to all sacubitril/valsartan, angiotensin receptor blocker and angiotensin-converting enzyme inhibitor prescriptions, with an OR of 2.04 (95% CI: 1.98 to 2.10, $p < 0.001$). Moreover, a 10% increase in the annual number of meal payments was associated with a 2.6% (95% CI: 2.5% to 2.6%, $p < 0.001$) increase in the annual number of Medicare claims and a 7.3% (95% CI: 7.1% to 7.5%, $p < 0.001$) increase in annual Medicare spending per physician.

Conclusions Given the underprescription of sacubitril/valsartan in the USA, the positive associations between meal payments and physicians' prescribing patterns suggest that industry-sponsored meals may contribute to the early adoption of this cost-effective, novel heart failure drug among US Medicare beneficiaries.

INTRODUCTION

Sacubitril/valsartan, the first angiotensin receptor-neprilysin inhibitor approved for heart failure in the USA, has demonstrated significant reductions in hospitalisations and mortality while offering higher cost-effectiveness compared with the current, less expensive standard of care.¹ However, the affordability of sacubitril/valsartan remains a challenge for many patients, leading to its gradual adoption in clinical practice.² In certain instances, industry promotion targeted at physicians may facilitate the early adoption of high-value care for patients in the US.³⁻⁴

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Industry marketing has been shown to influence prescribing patterns among physicians. Despite its high efficacy, sacubitril/valsartan, a novel treatment for heart failure, remains under-prescribed in the USA.

WHAT THIS STUDY ADDS

⇒ This study identifies a significant association between industry-sponsored meal payments and increased prescribing of sacubitril/valsartan in the United States.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Industry promotion may support the early adoption of novel drugs that improve patient outcomes.

METHODS

This cross-sectional analysis aimed to examine the association between industry payments to physicians and their prescribing patterns of sacubitril/valsartan, as well as related Medicare spending in the USA. Four publicly accessible databases—Centres for Medicare and Medicaid Services Medicare Part D, Open Payments, National Plan and Provider Enumeration System and the Physician and Clinician databases—were matched using physician National Provider Identifier numbers from 2015 to 2021, as noted in previous research.³⁻⁵⁻⁷

The Physician Payments Sunshine Act, enacted in 2010 as part of the Affordable Care Act, mandates that all pharmaceutical and medical device companies manufacturing products approved by the US Food and Drug Administration report their financial transfers to physicians and teaching hospitals for both research and non-research purposes.⁸⁻⁹ These reported payments have been publicly available on the Open Payments Database since August 2013.

This study included all physicians who prescribed more than 10 claims per year for sacubitril/valsartan, angiotensin receptor blockers (ARBs) and/or angiotensin-converting enzyme inhibitors (ACEis) between 2015 and 2021, as recorded in the publicly accessible Medicare Part D database. Non-physician prescribers were excluded, as the Open Payments data covered only payments to physicians for the study period. Additionally, to focus on physicians likely to treat heart failure, those whose



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specialties were neither cardiology nor primary care (internal medicine, family medicine, general practice and hospitalist) were excluded from this study. Meal payments related to sacubitril/valsartan to physicians were extracted from the Open Payments between 2015 and 2021, as meal payments have demonstrated significant associations with physician prescribing patterns in other specialties.^{5 10 11}

The association between receipt of meal payments related to sacubitril/valsartan and the proportion of sacubitril/valsartan prescriptions among all prescriptions of sacubitril/valsartan, ARBs and ACEis was evaluated using multivariable population-averaged logistic generalised estimating equations (GEE) with the robust adjustment at the individual physician-year level, adjusting for covariates including gender, practice region, years in practice, medical school attended, specialty and year of payment/prescription. Physician specialties were classified into three groups based on the National Plan and Provider Enumeration System specialty classification: primary care (internal medicine, family medicine, general practice and hospitalist), cardiology (cardiovascular disease, adult congenital heart disease, clinical cardiac electrophysiology, hypertension specialist and interventional cardiology) and heart failure specialty (advanced heart failure and transplant cardiology). Additionally, the associations between the annual number of meal payments and the annual number of claims (standardised to 30-day prescriptions, including refills) and Medicare spending for sacubitril/valsartan were evaluated using multivariable linear GEE models with the robust adjustment. To account for non-linearity, the number of meal payments, Medicare claims and Medicare spending were log-transformed. Furthermore, as sensitivity analyses, this study also examined the association between payments made 1 year prior and subsequent prescription patterns. Specifically, payments made in 2015 were matched with prescriptions in 2016, and this pattern continued across successive years. These sensitivity analyses employed the same GEE models and adjusted for the same covariates.

All statistical analyses were performed using STATA V.17.0 (StataCorp). Payments and Medicare expenditures were adjusted for inflation and converted to 2021 US dollars.

As this analysis was based on publicly available data and did not involve human participants, no institutional ethics review was required, in accordance with the Common Rule (45 CFR §46). Patients or the public were not involved in the design, conduct, reporting or dissemination of this research.

RESULTS

A total of 220 147 physicians reported more than 10 claims for sacubitril/valsartan, ARBs or ACEis between 2015 and 2021. Of these, 88.5% were primary care physicians, 11.2% were cardiologists, 0.3% were heart failure specialists, 62.1% were male and 31.8% had been in practice for more than 30 years (table 1).

During the study period, 85.1% (187 258) and 97.8% (215 201) of physicians prescribed ARBs and ACEis to Medicare beneficiaries, while only 13.9% (30 493) prescribed sacubitril/valsartan. A total of 5 545 902 Medicare claims were filed for sacubitril/valsartan, resulting in US\$2.8 billion in Medicare spending over the 7 years (table 2). Mean Medicare spending per claim (\$) was US\$492 (SD: US\$96) for sacubitril/valsartan, US\$10 (SD: US\$12) for ARBs and US\$5 (SD: US\$5) for ACEis. The median annual Medicare spending per physician for sacubitril/valsartan was US\$18 653 (IQR: US\$9872–US\$40 553). The median annual number of Medicare claims was higher for heart failure specialists (median: 83 (IQR: 38–178)) than for other

Table 1 Characteristics of physicians who prescribed more than 10 claims per year for sacubitril/valsartan, angiotensin receptor blockers and/or angiotensin-converting enzyme inhibitors between 2015 and 2021

Variables	Number of physicians, n (%)
All eligible physician prescribers	220 147
Specialty*	
Primary care specialty†	194 840 (88.5)
Cardiology specialty other than heart failure specialists‡	24 562 (11.2)
Heart failure specialty§	745 (0.3)
Gender	
Male	136 710 (62.1)
Female	83 437 (37.9)
Years in practice¶	
Less than 10 years	38 311 (17.4)
10–19 years	55 408 (25.2)
20–29 years	56 422 (25.6)
30 or more years	70 006 (31.8)
Practice region	
Northeast	44 187 (20.1)
South	76 866 (34.9)
Midwest	49 727 (22.6)
West	46 988 (21.3)
US territories**	2379 (1.1)
Graduated medical school ranking††	
Top 20 US medical schools	13 873 (6.3)
Top 21–50 US medical schools	27 088 (12.3)
Other medical schools	179 186 (81.4)

*Specialty categorisation was based on the National Plan and Provider Enumeration System database.
†Primary care specialties included internal medicine, family medicine, general practice and hospitalist.
‡Cardiology specialty included cardiovascular disease, adult congenital heart disease, clinical cardiac electrophysiology, hypertension specialist and interventional cardiology.
§Heart failure specialty included advanced heart failure and transplant cardiology.
¶Years in practice were estimated from graduation year from medical school registered in the Centers for Medicare and Medicaid Services Physician and Clinician database as of 2021.
**US territories included Guam, Northern Mariana Islands, Puerto Rico and Virgin Islands.
††Graduated medical schools registered in the Physician and Clinician database was grouped into three categories based on 2023 US News and World Report medical school research ranking: top 20 US medical schools, top 21–50 US medical schools and other medical schools.

cardiologists (median: 54 (IQR: 30–105)) and primary care physicians (median: 22 (IQR: 15–33)).

Regarding payments from the manufacturer, 60 568 physicians (27.5%) received at least one meal payment related to sacubitril/valsartan, totalling US\$13.9 million. The median annual meal payments per physician were US\$41 (IQR: US\$20–US\$107) in monetary value and 2 (IQR: 1–4) in number. The median value per meal payment was US\$17 (IQR: US\$15–US\$22). The median annual meal payments were highest for heart failure specialists (median: US\$95 (IQR: US\$28–US\$231)), followed by other cardiologists (median: US\$70 (IQR: US\$29–US\$155)) and primary care physicians (median: US\$31 (IQR: US\$18–US\$67)).

Physicians who received meal payments for sacubitril/valsartan had a significantly higher proportion of sacubitril/valsartan prescriptions relative to all sacubitril/valsartan, ARB and ACEi prescriptions, with an OR of 2.04 (95% CI: 1.98

Table 2 Medicare claims and meal payments for sacubitril/valsartan from 2015 to 2021

Variables	Sacubitril/valsartan	Angiotensin receptor blockers	Angiotensin-converting enzyme inhibitors
Medicare claims			
Total amounts of Medicare spending during 2015–2021, US\$	2 841 532 185	3 427 830 502	2 131 206 105
Total number of 30-day standardised Medicare claims including refills during 2015–2021, n	5 545 902	3 180 458 814	4 514 665 688
Number of physicians who prescribed sacubitril/valsartan during 2015–2021, n (%)	30 493 (13.9)	187 258 (85.1)	215 201 (97.8)
Mean Medicare spending per claim (SD), US\$	492 (96)	10 (12)	5 (5)
Median annual Medicare claims per physician (IQR)			
Medicare spending, US\$	18 653 (9872–40 553)	1636 (523–4045)	1118 (325–2603)
Number of Medicare claims, n	38 (22–80)	216 (86–437)	271 (87–582)
Meal payments for sacubitril/valsartan			
Total payment amounts during 2015–2021			
Monetary amounts, US\$	13 923 873	–	–
Number of payments, n	661 793	–	–
Median payment value per payment (IQR), US\$	17 (15–22)	–	–
Number of physicians who received meal payments during 2015–2021, n (%)	60 568 (27.5)	–	–
Median annual payments per physician (IQR)			
Monetary amounts, US\$	41 (20–107)	–	–
Number of payments, n	2 (1–4)	–	–

to 2.10, $p < 0.001$) (table 3). Furthermore, there were significant dose–response associations between the number of meal payments for sacubitril/valsartan and the volume of sacubitril/valsartan prescriptions. A 10% increase in the annual number of meal payments was significantly associated with a 2.6% (95% CI: 2.5% to 2.6%, $p < 0.001$) increase in the annual number of Medicare claims and a 7.3% (95% CI: 7.1% to 7.5%, $p < 0.001$) increase in annual Medicare spending per physician. These associations were also observed in the sensitivity analyses (table 3).

DISCUSSION

This study provides evidence of positive associations between industry-sponsored meals provided to physicians and their prescribing behaviours concerning sacubitril/valsartan among US Medicare beneficiaries. These findings align with numerous previous studies conducted in other specialties,^{3 5 10–12} further

highlighting the influence of industry promotion on prescribing practices and Medicare spending for this highly effective drug. In this context, the study indicates that even a small meal payment from the pharmaceutical company significantly increased the use of sacubitril/valsartan in the USA. Given the underprescription of sacubitril/valsartan in the USA,¹³ the positive associations between meal payments and physicians' prescriptions for sacubitril/valsartan could help early introduction of this cost-effective, novel heart failure drug to patients.

However, it is noteworthy that physicians typically do not disclose these financial relationships between physicians and industry to their patients. Even though patients can search for the financial relationships of their own physicians on the Open Payments Database, the awareness of the database remains very low among the general public and patients in the USA.^{14 15} Therefore, physicians should pay more attention to the influence

Table 3 Associations between the annual number of meal payments related to sacubitril/valsartan and the annual number of Medicare claims and Medicare spending

Variables	OR for proportion of sacubitril/valsartan prescriptions relative to all sacubitril/valsartan, ARB and ACEi prescriptions (95% CI), OR	P value	Percentage difference in the annual medicare claims per physician (95% CI), %	P value	Percentage difference in the annual medicare spending per physician (95% CI), %	P value
Meal payments related to sacubitril/valsartan						
Same-year model						
Receipt of meal payments related to sacubitril/valsartan in same year of prescription (yes or no)	2.04 (1.98 to 2.10)	<0.001	–	–	–	–
10% increase in the annual number of meal payments in same year of prescription	–	–	2.6 (2.5 to 2.7)	<0.001	7.3 (7.1 to 7.5)	<0.001
One-year gap model						
Receipt of meal payments related to sacubitril/valsartan 1 year prior to prescription (yes or no)	1.97 (1.91 to 2.02)	<0.001	–	–	–	–
10% increase in the annual number of meal payments 1 year prior to prescription	–	–	3.6 (3.5 to 3.7)	<0.001	9.6 (9.4 to 9.9)	<0.001

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

of financial relationships with the industry, and this information should be integrated into shared decision-making processes when discussing treatment options with patients.

The study has several limitations that should be acknowledged. First, due to privacy protections, data with fewer than 10 claims and detailed demographic information of Medicare beneficiaries who received the drugs were not available from the publicly accessible databases. Additionally, specific details regarding physicians' clinical settings and prescription practices (eg, the number of patients with heart failure treated by the individual physicians who were included in this study) were not accessible through the Medicare databases. However, previous research indicates that patient-level models show stronger associations between industry payments and prescribing patterns.¹⁰ Therefore, this physician-level study of industry payments for sacubitril/valsartan may underestimate the real-world impact. In addition, the generalisability to non-Medicare populations may also be limited, and there is potential for inaccuracies within the databases used.⁹

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Data availability statement Data are available upon reasonable request. These data were derived from the following resources available in the public domain: Open Payments Database at <https://openpaymentsdata.cms.gov/>, and the Centers for Medicare and Medicare Services Medicare Part D database at <https://data.cms.gov/>. The data that support the findings of this study are available on request from the corresponding author.

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REFERENCES

- Gaziano TA, Fonarow GC, Velazquez EJ, *et al*. Cost-effectiveness of Sacubitril-Valsartan in Hospitalized Patients Who Have Heart Failure With Reduced Ejection Fraction. *JAMA Cardiol* 2020;5:1236–44.
- DeJong C, Kazi DS, Dudley RA, *et al*. Assessment of National Coverage and Out-of-Pocket Costs for Sacubitril/Valsartan Under Medicare Part D. *JAMA Cardiol* 2019;4:828–30.
- Murayama A. Pharmaceutical industry-sponsored meals and prescriptions of biologics for asthma. *J Allergy Clin Immunol Pract* 2023;11:2916–8.
- Inoue K, Figueroa JF, DeJong C, *et al*. Association Between Industry Marketing Payments and Prescriptions for PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) Inhibitors in the United States. *Circ Cardiovasc Qual Outcomes* 2021;14:e007521.
- Murayama A, Marshall DC. Associations between pharmaceutical industry payments to physicians and prescription of PARP inhibitors in the United States. *Gynecol Oncol* 2024;181:83–90.
- Murayama A. Pharmaceutical industry-sponsored meals are associated with increased prescriptions and Medicare spending for dupilumab among dermatologists in the United States. *J Eval Clin Pract* 2024;30:435–9.
- Murayama A. Evaluation of research and non-research industry payments to endocrinologists in the United States: An analysis of the Open Payments Database from 2014 to 2022. *Diabet Med* 2024;41:e15253.
- Pham-Kanter G. Act II of the Sunshine Act. *PLoS Med* 2014;11:e1001754.
- Murayama A. Industry Payments to Pediatricians in the United States Between 2013 and 2021. *Clin Pediatr (Phila)* 2024;63:1308–17.
- Mitchell AP, Trivedi NU, Gennarelli RL, *et al*. Are Financial Payments From the Pharmaceutical Industry Associated With Physician Prescribing?: A Systematic Review. *Ann Intern Med* 2021;174:353–61.
- Mitchell AP, Dusetzina SB, Mishra Meza A, *et al*. Pharmaceutical industry payments and delivery of non-recommended and low value cancer drugs: population based cohort study. *BMJ* 2023;383:e075512.
- Murayama A. Industry-sponsored meal payments are associated with prescriptions and Medicare expenditures on brand-name colchicine in the United States. *Int J Rheum Dis* 2024;27:e14962.
- Sangaralingham LR, Sangaralingham SJ, Shah ND, *et al*. Adoption of Sacubitril/Valsartan for the Management of Patients With Heart Failure. *Circ Heart Fail* 2018;11:e004302.
- Pham-Kanter G, Mello MM, Lehmann LS, *et al*. Public Awareness of and Contact With Physicians Who Receive Industry Payments: A National Survey. *J GEN INTERN MED* 2017;32:767–74.
- Kanter GP, Carpenter D, Lehmann LS, *et al*. US Nationwide Disclosure of Industry Payments and Public Trust in Physicians. *JAMA Netw Open* 2019;2:e191947.