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Provider-directed marketing may increase prescribing of medications for opioid use disorder

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ABSTRACT

Background: Opioid use disorder (OUD) has become an increasingly grave public health concern, especially in the United States where approximately 80% of the global opioid supply is consumed. Despite greater awareness of the present overdose crisis, potentially life-saving OUD pharmacotherapy (medications for opioid use disorder or MOUD) utilization remains low. This study examines the extent of provider-directed marketing (detailing) for MOUD drugs and identifies any associations between a provider's receipt of detailing and their prescribing of MOUD drugs to Medicare Part D beneficiaries.

Method: We combined Open Payments data on all provider-directed payments from pharmaceutical manufacturers with physician-level data on all MOUD prescriptions filled in Medicare Part D. We estimated the adjusted difference in Medicare days supply for all MOUD drugs (collectively) and separately for each MOUD drug that was associated with receipt of payments.

Results: The Open Payments data show that $7.0 million MOUD-specific promotional payments were made by pharmaceutical manufacturers to 12,056 US physicians from 2014 to 2016, which is < 1/6th of the $50.3 million made in overall non-MOUD opioid-related promotional payments to 76,992 US physicians during that same period. Prescribers who received any MOUD-specific payments prescribed 1080 daily MOUD-related doses per year more than peers who did not receive any MOUD-specific payments ($p < 0.001$). The data also show the relatively greater association between receipt of detailing and Suboxone prescriptions compared to Vivitrol.

Conclusions: Provider-directed marketing by MOUD manufacturers has been found to be significantly and positively associated with incidence of MOUD prescribing in Medicare Part D, as well as with the quantity of MOUD prescribed.

1. Introduction

Approximately 2.1 million adults in the U.S. have an opioid use disorder (OUD) (Center for Behavioral Health Statistics and Quality, 2017). OUD is associated with a significantly increased risk of death from opioid overdose, as well as an increased risk of contracting HIV and Hepatitis C (SAMHSA, 2018). Between 2000 and 2015, rates of opioid-related overdose deaths quadrupled (Dowell, Haegerich, & Chou, 2016), prompting public officials to declare an opioid crisis and the U.S. federal government to declare a public health emergency in 2017 (DHHS, 2017). Despite greater awareness of the overdose crisis, the rate of OUD treatment has not significantly increased since 2004, with only 20% of individuals with OUD receiving treatment (Saloner et al., 2015).

Evidence-based treatments for OUD include behavioral health treatment (e.g. mental health therapy) and pharmacotherapy (medications for OUD or "MOUD") approved by the U.S. Food and Drug Administration (FDA) for OUD.[1] MOUD is significantly more effective at preventing relapse and decreasing opioid overdose than behavioral health treatment alone (Nielsen et al., 2016); however, for many individuals the two types of treatment should be combined (SAMHSA, 2018). Currently, MOUD options include various formulations of

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[1] We refer to pharmacotherapy for opioid use disorder as medication for opioid use disorder (MOUD) rather than medication-assisted treatment (MAT), as the latter term implies the combination of medications with behavioral therapy whereas our study only explores the associated medications.

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methadone, buprenorphine, and naltrexone (SAMHSA, 2018).

Decades of studies demonstrate that buprenorphine and methadone treatment decrease opioid overdose death rates, help prevent relapse, and decrease incidence rates of communicable diseases like HIV (Hedrich et al., 2012; Larney, 2010; Larochelle, Liebschutz, Zhang, Ross-Degnan, & Wharam, 2016; Nielsen et al., 2016). The most common forms of buprenorphine are taken orally daily and include the brand-names Suboxone, Zubsolv, Cassipa, Bunavail, and Subutex (the last lacks the abuse-deterrent ingredient naloxone). Recent versions of buprenorphine also include a six-month surgical implant, Probuphine, and a once-per-month depot injection, Sublocade (FDA, 2019). Recent studies of the once-per-month depot injection version of naltrexone (under the brand name Vivitrol) suggest that it is likewise effective at decreasing overdose death and relapse rates (Gordon et al., 2015; Kjome & Moeller, 2011; Tanum et al., 2017). However, oral naltrexone alone is not recommended for OUD due to low adherence rates (Nielsen et al., 2016).

Government agencies (including the Substance Abuse & Mental Health Services Administration, Food & Drug Administration, and National Institutes of Health), as well as health care organizations (including the American Society of Addiction Medicine and the American Medical Association) have called for an expansion of MOUD prescribing to counter the current opioid crisis (FDA, 2018; Rinaldo & Rinaldo, 2013; SAMHSA, 2018) Unfortunately, MOUD utilization remains low (Alderks, 2017; Morgan, Schackman, Leff, Linas, & Walley, 2018), despite the fact both buprenorphine and naltrexone may be prescribed and dispensed in office-based settings, unlike methadone, which may only be dispensed in highly-regulated and stigmatized Opioid Treatment Programs, also called “methadone clinics” (SAMHSA, 2018).

Studies that have examined underuse of buprenorphine and naltrexone describe multiple prescribing barriers, including stigma, insurance prior authorization requirements, inadequate insurance reimbursement, and limited physician education and training in addiction medicine (DeFlavio, Rolin, Nordstrom, & Kazal, 2015; Huhn & Dunn, 2017; Kermack, Flannery, Tofighi, McNeely, & Lee, 2017; Oliva, Maisel, Gordon, & Harris, 2011; Roman, Abraham, & Knudsen, 2011; Vranken et al., 2017). Buprenorphine prescribing barriers also include concerns of medication diversion and misuse, as well as regulatory barriers (Andraka-Christou & Capone, 2018; Vranken et al., 2017). Specifically, buprenorphine may only be prescribed by physicians, nurse practitioners, or physician assistants (Comprehensive Addiction and Recovery Act of 2016) who have received a waiver from the Substance Abuse & Mental Health Services Administration following special education; and prescribers are then limited in the number of patients to whom they may prescribe buprenorphine at any time (SAMHSA, 2018).

Extended-release naltrexone, in contrast, may be prescribed by physicians, nurse practitioners, or physician assistants without any special education requirements or patient limits; nevertheless, utilization rates remain low for this form of MOUD as well (Alderks, 2017; Morgan et al., 2018). Barriers specific to extended-release naltrexone prescribing include relatively low patient interest in and awareness of the medication, required complete detoxification prior to induction, inadequate insurance coverage of inpatient detoxification, and high out-of-pocket patient costs (Alanis-Hirsch et al., 2016; Andraka-Christou & Capone, 2018; Lee et al., 2017).

Since limited physician training in addiction medicine is one of strongest barriers to prescribing buprenorphine and naltrexone (Wood, Samet, & Volkow, 2013), government agencies, professional health organizations, and researchers have developed policies and programs to increase healthcare providers' education about MOUD. SAMHSA has funded the Providers' Clinical Support System for Medication Assisted Treatment initiative to train and mentor primary care physicians in partnership with national professional organizations (Levin, Bisaga, Sullivan, Robin Williams, & Cates-Wessel, 2016). Also, through the Project Extension for Community Healthcare Outcomes (ECHO), addiction specialists at academic health centers are using tele-education to bridge knowledge gaps among primary care providers in remote areas (Komaromy et al., 2016).

Pharmaceutical detailing is another known route for increasing prescribing rates of medication in general, typically consisting of pharmaceutical direct-to-provider marketing (Datta & Dave, 2017). One form of pharmaceutical detailing includes payments from pharmaceutical companies to prescribers, such as through speaking-engagement fees or purchases of food and beverages. Previous research suggests that pharmaceutical detailing is more effective at increasing prescribing rates than direct-to-consumer advertising (Datta & Dave, 2017).

In light of limited physician education and training in addiction medicine (Polydorou, Gunderson, & Levin, 2008; Yoast et al., 2008), pharmaceutical detailing may be one of the primary methods for practicing physicians to learn about MOUD efficacy, as well as recent formulations. However, neither the extent of pharmaceutical detailing nor its association with prescribing rates has been examined in the context of MOUD.

Additionally, MOUD prescribing has been understudied in the Medicare population, even though Medicare beneficiaries are frequently exposed to prescription medication with addiction potential (Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005). A retrospective review of Medicare Part D data from 2010 to 2011 found that 204,052 FFS beneficiaries had an OUD; and of those, 76% were receiving benefits due to a disability (Roland, Ye, Stevens, & Oderda, 2018). Another study of records from 2008 to 2010 found that the rate of OUD use increased faster among Medicare beneficiaries than among commercial insurance beneficiaries during that time period (Dufour et al., 2014). Furthermore, Medicare Part D beneficiaries with OUD have significantly higher inpatient, outpatient, pharmacy, and emergency department costs than do Medicare Part D beneficiaries without OUD (Roland et al., 2018).

Therefore, the aims of our study were two-fold: first, to explore the extent of pharmaceutical detailing for MOUD; and second, to identify any associations between pharmaceutical detailing and prescribing of MOUD to Medicare Part D beneficiaries. We specifically examined buprenorphine and naltrexone prescribing and detailing practices.

2. Material and methods

2.1. Data

The Part D Prescriber Public Use File (Prescriber PUF) data 2014–2016 from Centers for Medicare and Medicaid Services (CMS) were linked at the individual provider level to the Sunshine Act's CMS Open Payments data. Since 2014 was the first full year of Open Payments data we selected that as the starting year for our analysis. All provider-directed payment records, mentioning at least one MOUD drug, were extracted and collapsed to the physician-year level. We compiled a list of all prescription drugs containing buprenorphine or naltrexone that were FDA-approved for treatment of OUD prior to December 31, 2016 (FDA, 2019) and were available in Open Payments and Prescriber PUF Data. We did not include methadone, because it is not prescribed in office-based settings for OUD. We then excluded Revia and all generic forms of naltrexone hydrochloride, because these drugs are not evidence-based for OUD due to low-adherence rates, and therefore are most likely to be prescribed for alcohol use disorder rather than for OUD (Nielsen et al., 2016). Our final drug list included Bunavail, Suboxone, Probuphine, Zubsolv, generic forms of buprenorphine-naloxone, and extended-release naltrexone (Vivitrol). Sublocade and Cassipa, the very recent FDA approved buprenorphine class drugs, as well as Subutex (the buprenorphine mono product) were excluded, because they were not found in Open Payments and Prescriber PUF data. Probuphine was excluded from the analyses of individual MOUD drugs, as it was not found in the Prescriber PUF data.

In line with prior studies, this study was limited to non-research,

non-equity, drug-related payments to physicians, referred to herein as promotional payments (Hadland, Krieger, & Marshall, 2017). Pursuant to previous literature and CMS recommendations in regard to merging Prescriber PUF data to other public datasets, Open Payments and Prescriber PUF data were linked using physician name and ZIP code (CMS, 2017; Nguyen, Bradford, & Simon, 2019; Perlis & Perlis, 2016). First names and last names of physicians in Prescriber PUF 2014–2016 were normalized by removing special non-letter characters. Fewer than 1500 physician entries in Prescriber PUF each year were dropped due to identical normalized names and 5-digit ZIP code. Using these normalized names with paired ZIP codes, 85.4% of all MOUD-related provider-directed promotional activities, in terms of dollar amounts in the Open Payment data, were matched successfully to National Providers Identifiers (NPIs). Due to the Sunshine Act's legally mandated reporting requirement, a reasonable assumption was made that providers in the Prescriber PUF data without any reported payments received no payments from MAT pharmaceutical makers. Also, the Prescriber PUF captures > 99% of physicians who write > 11 Medicare-paid claims for any drug in a given year (CMS, 2016). Noticeably, in order to protect the identity of patients before releasing data, CMS excluded the data of any provider-by-drug combination with < 11 claims for one drug from at least one provider (CMS, 2017).

Physicians in the Open Payments data were assumed not to have received any Medicare reimbursement for prescription services if they had no reported drug claims and profile information in the PUF data, and thus were excluded from the analysis. All regression analyses controlled for various observable characteristics of the prescriber obtained from Prescriber PUF data, and county-level characteristics obtained from the Robert Wood Johnson Foundation County Health Rankings file ("County Health Rankings", 2018). The number of opioid-related deaths per 100k residents for counties was estimated from the National Vital Statistics System of the Centers for Disease Control and Prevention Multiple Cause of Death files in 2014–2016. We estimated the number of substance abuse treatment facilities for counties from the directories associated with the National Survey of Substance Abuse Treatment Services files in 2014–2016. We mapped the physician-level data to their corresponding Federal Information Processing Standards (FIPS) codes using the ZIP-county crosswalk file in the R package noncensus (Boland, Parhi, Gentine, & Tatonetti, 2017; Ramey, 2016).

2.2. Measures

2.2.1. Outcome variable

The first set of dependent variables included the number of days of supply dispensed by each prescriber in the Prescriber PUF each year for all MOUD drugs (collectively) and then for each individual MOUD drug separately: Bunavail; Suboxone; Zubsolv; Buprenorphine-naloxone; and Vivitrol. The second set of dependent variables were the binary indicators for whether a physician prescribed MOUD drugs (all MOUD drugs and each individual drug) at all each year, noting that we were only able to observe whether a physician prescribed at least 11 prescriptions a year.

2.2.2. Key predictors

Receipt of MOUD-related payments, defined as an indicator variable for whether a Medicare Part D prescriber was linked to any MOUD-related payment record in Open Payments data each year, was the key predictive measure of pharmaceutical direct-to-physician marketing activities. The exposure to direct-to-physician marketing activities was measured by receipt of any MOUD-related payment.

2.2.3. Covariates

Adjustments were made for local sociodemographic characteristics and physician-level characteristics when studying the associations between outcome variables and key predictors. All county information was year specific. Local sociodemographic characteristics included: county population; county unemployment rate; percent of county that was male; percent of county aged 65 or older; percent of county that was non-Hispanic African-American; percent of county that was Hispanic; and percent of county that was non-Hispanic Caucasian. Physician-level characteristics included the following: sex; years of practice; specialty; and number of unique Medicare beneficiaries to whom the physician prescribed.

2.3. Statistical analysis

We estimated the association between opioid prescribing and payment receipt using multivariate linear regression in Stata (version 15.1). We estimated four models: (1) days supply of MOUD drugs (collectively) as a function of receipt of any MOUD-related payment; (2) days supply of each individual MOUD drug as a function of receipt of drug-specific payments; (3) likelihood of prescribing any MOUD drug as a function of receipt of any MOUD-specific payments; and (4) likelihood of prescribing each individual MOUD drug as a function of receipt of drug-specific payments. In each model we controlled for the sociodemographic and physician characteristics listed in the previous paragraph. A full set of county and year fixed effects were included with each regression in order to control for unobserved temporal and geographic factors. We clustered standard errors at the state level when calculating 95% confidence intervals and p-values.

3. Results

3.1. Descriptive analyses

The complete Open Payments data show that $7.0 million in MOUD-specific promotional payments were made by drug manufacturers to 12,056 US physicians from 2014 to 2016, which is < 1/6th of the $50.3 million total in non-MOUD opioid-related payments to 76,992 physicians during that same period. The annual aggregate amount of MOUD-related payments increased from $1.7 million in 2014 to $3.2 million in 2015, and declined to $2.1 million in 2016. Unsurprisingly, most of these detailing expenditures were devoted to branded MOUD drugs. From 2014 to 2016, less than $10,000 was spent by Amneal Pharmaceuticals and Roxane Laboratories to promote their generic buprenorphine-naloxone.

Table 1 reports the descriptive statistics of our 865,347 US physicians who have complete data from CMS Open Payments Data and Medicare Part D Prescriber files in 2014–2016. Among these physicians, only 9922 physicians (1.1% of all physicians) who had received some MOUD-related detailing payments in this study period, 10,560 physicians (1.2% of all physicians) who had prescribed some MOUD prescriptions to Medicare Part D patients, and 4621 physicians (0.5% of all physicians) who had prescribed MOUD and received MOUD detailing.

Although a physician might receive speaking-engagement fees, consulting fees and traveling reimbursements, most receive only meal-form payments; a very small number of physicians in our dataset (695 out of 865,347 US physicians) received MOUD non-meal payments. In particular, among 9992 physicians, who received MOUD-related payments, 9741 physicians received meals in 2014–2016, yet only 695 physicians received any MOUD non-meal payments (including speaking fees, consulting fees, traveling expenses, and educational expenses). Therefore, we focused our analyses on the number of meals, the form of detailing a typical physician would receive from drug manufacturers, instead of non-meal payments. While the amount of overall payments is another interesting dimension of detailing, this measure was highly skewed in our dataset as well as in the other similar studies (Hadland, Cerdá, Li, Krieger, & Marshall, 2018; Nguyen et al., 2019). For instance, a typical physician who received at least some MOUD-related payments, received on average $37.8/year; 90% of these physicians received less than $208/year; and only 1% of these physicians received more than $7441/year (up to the max payment of $128,340/year).

Table 1
Descriptive statistics for explanatory variables, outcomes, and control variables.

	Mean	Std. dev	Median	Min	Max
MOUD pharmaceutical payments and written prescriptions					
Receive MOUD payments (%)	0.66	(8.10)	0	0	100
Receive Suboxone payments (%)	0.21	(4.61)	0	0	100
Receive Vivitrol payments (%)	0.22	(4.65)	0	0	100
Receive Zubsolv payments (%)	0.25	(5.02)	0	0	100
Receive Bunavail payments (%)	0.17	(4.15)	0	0	100
Receive Buprenorphine-naloxone payments (%)	0.00031	(0.17)	0	0	100
No. MOUD meals	0.017	(0.29)	0	0	10
No. Suboxone meals	0.0036	(0.11)	0	0	10
No. Vivitrol meals	0.0039	(0.11)	0	0	10
No. Zubsolv meals	0.0065	(0.18)	0	0	10
No. Bunavail meals	0.0036	(0.12)	0	0	10
No. Buprenorphine-naloxone meals	0	(0)	0	0	0
Prescribe MOUD (%)	1.01	(9.98)	0	0	100
Prescribe Suboxone (%)	0.93	(9.58)	0	0	100
Prescribe Vivitrol (%)	0.016	(1.26)	0	0	100
Prescribe Zubsolv (%)	0.022	(1.47)	0	0	100
Prescribe Bunavail (%)	0.0055	(0.74)	0	0	100
Prescribe Buprenorphine-naloxone (%)	0.40	(6.31)	0	0	100
Daily doses of MOUD	16.6	(278.6)	0	0	91,345
Daily doses of Suboxone	13.3	(225.5)	0	0	70,569
Daily doses of Vivitrol	0.079	(7.24)	0	0	2483
Daily doses of Zubsolv	0.087	(10.1)	0	0	8478
Daily doses of Bunavail	0.022	(4.72)	0	0	3719
Daily doses of Buprenorphine-naloxone	3.09	(75.1)	0	0	18,806
Physician characteristics					
Number of beneficiaries	156.0	(207.7)	80	11	36,943
Male physician	0.69	(0.46)	1	0	1
Years since NPI registration	7.67	(2.61)	8	0	11
Opioid prescriptions 2013 (1000 daily doses)	1.78	(7.29)	0	0	466.5
Internal medicine (%)	24.8	(43.2)	0	0	100
Family medicine and practice (%)	13.2	(33.9)	0	0	100
Surgery (%)	7.26	(26.0)	0	0	100
Hematology and oncology	1.04	(10.2)	0	0	100
Radiation oncology	0.47	(6.82)	0	0	100
Neurology	1.54	(12.3)	0	0	100
Pain medicine	0.12	(3.49)	0	0	100
Physical medicine and rehabilitation	0.91	(9.52)	0	0	100
Anesthesiology	0.26	(5.05)	0	0	100
Other specialties	50.4	(50.0)	100	0	100
County characteristics					
1000 residents per mile^2	3.39	(10.1)	0.9	0.000038	72.0
Unemployment rate (%)	0.054	(0.015)	0.05	0.010	0.24
Aged 18–64 population (%)	62.9	(3.33)	62.7	36.6	82.9
Aged > 64 population (%)	14.7	(3.56)	14.2	4.10	56.3
Non-Hispanic African American (%)	14.1	(13.2)	10	0	85.2
Hispanic American (%)	16.8	(15.4)	10.8	0.40	96.3
Asian and other race (%)	8.73	(7.69)	6.7	0.25	87.2
Opioid-related deaths/100k residents	12.5	(11.3)	9.8	0	120.8
Substance abuse treatment facilities/100k residents	3.80	(2.53)	3.5	0	93.4
Observations (physician × year)	**2,289,222**				

Notes: This table reports the basic statistics of 865,347US physicians who have complete data from CMS Open Payments Data 2014–2016 and Medicare Part D Prescriber 2014–2016. Data sources include the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The CMS Part D Prescriber is a public dataset published by the Centers for Medicare & Medicaid Services. This analysis is restricted to all prescribers who had a valid NPI and were included on both Medicare Part D and in the Open Payments data. The dataset represents one observation per physician per year, over the period of 2014–2016.

3.2. Regression results

Table 2 compares four separate groups of physicians (M1-M4) regarding their intensive measures of pharmaceutical detailing and prescribing for MOUD, physician characteristics, and county characteristics. Column M1 reports the means of MOUD prescriptions and detailing as well other characteristics of physicians who prescribed MOUD and received MOUD detailing payments. Column M2 reports those means of physicians who prescribed MOUD but did not receive any MOUD detailing payments. Column M3 shows the means for physicians who received some MOUD detailing payments bud who did not write any MOUD prescriptions. Column M4 reports the means for physicians who neither prescribed nor received any payments. We reported the *t*-tests for the differences in Columns D5-D7.

Interestingly, Column D5 implies that among MOUD prescribers, physicians who received MOUD-related pharmaceutical detailing were observed to have prescribed > 673 daily doses of MOUD per year more than non-recipients in 2014–2016 ($p < 0.001$). Among MOUDs, the similar and large difference was found for Suboxone only. Column D6 depicts the difference in the intensive degree of detailing among recipients of MOUD-specific detailing. Among recipients of such detailing, MOUD prescribers were found to receive 385 dollars per year more than non-prescribers ($p < 0.001$). Among MOUDs, we found the largest differences for Bunavail (183 dollars) and Zubsolv (107.5

Table 2
Physician and practice location characteristics of four groups: prescribed/received detailing, no prescriptions/received detailing, prescribed/no detailing, and neither prescribed or received detailing.

	(M1)	(M2)	(M3)	(M4)	(D5)	(D6)	(D7)
	Prescribed/ received	Prescribed/no detailing	No prescribing/ received	No prescribing/no detailing	Difference M1 − M2	Difference M1 − M3	Difference M1 − M4
MOUD pharmaceutical payments and written prescriptions							
Daily doses of MOUD	2089.0	1415.7	0	0	**673.3*****		
Daily doses of Suboxone	1738.9	1102.5	0	0	**636.4*****		
Daily doses of Vivitrol	10.3	6.59	0	0	**3.69*****		
Daily doses of Zubsolv	18.4	3.52	0	0	**14.8*****		
Daily doses of Bunavail	4.33	1.03	0	0	**3.31*****		
Daily doses of Buprenorphine-naloxone	317.1	302.1	0	0	**15.1**		
MOUD payments ($)	528.7	0	143.5	0		**385.2*****	
Suboxone payments ($)	96.3	0	28.3	0		**68.0*****	
Vivitrol payments ($)	98.4	0	73.3	0		**25.1**	
Zubsolv payments ($)	126.4	0	18.9	0		**107.5*****	
Bunavail payments ($)	202.5	0	19.1	0		**183.4*****	
Buprenorphine-naloxone payments ($)	0.25	0	0.39	0		**−0.14**	
No. MOUD meals	3.24	0	1.74	0		**1.50*****	
No. Suboxone meals	0.61	0	0.48	0		**0.13*****	
No. Vivitrol meals	0.50	0	0.70	0		**−0.21*****	
No. Zubsolv meals	1.53	0	0.38	0		**1.14*****	
No. Bunavail meals	0.85	0	0.21	0		**0.63*****	
No. Buprenorphine-naloxone meals	0	0	0	0		**0**	
Physician characteristics							
Number of beneficiaries	239.9	233.0	208.9	155.1	6.94*	31.1***	84.9***
Male physician	0.82	0.76	0.70	0.69	0.055***	0.12***	0.13***
Years since NPI registration	8.72	8.69	8.27	7.66	0.030	0.44***	1.06***
Opioid prescriptions 2013 (1000 daily doses)	10.5	9.59	5.27	1.68	0.89**	5.21***	8.79***
Internal medicine (%)	17.4	18.6	18.6	24.8	−1.22*	−1.17^{+}	−7.46***
Family medicine and practice (%)	28.4	27.5	25.8	13.0	0.85	2.54***	15.4***
Surgery (%)	0.94	0.86	0.98	7.35	0.082	−0.044	−6.41***
Hematology and oncology	0.063	0.11	0.24	1.06	−0.044	−0.18**	−0.99***
Radiation oncology	0	0.027	0.070	0.47	−0.027*	−0.070*	−0.47***
Neurology	0.96	0.85	0.77	1.55	0.11	0.19	−0.58***
Pain medicine	1.20	1.30	0.88	0.11	−0.10	0.32^{+}	1.09***
Physical medicine and rehabilitation	3.84	2.77	2.67	0.89	1.07***	1.18***	2.95***
Anesthesiology	2.20	2.26	1.68	0.23	−0.062	0.52*	1.97***
Other specialties	45.0	45.7	48.3	50.5	−0.66	−3.28***	−5.46***
County characteristics							
1000 residents per mile^2	1.98	3.10	2.73	3.40	−1.11***	−0.75***	−1.42***
Unemployment rate (%)	0.055	0.054	0.056	0.054	0.00051*	−0.0008***	0.0009***
Aged 18–64 population (%)	62.4	62.8	62.7	62.9	−0.41***	−0.26***	−0.48***
Aged > 64 population (%)	15.4	15.5	14.8	14.7	−0.11*	0.59***	0.70***
Non-Hispanic African American (%)	14.1	12.8	13.8	14.1	1.36***	0.34^{+}	−0.0028
Hispanic American (%)	12.7	13.2	16.5	16.8	−0.47**	−3.77***	−4.09***
Asian and other race (%)	6.85	7.57	8.24	8.75	−0.72***	−1.38***	−1.89***
Opioid-related deaths/100k residents	10.5	9.59	5.27	1.68	−0.89**	−5.21***	−8.79***
Substance abuse treatment facilities/100k residents	14.9	16.2	12.5	12.5	−1.35***	2.40***	2.36***
1000 residents per mile^2	3.61	4.42	3.60	3.79	−0.82***	0.0049	−0.19***
Observations (physician × year)	7992	15,060	7126	2,259,044			

Notes: This table compares means of four separate groups of physicians (M1–M4) regarding their intensive measures of pharmaceutical detailing and prescribing for MOUD, physician characteristics, and county characteristics. The p-values of the t-tests for the differences in means were reported in columns D5–D7.
$^{+}$ $p < 0.1$.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

dollars), but not for Suboxone (68 dollars). Additionally, among these recipients, MOUD prescribers were observed to receive 1.5 meals per year more than non-prescribers, which mostly were driven by payments for Zubsolv (1.3 meals/year) and Bunavail (0.63 meals/year). Surprisingly, Vivitrol prescribers were observed to receive 0.2 meals/year less than non-prescribers. These variations in the intensive degree of detailing and prescribing for different MOUDs suggest that the relationship between MOUD detailing and prescribing may not be a reward payment after prescribing. Comparing group M1 (prescribed and received) and M4 (neither prescribe nor receive) regarding their physician characteristics and county characteristics, we found that physicians with higher opioid prescriptions prescribed in the previous year

Table 3
Regression results: Relationship between Medicare MOUD days supply prescribed and receipt of MOUD-related payments.

	Average days supply (thousand daily doses)	Adjusted difference in days supply (thousand daily doses) associated with receipt of payments		
		Estimate	95% CI	p-Value
MOUD	0.017	1.080	0.882 to 1.278	< 0.001
Suboxone	0.013	0.791	0.625 to 0.958	< 0.001
Vivitrol	0.00008	0.014	0.008 to 0.019	< 0.001
Zubsolv	0.00009	0.022	0.013 to 0.031	< 0.001
Bunavail	0.00002	0.008	0.003 to 0.012	0.002
Buprenorphine-naloxone	0.003	0.287	−0.171 to 0.744	0.215

Notes: Authors analyzed records from the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The CMS Part D Prescriber is a public dataset published by the Centers for Medicare & Medicaid Services. MOUDs in this analysis include Bunavail, Suboxone, Probuphine, Zubsolv, Buprenorphine-naloxone, and Vivitrol. This analysis is restricted to all prescribers who had a valid NPI and were included on both Medicare Part D and in the Open Payments data. The dataset represents one observation per physician per year, over the period of 2014–2016.The dependent variable is the number of daily doses (thousand daily doses) for MOUD annually prescribed by a physician. "Receipt of payments" equals 1 if a physician received any payment in the data year. We controlled for 1) physician gender and years of experience; 2) county-level population density, unemployment rate, ratio of male population, and ratios of races from the previous year; 3) specialty fixed effects; 4) county fixed effects; and 5) year fixed effects. Each OLS regression clusters the standard errors at the state.

are more likely to both prescribe MOUD and receive MOUD-specific detailing. Additionally, physicians with more patients, or male physicians, or physicians with more years of practice under their NPI tended to belong to the M1 group. Among county characteristics, M1 physicians tended to be located in counties with more substance abuse treatment facilities. Therefore, it was important to control for these physician and county characteristics in the multivariate cross-sectional linear regression models.

Table 3 reports the multivariate regression results that described the relationship between a provider's Medicare prescribing of MOUD-related pharmaceuticals (by days of supply) and their receipt of any MOUD-related payments. Each row presents the adjusted difference in Medicare days supply for all MOUD drugs (collectively) and separately for each drug, between physicians receiving payments and those that did not. These differences were potentially attributable to receipt of these payments, as we adjusted for other covariates; but, we caveat that we did not have an experimental setting from which causation could be verified. Prescribers (9922 physicians with complete data) who received any MOUD-specific payments prescribed 1080 daily doses per year more than their peers (863,405 physicians) who did not receive such payments ($p < 0.001$). We found heterogeneous and statistically significant associations with promotion for each MOUD drug. The associations between the receipt of payments and prescribing were largest for Suboxone (791 daily doses, $p < 0.001$) and modest for Vivitrol (14 daily doses, $p < 0.001$), Bunavail (8 daily doses, $p < 0.001$), and Zubsolv (9 daily doses, $p < 0.01$). A smaller number of physicians who received promotions related to a generic form of buprenorphine-naloxone were not observed to increase their prescriptions for Medicare patients in a statistically significant way.

Table 4 presents the associations between a provider's likelihood of prescribing MOUD to Medicare patients and the provider's receipt of any MOUD-related payments in a manner very similar to Table 3, except that Table 4 presents the probability of any MOUD prescriptions (as long as the total number of claims for each drug exceeded 11 per year), while Table 1 focuses on number of daily doses prescribed. Prescribers who received any MOUD-specific payments were 51.42% more likely to prescribe MOUD than their peers ($p < 0.001$). We also found heterogeneous and statistically significant associations with promotion for each MOUD drug. The associations between payments and prescribing were largest for Suboxone (46.09 percentage points, $p < 0.001$) and modest for Vivitrol, Bunavail, and Zubsolv (< 5 percentage points).

Although consulting fees represented the largest share of promotion in dollars, the most common type of promotion was spending on food and beverage. Fig. 1 visualizes the results of multivariate regression models by presenting the adjusted difference and their 95% confidence interval in two measures of MOUD prescribing associated with one additional meal among targeted recipients. Fig. 1(a) reinforces the aforementioned association between Medicare days supply of MOUD drugs and receipt of MOUD detailing. One additional MOUD-specific promotional meal was significantly associated with 210 more daily doses per year ($p < 0.001$), while one additional Suboxone-specific promotional meal was significantly associated with 197 more daily doses per year ($p = 0.004$). These results suggest that the collective associations between promotions and written prescriptions might have been primarily driven by Suboxone-related promotions.

Fig. 1(b) shows that one additional MOUD-specific promotional meal significantly increased the likelihood of prescribing MOUD drugs to Medicare patients by 5.8 percentage points ($p < 0.001$). The associations between these industry-sponsored meals and prescribing were largest for Suboxone (a 6.3 percentage point increase, $p < 0.001$). One additional Vivitrol-specific meal significantly increased the likelihood of prescribing Vivitrol to Medicare patients by 1.4 percentage points ($p < 0.001$).

We sought to place our findings in context by estimating the associations between direct-to-physician marketing and Medicare Part D prescribing for 3 drug categories from the CMS Prescriber Drug Category List (antibiotics, antipsychotics, and opioids). Fig. 2 compares the associations between Medicare days supply and promotion for opioids, antibiotics, and anti-psychotics, relative to MOUD drugs. The association with detailing was largest for opioids; indeed, the detailing-related differential was modest for MOUD drugs compared to opioids. Particularly, prescribers who received any non-MOUD opioid-related payments prescribed 8780 daily doses per year more than their peers who did not receive any opioid-specific, direct-to-physician promotions ($p < 0.001$).

3.3. Sensitivity analyses

We provided the first additional analysis (Table A.1) where we controlled for opioid prescriptions written by individual physicians in the pre-period of this study (2013) and two measures of OUD problems in the county (opioid-related deaths per 100k residents and the number of substance abuse treatment facilities per 100k residents). The estimated association between Medicare MOUD days' supply prescribed and receipt of MOUD detailing is slightly smaller than our baseline estimate (1069 daily doses vs. 1080 daily doses). In particular, opioids prescribed in the previous year are statistically associated with a relatively trivial increase in MOUD prescriptions written in the subsequent periods. Controlling for these factors, which would lessen endogeneity

Table 4
Regression results: Relationship between any MOUD prescribing and receipt of MOUD-related payments.

	Average likelihood of any prescribing (%)	Adjusted difference in the likelihood of prescribing MOUD (%) associated with receipt of payments		
		Estimate	95% CI	p-Value
MOUD	0.66	51.42	46.80 to 56.04	< 0.001
Suboxone	0.21	46.09	41.03 to 51.14	< 0.001
Vivitrol	0.22	2.43	1.60 to 3.26	< 0.001
Zubsolv	0.25	4.70	3.93 to 5.46	< 0.001
Bunavail	0.17	1.61	1.04 to 2.18	< 0.001
Buprenorphine-naloxone	0.0003	27.69	−8.78 to 64.17	0.134

Notes: Authors analyzed data from the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The CMS Part D Prescriber is a public dataset published by the Centers for Medicare & Medicaid Services. MOUDs in this analysis include Bunavail, Suboxone, Probuphine, Zubsolv, Buprenorphine-naloxone, and Vivitrol. This analysis is restricted to all prescribers who had a valid NPI and were included on both Medicare Part D and in the Open Payments data. The dataset represents one observation per physician per year, over the period of 2014–2016. The dependent variable is the likelihood to prescribe any MOUD each year. "Receipt of payments" equals 1 if a physician received any payment in the data year. We controlled for 1) physician gender and years of experience; 2) county-level population density, unemployment rate, ratio of male population, and ratios of races from the previous year; 3) specialty fixed effects; 4) county fixed effects; and 5) year fixed effects. Each OLS regression clusters the standard errors at the state.

bias concerns, does not considerably change our estimated large associations between MOUD-related detailing and MOUD prescribing. This additional analysis helps to justify our assumption that the models may not face a very serious endogeneity problem; consequently we have not controlled for endogeneity. Nonetheless, we continue to emphasize that our study design does not support a strong claim of causality.

In the base estimations of our study, each regression controlled for county fixed effects to account for unobserved geographic factors at county and state levels. Column 2 of Table A.2 (Appendix A) provides results of an alternative specification in which only state fixed effects were controlled. The estimated association between Medicare MOUD days' supply prescribed and receipt of MOUD detailing is slightly larger than our baseline estimate (1084 daily doses vs. 1080 daily doses).

In the base estimations of our study, the two models (regressing on the number of days supply and the binary indicator of prescribing MOUD drugs) were fit separately with standard linear regression software (Stata). We chose this approach due to our relatively large dataset, county fixed effects setting as well as various outcome measures. The

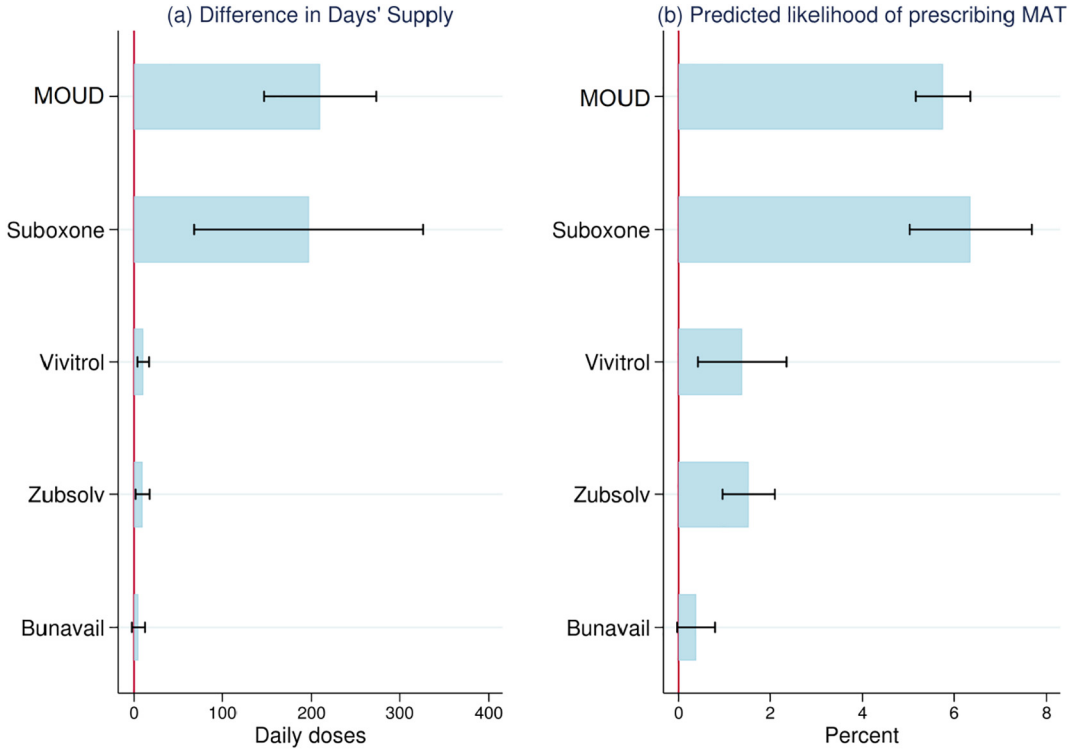

Fig. 1. Difference in MOUD days supply and the likelihood of prescribing MOUD for Medicare patients associated with one additional industry-sponsored meal.
Notes: (a) presents the adjusted difference (bar) and its 95% confidence interval (in error bars) in days' supply associated with one additional industry-sponsored meal. The outcome variable was the number of days supply dispensed by each prescriber each year for all MOUD drugs (collectively) and then separately for each MOUD drug. (b) presents the adjusted difference (bar) and its 95% confidence internal (in error bars) in the likelihood of prescribing MOUD to Medicare patients associated with one additional industry-sponsored meal. The dataset represents one observation per physician per year, over the period of 2014–2016. This analysis is restricted to all prescribers who had a valid NPI, were included on both Medicare Part D and in the Open Payments data and received at least some payments. We controlled for 1) receipt of any non-meal payments; 2) physician gender and years of experience; 3) county-level population density, unemployment rate, ratio of male population, and ratios of races from the previous year; 4) specialty fixed effects; 5) county fixed effects; and 6) year fixed effects. Each OLS regression clusters the standard errors at the state.

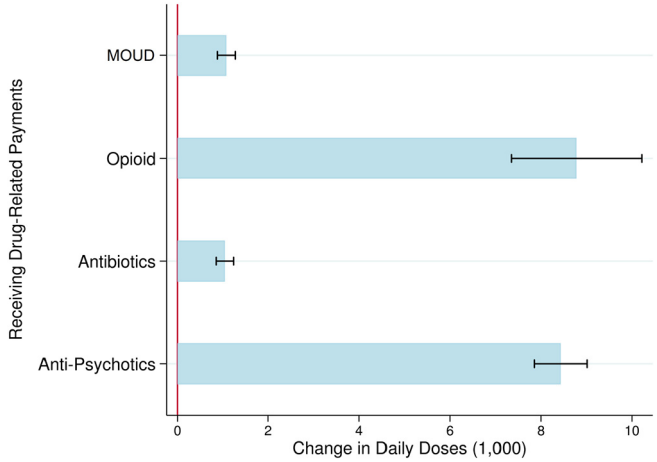

Fig. 2. Relationship between Medicare days supply and promotions: Opioid, antibiotics, and anti-psychotics, relative to MOUD.
Notes: Authors analyzed data from the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The CMS Part D Prescriber is a public dataset published by the Centers for Medicare & Medicaid Services. "Receiving detailing" equals 1 if a physician received any payment in the data year. The dependent variable is the number of daily doses for relevant drugs annually prescribed by a physician. We controlled for 1) physician gender and years of experience; 2) county-level population density, unemployment rate, ratio of male population, and ratios of races from the previous year; 3) specialty fixed effects; 4) county fixed effects; and 5) year fixed effects. Each OLS regression clusters the standard errors at the state.

two-part regression models have applied to both continuous and count data with excess zeros in empirical analyses since the 1980s (Duan, Manning, Morris, & Newhouse, 1983; Olsen & Schafer, 2001). Zero-inflated models, such as zero-inflated negative binomial and zero-inflated Poisson models, are another model class capable of fitting excess zero counts (Zeileis, Kleiber, & Jackman, 2008). In the third sensitivity analysis, we conducted several estimations using the zero-inflated negative binomial (ZINB) for MOUD prescriptions which were reported in columns 3–5, Table A.2 (Appendix A). The negative binomial regression enables the model to have greater flexibility in modeling the relationship between the conditional variance and the conditional mean compared to the Poisson model. Particularly, in the count model of our zero-inflated negative binomial models, we include: (1) key predictors consisting of receipt of MOUD-related payments and the amount of MOUD-related payments (in one specification), (2) similar covariates from the base estimations, (3) state fixed effects (instead of county fixed effects), and (4) year fixed effects. In the zero-inflation model (the logit model predicting whether a physician wrote any MOUD prescription or not), we use two specifications: (1) only including specialties; (2) including receipt of MOUD-related payments, similar covariates from the base estimations, state fixed effects (instead of county fixed effects), and year fixed effects.

The various specifications of the zero-inflated negative binomial models provide estimates that are consistent with our base estimations that receipt of any MOUD-specific payments is positively associated with MOUD daily doses per year prescribed by physicians. Unlike the straightforward interpretations of OLS estimates in columns 1–2, the coefficients in columns 3–5 should be exponentiated and interpreted as a multiplicative term relative to the base. In particular, the results in column 5 suggest that receipt of any MOUD-specific payments is associated with a 40% increase in daily doses per year. Additionally, one additional dollar in these payments is associated with a 0.003% in daily doses per year. In the zero-inflation models, the coefficient of receipt of payments suggests that receipt of these payments decreases the odds of not writing any MOUD prescriptions by 99.3%. The ZINB estimates are consistent across several selected specifications.

4. Discussion

Our study examined pharmaceutical manufacturer promotion toward providers for MOUD medication and the association with provider prescribing in MOUD, given widespread concern regarding low utilization of MOUD. While we find that prescribers who received any MOUD-specific payments prescribed more MOUD-related doses than their peers who did not receive any MOUD-specific payments, the association, though still significant, was smaller than found in the case of non-MOUD opioids and antipsychotics. These relatively smaller associations in the MOUD context may reflect providers' lower levels of pre-existing knowledge about MOUD, since previous studies have found that physicians have minimal education and training in MOUD (Egan et al., 2010; Ram & Chisolm, 2016; Wood et al., 2013). In other words, pharmaceutical detailers may have a larger hurdle of information provision to overcome for MOUD drugs as compared to the other medications that we examined. MOUD information provided through pharmaceutical detailing may be the first information providers have received about these treatment methods, thereby such education may have a smaller effect than education about treatments for other health conditions about which providers may already have pre-existing knowledge and experience utilizing in treatment.

Relatedly, physicians may be more likely to have pre-existing inaccurate information about MOUD than about treatments for other conditions, because MOUD is highly stigmatized and mythicized (Hutchinson, Catlin, Andrilla, Baldwin, & Rosenblatt, 2014; Matusow et al., 2013; Roman et al., 2011). Therefore, to influence prescribing behavior pharmaceutical detailing may need to not only fill an information gap but also to address pre-existing inaccurate beliefs about MOUD efficacy and safety. Additionally, even if pharmaceutical detailing helps fill prescribers' pre-existing information gaps and addresses inaccurate beliefs, physicians may still have difficulty prescribing medications due to well-known MOUD prescribing barriers, such as SAMHSA waiver requirements for buprenorphine, insurance prior authorization requirements, and resistance from their institution or colleagues to treating a highly stigmatized and "difficult" population (Hutchinson et al., 2014; Molfenter et al., 2015; Oliva et al., 2011; Roman et al., 2011). Finally, patient demand for MOUD drugs may simply be lower than demand for opioids and anti-psychotics.

The relatively greater association between pharmaceutical detailing and Suboxone prescriptions compared to Vivitrol prescriptions was noteworthy, given the amount of media attention recently paid to promotions by the manufacturers of Vivitrol in drug courts and state legislatures (Harper, 2017a, 2017b). This relatively greater association of Suboxone detailing and written prescriptions may be explained in several ways. First, it may mean that there are more pre-existing barriers to prescribing Vivitrol than to prescribing Suboxone. For example, previous studies suggest that patients with OUD were likely to have already heard of Suboxone but may have limited knowledge or interest in Vivitrol (Andraka-Christou & Capone, 2018). Therefore, even if the provider would like to prescribe Vivitrol, the patient may resist. In particular, patients may fear the longer, potentially more painful detoxification process (approximately two weeks) required for initiating Vivitrol than the shorter detoxification process (approximately three days) required for initiating Suboxone. If inpatient detoxification (which would provide palliative comfort) is not covered by the patient's insurance, then the patient may experience less comfort beginning Vivitrol than Suboxone. Additionally, Vivitrol inherently requires a greater commitment to recovery, as each injection blocks opioid-related euphoria for 28 days. In contrast, individuals may feel opioid-related euphoria within as little as 72 h following their last dose of Suboxone. Finally, even though both Suboxone and Vivitrol prescribing are

associated with significant insurance barriers (such as tedious prior authorization process) (Andraka-Christou & Capone, 2018; Vranken et al., 2017), it is possible that insurers put greater barriers in place for Vivitrol than Suboxone, since Vivitrol is a significantly more expensive medication. It should be noted, however, that few studies have directly compared prescribing barriers between these two medications.

In total, only 1% of physicians in our dataset received any MOUD detailing. This percentage may appear small, but only 2% of physicians have a SAMHSA waiver to prescribe buprenorphine (Rosenblatt, Andrilla, Catlin, & Larson, 2015). Furthermore, a 2013 study found that among physician specialties, physicians with board certification in addiction medicine prescribe the most buprenorphine-naloxone per prescriber, but only 100 Medicare physicians in the nation have this specialty (Lembke & Chen, 2016). Additionally, most physicians with a SAMHSA waiver prescribe to far fewer patients than their limit allows, typically with many months passing between accepting a new buprenorphine patient (Thomas et al., 2017).

Pharmaceutical detailing may help fill a well-known gap in physician education and training about MOUD (Cunningham, Sohler, McCoy, & Kunins, 2006; Egan et al., 2010; Rieckmann, Abraham, Kovas, McFarland, & Roman, 2014). Furthermore, by increasing prescribing rates, pharmaceutical detailing may have a positive impact on population health, since MOUD is associated with decreased overdose death rates, HIV rates, and relapse rates (Nielsen et al., 2016; Parks Thomas et al., 2014). On the other hand, information provided by pharmaceutical detailing may be biased, because pharmaceutical companies aim to maximize profits, creating an incentive to overemphasize the benefits of their product and downplay the risks. Pharmaceutical companies also may inaccurately compare their products to other companies' products, presenting a one-sided picture through which providers may not learn accurate information (or any information) about alternative medications. Finally, pharmaceutical companies might target detailing efforts at high-volume MOUD prescribers after purchasing prescription records from information distribution companies (Fugh-Berman & Ahari, 2007). In such a case, pharmaceutical companies may not help fill preexisting knowledge gaps among providers, as high-volume prescribers presumably already have information about MOUD.

A potential remedy for the implicit biases in pharmaceutical detailing is academic detailing, wherein health care professionals trained by academics provide balanced information about a range of treatments with the purpose of remedying limits in education and helping providers adopt best practices. A Cochrane review found that academic detailing has a moderate impact on physician practice (O'Brien et al., 2007); however, limited research exists on academic detailing in the context of OUD treatment. In one study, a team of academic researchers trained health professionals to engage in pharmaceutical detailing about medications for treating alcohol use disorders. Study results included a 68% increase in prescribing of these medications in relative terms by providers who were not previously prescribing them (Harris et al., 2016).

Despite promising results of academic detailing studies, it is unlikely that academic detailing can ever scale-up to levels of pharmaceutical detailing. A significant imbalance exists between the existing number of pharmaceutical representatives and the number of academic representatives. For example, a study of Pennsylvania found one pharmaceutical representative per five providers versus one academic representative per 4800 providers (Grande, 2010). Another similar alternative is public health detailing, wherein state or local public health departments train a workforce to provide direct education to health care providers (Larson et al., 2006); but akin to academic detailing, the workforce is likely to be limited in size. Therefore, pharmaceutical detailing is likely to continue to serve as a key source of (potentially biased) education for physicians interested in treating OUD.

4.1. Limitations

Several limitations of this study should be briefly mentioned. The first and most significant limitation is that the findings of this paper do not imply causality; rather they should be interpreted as the association between physician payments and the volume of MOUD prescriptions by individual physicians. If pharmaceutical companies strategically target high-volume prescribers for payments then it would be possible that receipt of payment is endogenous in our regressions due to selection bias. Overall, pharmaceutical companies might track prescriptions and select high-volume prescribers by purchasing prescription records from information distribution companies (Fugh-Berman & Ahari, 2007). Our descriptive analyses of MOUD-related physician payments show that selection bias may not be prominent in MOUD-related detailing activities. In particular, only 46.6% of 9922 physicians who received some MOUD-related detailing payments had prescribed MOUD in this study period. The selection bias may be more relevant in the case of non-meal detailing payments such as speaking fee, consulting fee, and traveling expenses. Specifically, 74.4% of 695 physicians who received such payments had prescribed MOUD. Consequently, we excluded these payments in our regression analyses on the associations of additional meal payments and measures of MOUD prescribing. Although these empirical strategies may mitigate endogeneity concerns, our findings should be interpreted as addressing associations between MOUD pharmaceutical payments and prescribing behavior of individual physicians rather than as identifying a causal relationship. Use of a rigorous identification strategy in future research could formally address these endogeneity concerns.

The second notable limitation is due to our use of Medicare Part D data. It is conceivable that clinicians prescribe differently to patients in other plan types (e.g. Medicaid or private insurance) due to differences in formularies and the underlying patient populations such that our findings for Medicare may not be representative of associations under other payment types. Nonetheless, Medicare Part D is large and worthy of study in its own right. One particular benefit of Medicare data is that its population has one of the highest and fastest growing prevalence rates of opioid use disorder of any group (Dufour et al., 2014). Medicare Part D also accounts for a large share of all US drug spending (30%) (Yu, Atteberry, & Bach, 2018). In order to better understand physician-level associations for different patient populations and patient-level associations, additional research using privately insured and Medicaid populations will be necessary.

The last limitation worth mentioning is our reliance upon the pharmaceutical manufacturers' self-reports regarding which drugs were linked (marketed) to each payment. Potential for illicit provider-directed payments, such as “under the table” kickbacks, which likely would not be reported in the Open Payment data, leads to the distinct possibility of measurement error.

4.2. Contributions

To the best of our knowledge, this study is the first work aimed toward better understanding the roles of provider-directed marketing by MOUD manufacturers. We found MOUD provider-directed marketing was less common and the positive associations between these promotions and MOUD prescriptions for Medicare Part D patients were modest compared to pharmaceutical detailing of opiates and antipsychotic drugs. Therefore, although the findings of this paper do not imply causality, these findings highlight the limited physician education and training in MOUD provided by informal education furnished through pharmaceutical detailing.

Similar to the recent publications that explored the controversial and contentious relationship between pharmaceutical payments and opioid prescribing (Hadland et al., 2018; Nguyen et al., 2019), our paper has employed the highest quality publicly available data sets to consider the associations between physician-level pharmaceutical

payments and MOUD prescriptions within a national scope. In addition, we cautiously controlled for various physician characteristics and county characteristics in order to reduce the endogenous bias when using the multivariate cross-sectioned linear regression analyses. A descriptive analysis comparing four groups of physicians regarding their detailing payments received and prescriptions of MOUD pharmaceuticals was supplementary to the regression analyses.

Declaration of Competing Interest

No known conflicts of interest for any.

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Appendix A

Table A.1
Relationship between Medicare MOUD days supply prescribed and receipt of MOUD-related payments.

Outcome	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	Daily doses of MOUD	Daily doses of Suboxone	Daily doses of Vivitrol	Daily doses of Zubsolv	Daily doses of Bunavail	Daily doses of Buprenorphine-naloxone
Receipt of payments	**1.069**	**0.778**	**0.014**	**0.022**	**0.008**	**0.287**
	(< 0.001)	**(< 0.001)**	**(< 0.001)**	**(< 0.001)**	**(0.002)**	**(0.214)**
No. opioid prescriptions 2013 (1000)	0.003	0.003	−0.000002	0.00002	0.00001	0.0004
	(< 0.001)	(< 0.001)	(0.029)	(0.020)	(0.156)	(0.000)
Opioid-related deaths/100,000 residents	0.003	0.0001	0.000002	0.00002	0.000002	−0.00001
	(0.138)	(0.040)	(0.219)	(0.068)	(0.068)	(0.134)
Substance abuse treatment facilities/100-,000 residents	0.003	0.009	0.00005	0.0002	0.00002	−0.002
	(0.703)	(0.237)	(0.588	(0.241)	(0.809)	(0.053)
Number of beneficiaries	−0.000003	−0.000005	0.0000002	−0.000000	−0.000000	−0.000002
	(0.334)	(0.079)	(0.003	(0.470)	(0.993)	(0.852)
Male physician	0.006	0.005	0.000003	0.00002	0.000003	0.001
	(< 0.001)	(< 0.001)	(0.876	(0.155)	(0.531)	(< 0.001)
Years since NPI registration	0.001	0.001	0.00001	0.000003	−0.000001	0.0004
	(< 0.001)	(< 0.001)	(< 0.001)	(0.191)	(0.584)	(0.002)
1000 residents per mile^2	0.005	−0.001	0.000001	0.00003	−0.0001	0.001
	(0.396)	(0.785)	(0.983	(0.763)	(0.045)	(0.403)
Unemployment rate (%)	−0.028	−0.029	0.001	0.000007	−0.001	0.010
	(0.360)	(0.406)	(0.495	(0.993)	(0.149)	(0.310)
Aged 18–64 population (%)	0.000	0.0001	0.00002	−0.00004	−0.00002	0.0001
	(0.842)	(0.948)	(0.507	(0.822)	(0.483)	(0.595)
Aged > 64 population (%)	0.006	0.004	0.00004	0.000	0.00001	0.0005
	(0.013)	(0.079)	(0.333	(0.270)	(0.781)	(0.125)
Non-Hispanic African American population (%)	−0.0001	0.0001	0.00001	0.00003	0.00003	−0.0001
	(0.920)	(0.934)	(0.516	(0.469)	(0.371)	(0.499)
Hispanic American population (%)	−0.001	−0.001	0.00001	−0.00002	−0.00001	−0.0004
	(0.684)	(0.660)	(0.756	(0.303)	(0.773)	(0.122)
Asian and other race (%)	−0.001	−0.002	0.000005	0.00002	−0.000002	0.0001
	(0.504)	(0.081)	(0.874	(0.626)	(0.928)	(0.574)
Dep. variable mean	0.017	0.013	0.0001	0.0001	0.00002	0.003
Dep. variable SD	0.28	0.23	0.01	0.01	0.00	0.08
Obs.	2,289,222	2,289,222	2,289,222	2,289,222	2,289,222	2,289,222
R^2	0.11	0.04	0.01	0.01	0.01	0.01

Notes: Authors analyzed records from the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The CMS Part D Prescriber is a public dataset published by the Centers for Medicare & Medicaid Services. MOUDs in this analysis include Bunavail, Suboxone, Probuphine, Zubsolv, Buprenorphine-naloxone, and Vivitrol. This analysis is restricted to all prescribers who had a valid NPI and were included on both Medicare Part D and in the Open Payments data. The dataset represents one observation per physician per year, over the period of 2014–2016.The dependent variable is the number of daily doses for MOUD annually prescribed by a physician. "Receipt of payments" equals 1 if a physician received any payment in the data year. We controlled for 1) physician gender and years of experience; 2) county-level population density, unemployment rate, ratio of male population, and ratios of races from the previous year; 3) specialty fixed effects; 4) county fixed effects; and 5) year fixed effects. Each OLS regression clusters the standard errors at the state.

Table A.2
Robustness checks: Zero-inflated regression models.

Model	Model 1	Model 2	Model 3	Model 4	Model 5
	OLS	OLS	ZINB	ZINB	ZINB
Count models					
Receipt of payments	1080.110	1084.580	0.370	0.369	0.349
	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)
Amount of Payments					0.00003

(*continued on next page*)

Table A.2 (*continued*)

Model	Model 1	Model 2	Model 3	Model 4	Model 5
	OLS	OLS	ZINB	ZINB	ZINB
					(0.012)
Number of beneficiaries	0.027	0.027	0.001	0.001	0.0005
	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)
Male physician	6.223	5.900	0.151	0.151	0.149
	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)
Years since NPI registration	1.425	1.305	0.045	0.045	0.045
	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)	(< 0.001)
1000 residents per mile^2	3.857	−0.125	−0.005	−0.005	−0.005
	(0.442)	(0.001)	0.001	0.001	(0.001)
Unemployment rate	−37.510	264.334	3.784	3.783	3.868
	(0.246)	(0.018)	0.023	0.023	(0.019)
Aged 18–64 population (%)	−0.062	1.114	0.022	0.022	0.022
	(0.962)	(0.002)	0.014	0.014	(0.015)
Aged > 64 population (%)	4.845	0.589	0.009	0.009	0.009
	(0.025)	(0.031)	0.204	0.205	(0.218)
Non-Hispanic African American population (%)	−0.261	−0.172	−0.001	−0.001	−0.001
	(0.807)	(0.167)	0.796	0.796	(0.660)
Hispanic American population (%)	−0.643	−0.147	−0.004	−0.004	−0.004
	(0.622)	(0.007)	0.111	0.111	(0.109)
Asian and other race (%)	−1.024	−0.126	−0.010	−0.010	−0.010
	(0.385)	(0.095)	0.007	0.007	(0.007)
Specialty dummies	Yes	Yes	Yes	Yes	Yes
State fixed effects	Yes	Yes	Yes	Yes	Yes
County fixed effects	Yes	No	No	No	No
Zero-inflation models					
Receipt of payments				−4.902	−4.902
				(< 0.001)	(< 0.001)
Number of beneficiaries				−0.0003	−0.0003
				(< 0.001)	(< 0.001)
Male physician				−0.382	−0.382
				(< 0.001)	(< 0.001)
Years since NPI registration				−0.207	−0.207
				(< 0.001)	(< 0.001)
1000 residents per mile^2				0.005	0.005
				(0.026)	(0.026)
Unemployment rate				−8.934	−8.934
				(< 0.001)	(< 0.001)
Aged 18–64 population (%)				−0.064	−0.064
				(< 0.001)	(< 0.001)
Aged > 64 population (%)				−0.038	−0.038
				(0.002)	(0.002)
Non-Hispanic African American population (%)				0.003	0.003
				(0.401)	(0.401)
Hispanic American population (%)				0.010	0.010
				(0.047)	(0.047)
Asian and other race (%)				0.015	0.015
				(< 0.001)	(< 0.001)
Specialty dummies			Yes	Yes	Yes
State fixed effects			No	Yes	Yes
County fixed effects			No	No	No

Notes: Authors analyzed data from the CMS Open Payments Data 2014–2016, Medicare Part D Prescriber 2014–2016, and County Health Rankings data. The CMS Open Payments data is a national disclosure program created by the Sunshine Act (a provision of the Affordable Care Act), capturing the industry payments to physicians and teaching hospitals. The dependent variable is the number of daily doses for MOUD annually prescribed by a physician.

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