Contaminated Relationships in the Opioid Crisis

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Unlike past public health crises, the opioid crisis arose from within the healthcare system itself. Entities within that system, particularly opioid manufacturers, may bear some liability in sparking and perpetuating the current crisis. Unsurprisingly, the allegations underlying the thousands of claims filed in connection with the opioid crisis differ substantially. However, almost all of those claims rely, to some degree, on the strength of the relationship between opioid manufacturers and the healthcare providers who prescribed their products. This Article argues that the underlying relationship is the heart of the crisis and that this problematic relationship is by no means a thing of the past.

This Article provides critically important empirical evidence on the provider-manufacturer relationship. Analyzing a novel dataset constructed solely for this Article, the Article examines the role of payments from pharmaceutical companies to healthcare providers in inducing the latter to prescribe more opioids. This analysis reveals robust and consistent empirical evidence that pharmaceutical companies continue to pay healthcare providers, and providers receiving higher levels of payments prescribe more opioids. This analysis is limited to legal payments, so it cannot establish any basis of liability by itself. However, the relationships elucidated by this empirical evidence are the types that can facilitate the activities plaintiffs in the ongoing opioid litigation have alleged. Thus, the evidence developed and presented in this Article provides critically important insight into the role of manufacturers in the opioid crisis and into the litigation that crisis has generated.

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INTRODUCTION

Are the forces fueling the opioid epidemic truly extinguished? To believe so is tremendously tempting: for the first time since the crisis's beginning, opioid-related deaths declined in 2018.[1] In the wake of the devastation wreaked by the epidemic, litigation accelerated, with victims and governments filing hundreds of claims. Though different theories underlie these claims, many share a common component—the relationship between the pharmaceutical companies that manufacture opioids and the healthcare providers who prescribe them. This Article argues that this relationship is at the heart of the opioid crisis and presents empirical evidence suggesting that, despite being past the peak of the crisis, the current relationship between payments from pharmaceutical companies and opioid prescriptions remains problematic.

The opioid crisis represents the greatest threat to the public health of this generation.[2] Near the peak of the crisis in 2017, an American died every eleven minutes from a drug overdose involving an opioid.[3] Unlike public health crises of the past—such as the influenza pandemic of the late 1910s or the spread of the human immunodeficiency virus (HIV) of the 1980s and 1990s—the opioid epidemic arose within the healthcare system itself. Indeed, a former Director of the Food and Drug Administration (FDA) has explained that the opioid crisis "start[ed] in doctor's offices and hospitals."[4]

The opioid crisis began in earnest around 2000,[5] and over the next fifteen years, the number of opioid prescriptions quadrupled.[6] This explosion in prescription opioid use has led to profound consequences. By 2015, over 63% of the 52,404 drug overdose deaths recorded by the Centers for Disease Control

1. Holly Hedegaard, Arialdi M. Miniño & Margaret Warner, *Drug Overdose Deaths in the United States, 1999–2018*, 356 NCHS DATA BRIEF, Jan. 2020, at 1, 1.

2. *See* RICHARD J. BONNIE, MORGAN A. FORD & JONATHAN K. PHILLIPS, PAIN MANAGEMENT AND THE OPIOID EPIDEMIC: BALANCING SOCIETAL AND INDIVIDUAL BENEFITS AND RISKS OF PRESCRIPTION OPIOID USE 187 (2017) ("Not since the HIV/AIDS epidemic has the United States faced as devastating and lethal a health problem as the current crisis of opioid misuse and overdose and opioid use disorder (OUD).").

3. *The Evolution of the Opioid Crisis: 2000–2017*, NAT'L INST. FOR HEALTH CARE MGMT. (Aug. 2019), https://www.nihcm.org/categories/the-evolution-of-the-opioid-crisis-2000-2017; *The Evolution of the Opioid Crisis: 2000–2018*, NAT'L INST. FOR HEALTH CARE MGMT. (May 2020), https://nihcm.org/publications/the-evolution-of-the-opioid-crisis-2000-2018.

4. WHITE HOUSE COMM'N ON COMBATING DRUG ADDICTION & THE OPIOID CRISIS, DRAFT INTERIM REPORT 1 (July 31, 2017), https://www.whitehouse.gov/sites/whitehouse.gov/files/ondcp/commission-interim-report.pdf.

5. *See* Richard C. Dart, Hilary L. Surratt, Theodore J. Cicero, Mark W. Parrino, S. Geoff Severtson, Becki Bucher-Bartelson & Jody L. Green, *Trends in Opioid Analgesic Abuse and Mortality in the United States*, 372 NEW ENG. J. MED. 241, 242 (2015); Marcia K. Merboth & Susan Barnason, *Managing Pain: The Fifth Vital Sign*, 35 NURSING CLINICS N. AM. 375, 377 (2000); Rose A. Rudd, Noah Aleshire, Jon E. Zibbell & R. Matthew Gladden, *Increases in Drug and Opioid Overdose Deaths—United States, 2000–2014*, 64 MORBIDITY & MORTALITY WKLY. REP. 1378, 1378–82 (2016); D. Andrew Tompkins, J. Greg Hobelmann & Peggy Compton, *Providing Chronic Pain Management in the "Fifth Vital Sign" Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma*, 173 DRUG & ALCOHOL DEPENDENCE S11, S12–18 (2017); Michael R. Von Korff & Gary Franklin, *Responding to America's Iatrogenic Epidemic of Prescription Opioid Addiction and Overdose*, 54 MED. CARE 426, 428 (2016).

6. Rudd et al., *supra* note 5, at 1378–82.

and Prevention (CDC) involved an opioid.[7] The opioid crisis's collateral damage, however, has not been limited to deaths. Increased opioid use has fueled growth in opioid addiction rates,[8] opioid-related traffic accidents,[9] admissions to facilities for substance abuse,[10] opioid-related emergency room visits,[11] opioid-related hospital admissions,[12] and the occurrence of neonatal abstinence syndrome (infants born addicted to opioids).[13] Experts have estimated the costs of the opioid epidemic to hospitals alone at roughly $11 billion annually,[14] and the societal costs at over $95 billion.[15] Once the value of lost human life is included, the costs surge to over $500 billion.[16]

This overwhelming impact begs for a tractable policy solution; however, the disjointed evolution of the opioid crisis—and the role that illegal opioids have played—have complicated efforts to address the crisis. The CDC has classified the opioid crisis into three separate waves based on the type of opioids responsible for increases in opioid-related deaths.[17] A surge in the use of prescription opioids, including those legally prescribed by healthcare providers, ignited the first wave of the crisis around 2000.[18] During the second wave in 2011, heroin—illicitly manufactured and distributed outside the healthcare

7. Rose A. Rudd, Puja Seth, Felicita David & Lawrence Scholl, *Increases in Drug and Opioid-Involved Overdose Deaths—United States, 2010–2015*, 65 MORBIDITY & MORTALITY WKLY. REP. 1145, 1145 (2016).

8. Andrew Kolodny, David T. Courtwright, Catherine S. Hwang, Peter Kreiner, John L. Eadie, Thomas W. Clark & G. Caleb Alexander, *The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction*, 36 ANN. REV. PUB. HEALTH 559, 559 (2015).

9. Guohua Li & Stanford Chihuri, *Prescription Opioids, Alcohol and Fatal Motor Vehicle Crashes: A Population-Based Case-Control Study*, 6 INJ. EPIDEMIOLOGY 1, 1–3 (2019).

10. Andrew S. Huhn, Eric C. Strain, D. Andrew Tompkins & Kelly E. Dunn, *A Hidden Aspect of the U.S. Opioid Crisis: Rise in First-Time Treatment Admissions for Older Adults with Opioid Use Disorder*, 193 DRUG & ALCOHOL DEPENDENCE 142, 142 (2018).

11. Christopher M. Jones & Jana K. McAninch, *Emergency Department Visits and Overdose Deaths from Combined Use of Opioids and Benzodiazepines*, 49 AM. J. PREVENTIVE MED. 493, 497–500 (2015).

12. Hilary Mosher, Yunshou Zhou, Andrew L. Thurman, Mary Vaughan Sarrazin & Michael E. Ohl, *Trends in Hospitalization for Opioid Overdose Among Rural Compared to Urban Residents of the United States, 2007–2014*, 12 J. HOSP. MED. 925, 925 (2017); Jennifer P. Stevens, Michael J. Wall, Lena Novack, John Marshall, Douglas J. Hsu & Michael D. Howell, *The Critical Care Crisis of Opioid Overdoses in the United States*, 14 ANNALS AM. THORACIC SOC'Y 1803, 1808 (2017).

13. Neonatal abstinence syndrome occurs when an infant born to an opioid-addicted mother experiences symptoms of opioid withdrawal. Stephen W. Patrick, Robert E. Schumacher, Brian D. Benneyworth, Elizabeth E. Krans, Jennifer M. McAllister & Matthew M. Davis, *Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000–2009*, 307 JAMA 1934, 1934–37 (2012).

14. Press Release, Premier, Opioid Overdoses Costing U.S. Hospitals an Estimated $11 Billion Annually (Jan. 3, 2019), https://www.premierinc.com/newsroom/press-releases/opioid-overdoses-costing-u-s-hospitals-an-estimated-11-billion-annually.

15. *See* CORWIN N. RHYAN, THE POTENTIAL SOCIETAL BENEFIT OF ELIMINATING OPIOID OVERDOSES, DEATHS, AND SUBSTANCE USE DISORDERS EXCEEDS $95 BILLION PER YEAR 1 (2017), https://altarum.org/sites/default/files/uploaded-publication-files/Research-Brief_Opioid-Epidemic-Economic-Burden.pdf.

16. COUNCIL OF ECON. ADVISERS, THE UNDERESTIMATED COST OF THE OPIOID CRISIS 1 (2017), https://www.whitehouse.gov/sites/whitehouse.gov/files/images/The%20Underestimated%20Cost%20of%20the%20Opioid%20Crisis.pdf.

17. *Understanding the Epidemic*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/drugoverdose/epidemic/index.html (last visited Feb. 25, 2021).

18. *The Evolution of the Opioid Crisis: 2000–2017*, *supra* note 3.

system—became a salient part of the crisis.[19] A third wave emerged in 2013, characterized by synthetic opioids—substances that mimic naturally occurring opioids such as codeine and morphine and tend to be highly potent.[20] These synthetic opioids, which may be produced and distributed through legal or illegal channels, contributed to many accidental overdoses, particularly when synthetic opioids were mistaken for, or mixed with, traditional opioids.[21]

The growth in deaths attributable to illicit opioids has caused some confusion about the responsibility of the healthcare system for the opioid crisis. Illegal drug usage is neither new nor unique to the opioid crisis. Illegal opioid use, however, differs from other illegal drug use in the closeness of its connection with the modern healthcare system. Prescription opioid use is often the catalyst for subsequent abuse of illegal opioids, as "the majority of users start taking opioids that are prescribed by their physicians, even if they later progress to illicit or illegal opioid use."[22] Scott Gottlieb, the former Commissioner of the FDA, explained that "[m]ost people who become addicted to opioids become medically addicted. Their first exposure is going to be a clinical prescription that they receive in a clinical setting, and then they'll go on to develop an addiction."[23]

Accordingly, despite the uptick in deaths attributable to illegal opioids, the heart of the opioid crisis remains within the healthcare system. Indeed, the use of illegal substances does not necessarily limit the responsibility of the healthcare system in the opioid crisis, as recently recognized by West Virginia—one of the states hardest hit by the opioid crisis.[24] In *Tug Valley Pharmacy v. All Plaintiffs*, the West Virginia Supreme Court refused to hold that the illegal consumption of opioids bars the imposition of liability on healthcare providers

19. *Id.*

20. *See Synthetic Opioid Overdose Data*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/drugoverdose/data/fentanyl.html (last visited Feb. 25, 2021); *Opioid Data Analysis and Resources*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/drugoverdose/data/analysis.html (last visited Feb. 25, 2021). Examples include tramadol and fentanyl, which may be produced and distributed through legal or illegal channels. *See Opioid Data Analysis and Resources*, *supra*; *Synthetic Opioid Overuse Data*, *supra*.

21. *See Synthetic Opioid Overdose Data*, *supra* note 20.

22. Janet Currie, Jonas Y. Jin & Molly Schnell, *U.S. Employment and Opioids: Is There a Connection?* 2 (Nat'l Bureau of Econ. Rsch., Working Paper No. 24440, 2018), https://www.nber.org/system/files/working_papers/w24440/w24440.pdf ("The epidemic is particularly shocking since the majority of users start taking opioids that are prescribed by their physicians, even if they later progress to illicit or illegal opioid use."); Jennifer L. Doleac & Anita Mukherjee, *The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime* 6 (IZA Inst. of Lab. Econ., Discussion Paper No. 11489, 2018), http://ftp.iza.org/dp11489.pdf ("Individuals are prescribed these drugs to treat pain, but many patients develop addictions that lead them to illegal use of prescription opioids and cheaper substitutes such as heroin.").

23. *FDA's Scott Gottlieb: Opioid Addiction Is FDA's Biggest Crisis Now*, CNBC (July 21, 2017, 8:24 AM), https://www.cnbc.com/video/2017/07/21/fdas-scott-gottlieb-opioid-addiction-is-fdas-biggest-crisis-now.html.

24. *See* Tug Valley Pharmacy, LLC v. All Plaintiffs Below in Mingo Cty., 773 S.E.2d 627, 628 (W. Va. 2015).

for their role in allowing patients to become addicted to opioids.[25] Importantly, the court held that the criminal consumption of illicit opioids by the patients does not extinguish the liability of the providers who originally prescribed legal opioids.[26] This decision provides an appropriate lens for the opioid crisis. While illegal opioids may have risen in importance based on the number of deaths caused, the path to those deaths often begins with legal prescription opioids.[27]

Given the importance of initial prescriptions of opioids and the follow-on effects of opioid over-prescription, this Article focuses on the relationship that arguably ignited the crisis: the relationship between pharmaceutical companies and the physicians who prescribe opioids. Part I examines the importance of the relationship between pharmaceutical companies and providers in initiating and perpetuating the opioid crisis. It details why, despite the multiplicity of claims made in the current litigation, the prescriber-pharmaceutical company relationship underlies almost all claims filed in connection with the opioid crisis. Given the importance of this relationship, Part II describes a theoretical model that differentiates between pharmaceutical companies playing a purely unbiased educational role and inappropriately persuading healthcare providers to prescribe more opioids. Part II also relies on this model to develop testable hypotheses about the nature of the relationship between pharmaceutical companies and prescribers.

Part III uses empirical analysis to test the hypotheses developed in Part II. Using statistical matching techniques to match multiple data sources, Part III provides novel evidence on the relationship between pharmaceutical payments and physician prescriptions. In general, the evidence suggests that payments from pharmaceutical companies are associated with increases in opioid prescriptions. Further, by exploiting the passage of state laws meant to educate providers on the prevalence of opioid prescriptions, Part III shows that this positive correlation is more consistent with pharmaceutical companies persuading healthcare providers to prescribe more opioids than with a legitimate educational function. Part IV examines the implications of these results, concluding that the continued importance of pharmaceutical payments in prescription decisions is problematic. It argues that this continued importance may support claims within the current opioid litigation. Part IV also explores the role of current state legislation in combatting the contamination within the manufacturer-provider relationship.

25. *Id.*

26. *Id.* at 636.

27. *See* WHITE HOUSE COMM'N ON COMBATING DRUG ADDICTION & THE OPIOID CRISIS, *supra* note 4, at 1.

I. ORIGINS OF THE OPIOID EPIDEMIC AND THE PRESCRIBER-PHARMACEUTICAL COMPANY RELATIONSHIP

The existence of the opioid crisis is as apparent as its origins are murky. As noted above, several factors have contributed to the opioid crisis. For example, underlying issues of mental health and socioeconomic instability may drive the demand for illegal opioids.[28] Relatedly, economic challenges for middle-aged whites without a college degree stemming from deindustrialization and cuts to social safety nets have been blamed for the rise of "diseases of despair"—drug overdose, alcohol-related disease, and suicide—which are often tightly connected with the opioid crisis.[29] These factors are perceived to have increased the long-term demand for opioids, particularly illegal opioids.[30] However, the focus here is the role of the relationship between providers and pharmaceutical companies in creating the initial demand for opioids and in supplying much of the prescription drugs that began the crisis two decades ago.

This Part examines the origins of the opioid epidemic and argues that it evolved from a mixture of well-meaning policies aimed at addressing undertreated pain and misleading scientific information from pharmaceutical companies. In July 2017, the White House Commission on Combating Drug Addiction and the Opioid Crisis explained that the opioid crisis "start[s] in doctor's offices and hospitals."[31] In offering this explanation, the Commission did not blame physicians, and this Article similarly does not seek to offer blanket accusations against those on the front lines of healthcare. However, understanding the opioid crisis necessarily requires understanding changes in physicians' approaches to pain management and opioid prescribing. This Part begins by exploring changes in these approaches that led to an increase in opioid prescriptions. In turn, the excess supply of opioids generated by such over-prescription fueled the crisis in at least three ways: (1) patients who are legally prescribed opioids for an extended period of time are more likely to become addicted, (2) the excess supply is diverted from legal uses and used by those without a prescription, or (3) the excess supply is sold on the black market.

Well-meaning prescribers were not alone in causing the opioid crisis, however. Pharmaceutical manufacturers took several courses of action which may have contributed to the current epidemic. Although some scholars maintain that the increase in supply was an unfortunate consequence of a genuine desire to cater to an undertreated population, a more cynical explanation—and one which is gaining popular and legal traction—views the development of the opioid crisis as a foreseeable consequence of interference by pharmaceutical

28. *See* Nabarun Dasgupta, Leo Beletsky & Daniel Ciccarone, *Opioid Crisis: No Easy Fix to Its Social and Economic Determinants*, 108 AJPH PERSPS. 182, 183 (2018).

29. *Id.*

30. *Id.*

31. WHITE HOUSE COMM'N ON COMBATING DRUG ADDICTION & THE OPIOID CRISIS, *supra* note 4, at 1.

companies.[32] This interference took various forms, including the use of false and misleading advertising.[33] Understanding the strategies these companies used to become involved in providers' prescribing decisions gives important context for the empirical analysis presented below.

A. THE UNDERTREATMENT OF PAIN

The initial change in prescribing patterns that precipitated the opioid crisis was spurred by the noblest of factors: (1) the recognition that pain has traditionally been undertreated, and (2) new evidence supporting the safety of opioids. Studies in the 1990s highlighted the systematic under-treatment of both cancer and non-cancer pain.[34] Related research suggested that inadequate treatment of pain disproportionately affected racial minorities and the elderly, noting the "significant disparities between those who received analgesic treatment for pain, particularly among racial and ethnic minorities as well as for differences in age."[35]

In response to such studies, two significant policy changes ensured that physicians would pay more attention to patient pain. First, the Joint Commission, an organization that monitors hospitals and medical centers and promulgates standards for accreditation, revised its standards for treating pain.[36] The new standards "emphasized the need to perform systematic assessments of patients' pain levels regularly and frequently while hospitalized."[37] Because Joint Commission accreditation of hospitals and medical centers is often relied upon by state governments in quality oversight,[38] these elevated standards encouraged providers to treat pain more aggressively.

Second, and working in conjunction with the Joint Commissions' new standards, the government changed the way it incorporated patient satisfaction as a measure of hospital quality. In response to an Institute of Medicine report criticizing the quality of health care in the United States, Congress required the

32. *See* Scott G. Weiner, Sayeed K. Malek & Christin N. Price, *The Opioid Crisis and Its Consequences*, 101 TRANSPLANTATION 678, 679 (2017).

33. *See infra* Part I.B.

34. *See* Weiner et al., *supra* note 32, at 679; Teresa A. Rummans, M. Caroline Burton & Nancy L. Dawson, *How Good Intentions Contributed to Bad Outcomes: The Opioid Crisis*, 93 MAYO CLINIC PROC. 344, 346 (2018).

35. Weiner et al., *supra* note 32, at 679 (citing Salimah H. Meghani, Eeeseung Byun & Rollin M. Gallagher, *Time to Take Stock: A Meta-Analysis and Systematic Review of Analgesic Treatment Disparities for Pain in the United States*, 13 PAIN MED. 150, 151 (2012); Karen O. Anderson, Carmen R. Green & Richard Payne, *Racial and Ethnic Disparities in Pain: Causes and Consequences of Unequal Care*, 10 J. PAIN 1187, 1187–89 (2009); Alexie Cintron & R. Sean Morrison, *Pain and Ethnicity in the United States: A Systematic Review*, 9 J. PALLIAT. MED. 1454, 1454–56 (2006); and Ula Hwang, Laura K. Belland, Daniel A. Handel, Kabir Yadav, Kennon Heard, Laura Rivera-Reyes, Amanda Eisenberg, Matthew J. Noble, Sudha Mekala, Morgan Valley, Gary Winkel, Knox H. Todd & Sean R. Morrison, *Is All Pain Is Treated Equally? A Multicenter Evaluation of Acute Pain Care by Age*, 155 PAIN 2568, 2568–72 (2014)).

36. Rummans et al., *supra* note 34, at 346.

37. *Id.*

38. *State Recognition*, JOINT COMM'N, https://www.jointcommission.org/en/accreditation-and-certification/state-recognition/ (last visited Feb. 25, 2021).

Centers for Medicare and Medicaid Services (CMS) to promulgate the Hospital Consumer of Healthcare Providers and Systems Survey to measure quality.[39] To address the concern about patient experience, three out of the twenty-five questions in this survey inquired about how well hospital providers managed patients' pain.[40] Because this measure affected providers' reimbursement from Medicare, they began concentrating on delivering more intensive pain management treatments.[41] Thus, a well-intentioned effort to increase the quality of medical services resulted in an overemphasis on the provision of pain medication.

Compounding these various institutional factors pushing physicians to treat pain more intensively was the recognition of "a moral imperative for physicians to treat pain and relieve suffering."[42] The moral obligation is documented in the Declaration of Montreal, which recognized the "fundamental human right" of pain management.[43] That document acknowledges "[t]he right of all people to have access to pain management without discrimination," and emphasizes the "inadequate access to treatment for acute pain" and the "severe restrictions on the availability of opioids and other essential medications, [which are] critical to the management of pain."[44] Similarly, scholarly work began to emphasize the importance of pain as a "fifth vital sign," encouraging physicians to treat it more aggressively.[45] In 1996, the American Academy of Pain Medicine and the American Pain Society issued a statement arguing that opioids should be used even in chronic noncancer pain.[46]

In response to this increase in opioid use, most states passed intractable pain statutes.[47] These states provided safe harbors for physicians prescribing long-term opioid therapy.[48] Further insulated from board discipline, spurred by a sense of professional duty, and incentivized by institutional evaluations that affected payment, physicians unsurprisingly increased opioid prescription rates.[49] Importantly, however, these factors alone were not enough to spark the

39. Rummans et al., *supra* note 34, at 346–347.

40. *Id.*

41. *Id.* at 346.

42. Weiner et al., *supra* note 32, at 679.

43. *Id.*

44. *Declaration of Montréal*, INT'L ASS'N FOR THE STUDY OF PAIN, https://www.iasp-pain.org/DeclarationofMontreal?navItemNumber=582 (last visited Feb. 25, 2021).

45. Merboth & Barnason, *supra* note 5, at 377; Tompkins et al., *supra* note 5, at S11–S21; Richard A. Mularski, Foy White-Chu, Devorah Overbay, Lois Miller, Steven M. Asch & Linda Ganzini, *Measuring Pain as the 5th Vital Sign Does Not Improve Quality of Pain Management*, 21 J. GEN. INTERNAL MED. 607, 607 (2006).

46. Rummans et al., *supra* note 34, at 345.

47. *See* FED'N OF STATE MED. BDS., PAIN MANAGEMENT POLICIES, https://www.fsmb.org/siteassets/advocacy/key-issues/pain-management-by-state.pdf (last visited Feb. 25, 2021) (listing statutes by state).

48. *Id.* at 345–46. The level of protection provided by each statute varies, but physicians were somewhat protected from discipline for long-term opioid prescription. *Id.*

49. *Id*. at 345–48.

opioid crisis. As the following Subpart details, pharmaceutical companies played a vital role as well.

B. NEW INFORMATION ON OPIOIDS FROM PHARMACEUTICAL COMPANIES

As providers and regulators increasingly acknowledged and even touted the benefits of pain management with opioids, emerging research began to suggest that the risk of harm associated with these medications—including addiction—was lower than previously believed.[50] Plaintiffs in the current litigation assert, however, that much of this research was paid for by the pharmaceutical industry and did not offer valid scientific conclusions.[51] Indeed, several particularly relevant announcements, which fell far below the standard of rigorous research, garnered disproportionate attention and credibility.[52] These focal announcements spurred the push for more opioids.[53] For example, a one-paragraph letter in the *New England Journal of Medicine* reported the results of a retrospective review of pain patients, finding that only 4 of the 11,882 patients became addicted.[54] This letter was cited over 600 times as support for providers seeking to expand the use of prescription opioids.[55] Similarly, in 1998, Purdue Pharma ("Purdue")—an opioid manufacturer at the center of many current lawsuits—circulated a video entitled "I Got My Life Back," which documented six patients whose chronic, non-cancer pain was treated by opioids.[56] Following this promotional message, prescriptions for OxyContin increased from 670,000 in 1997 to 6.2 million in 2002, and the total number of opioid prescriptions increased by 45 million.[57]

In addition to media attention, research on "pseudoaddiction" encouraged physicians to continue prescribing opioids to patients who appeared to suffer similar symptoms as addicts. Researchers David Weissman and J. David Haddox first outlined pseudoaddiction in 1989.[58] David Haddox later became a Senior Medical Director for Purdue.[59] Designated an "iatrogenic" syndrome, a syndrome induced by a healthcare provider as opposed to arising from natural causes,[60] pseudoaddiction ostensibly affects patients receiving inadequate pain

50. *See* Rummans et al., *supra* note 34, at 345.
51. *See infra* Part I.C.
52. *See* Rummans et al., *supra* note 34, at 345.
53. *See id.*
54. *Id.*
55. *Id.* at 346.
56. *Id.*
57. *Id.*
58. Marion S. Greene & R. Andrew Chambers, *Pseudoaddiction: Fact or Fiction? An Investigation of the Medical Literature*, 2 CURRENT ADDICTION REPS. 310, 311 (2015).
59. Complaint at 55, Bradford Cnty. v. Purdue Pharma L.P., No. 19-00702 (M.D. Fla. June 11, 2019).
60. Iatrogenic is defined as a condition "induced inadvertently by a physician or surgeon or by medical treatment or diagnostic procedures." *Iatrogenic*, MERRIAM-WEBSTER, https://www.merriam-webster.com/dictionary/iatrogenic?src=search-dict-box (last visited Feb. 25, 2021). Greene and Chambers note that in describing pseudoaddiction as an iatrogenic disease, Weissman and Haddox flipped the definition on its head

management.[61] Patients suffering from pseudoaddiction supposedly progress through three separate phases. First, a patient experiencing pain receives inadequate pain management and requests additional medication.[62] Second, the patient learns that in order to receive more medication, he or she must convince his or her physician of the need for such medication.[63] Third, the patient engages in drug-seeking behavior, creating mistrust in the physician-patient relationship.[64] The described symptoms of pseudoaddiction, perhaps unsurprisingly, are almost indistinguishable from true addiction.[65] Unlike the treatment for true addiction, however, research on pseudoaddiction recommended that physicians prescribe more, and not fewer, opioids.[66] A later study analyzing the medical literature regarding the validity of pseudoaddiction concluded that empirical evidence does not support its existence.[67]

In addition to the literature on pseudoaddiction, a few key opinion leaders—later alleged to have been paid by pharmaceutical companies[68]—became prolific sources of research, concluding that opioids are safe. A notable example is Dr. Russell Portenoy. Portenoy—hired as a consultant by several pharmaceutical companies—advocated for the increased use of opioids, particularly in the treatment of non-cancer pain.[69] Dubbed the "King of Pain,"[70] he published an article based on a study of thirty-eight cases, concluding that opioid treatment can be a safe option for patients with intractable non-malignant pain and no history of drug abuse.[71] He also allegedly served as a member of the American Pain Society and American Academy of Pain Medicine Guidelines Committee, organizations which "endorsed [the use of] opioids to treat chronic [non-cancer] pain."[72] Later, in exchange for legal immunity, Portenoy admitted that pharmaceutical companies "'overstated the benefits of chronic-opioid therapy' and 'understated the risks of opioids, particularly the risk of abuse, addiction and overdose.'"[73]

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since pseudoaddiction is theoretically caused by the withholding of treatment, not the provision of treatment. Greene & Chambers, *supra* note 58, at 311.

61. Greene & Chambers, *supra* note 58, at 311.

62. *Id.*

63. *Id.*

64. *Id.*

65. *See id.*

66. *Id.*

67. *Id.* at 314.

68. *See*, *e.g.*, Complaint, *supra* note 59, at 103–06.

69. Complaint at 19, City of Fargo v. Purdue Pharma L.P., No. 19-00139 (D. N.D. July 9, 2019); Jef Feeley, *Opioid Evangelist Switches Sides in Case Alleging Pharma Abuse*, BLOOMBERG (Apr. 8, 2019, 8:56 AM), https://www.bloomberg.com/news/articles/2019-04-08/opioid-evangelist-switches-sides-in-case-alleging-pharma-abuse.

70. Arthur H. Gale, *Drug Company Compensated Physicians Role in Causing America's Deadly Opioid Epidemic: When Will We Learn?*, 113 MO. MED. 244, 244 (2016).

71. Russell K. Portenoy & Kathleen M. Foley, *Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases*, 25 PAIN 171, 171–86 (1986).

72. Complaint, *supra* note 59, at 90.

73. Feeley, *supra* note 69.

Exposed to this new information on the safety of opioids even for noncancer pain, in conjunction with the new policy emphasis on relieving pain, providers understandably responded by prescribing more opioids.[74] While there are legitimate reasons to be sensitive to populations with truly undertreated pain,[75] the misinformation about the risks associated with opioids propagated by pharmaceutical companies helped ignite the current crisis. This misinformation would later become the basis for many of the lawsuits connected with that crisis, which is reviewed in the next Subpart.

C. CURRENT LITIGATION REFLECTS THE IMPORTANCE OF THE PRESCRIBER-PHARMACEUTICAL COMPANY RELATIONSHIP

As the full burden of the opioid crisis became clear, litigation over the harms associated with increased opioid use exploded. The first wave of that litigation has culminated in the multidistrict litigation under Judge Polster[76] and the first verdict against Johnson & Johnson in Oklahoma.[77] This Subpart engages with the theories underlying the current litigation and detail why, regardless of the specific claim, the dynamic between pharmaceutical companies and prescribers constitutes the heart of current litigation.[78]

At first glance, the most natural target of lawsuits filed by patients who become addicted to opioids would appear to be the healthcare providers who prescribed them. Providers have faced several lawsuits in connection with the opioid crisis. For example, the West Virginia Supreme Court recently addressed whether wrongful conduct of opioid addicts served as a complete bar to recovery against physicians for negligent over-prescription.[79] It held that patients could hold prescribers liable for their addiction even if those patients engaged in illegal activity—such as consuming heroin or other illicit opioids—in addition to the prescription opioids furnished by the providers.[80] Similarly, major drugstore chains have sued unnamed physicians, claiming that prescribers should pay some of the potential penalty levied against drugstores based on their over-prescription.[81] While it would come as no surprise to see more claims filed against providers in the future, the bulk of the opioid litigation has focused on

74. Rummans et al., *supra* note 34, at 347–48.

75. We do *not* mean to suggest that opioids should never be prescribed or that the unavailability of opioids negatively impacts some patients. We only mean to suggest that, consistent with existing research, opioids have been overprescribed in the aggregate.

76. *In re* Nat'l Prescription Opioid Litig., 290 F. Supp. 3d 1375, 1379 (J.P.M.L. 2017).

77. Jan Hoffman, *Johnson & Johnson Ordered to Pay $572 Million in Landmark Opioid Trial*, N.Y. TIMES, (Aug. 26, 2019), https://www.nytimes.com/2019/08/26/health/oklahoma-opioids-johnson-and-johnson.html.

78. Of course, current litigation also involves distributors and pharmacies accused of similar conduct, but we focus on pharmaceutical manufacturers.

79. Tug Valley Pharmacy, LLC v. All Plaintiffs Below in Mingo Cnty., 773 S.E.2d 627, 630 (W.Va. 2015).

80. *Id.* at 635–36.

81. Lenny Bernstein, *Major Drugstore Chains Sue Doctors in Sprawling Federal Opioid Case*, WASH. POST (Jan. 8, 2020, 8:30 AM), https://www.washingtonpost.com/health/major-drugstore-chains-sue-doctors-in-sprawling-federal-opioid-case/2020/01/07/3ac9cd70-317d-11ea-9313-6cba89b1b9fb_story.html.

pharmaceutical companies.[82] Accordingly, this Subpart focuses on claims filed against these defendants.

Litigation in connection with the opioid crisis has been ongoing since the early 2000s,[83] but this litigation has accelerated in the past few years. This Subpart concentrates on the most prominent current litigation—the multidistrict litigation (MDL) focused on holding pharmaceutical companies accountable for all the harms precipitated by the crisis. In general, these complaints assert numerous claims that pharmaceutical companies are responsible for the opioid crisis.[84] The heart of the complaints center on two general patterns of behavior. Pharmaceutical manufacturers and distributors either (1) engaged in misleading or fraudulent advertising or (2) failed to monitor supply chains of controlled substances.[85] This Subpart explains why both patterns inherently implicate the prescriber-pharmaceutical relationship.

1. False and Misleading Advertising

Many of the MDL complaints allege that pharmaceutical companies engaged in false and misleading advertisement, which led to physicians overprescribing opioids. This situation usually occurs in at least two ways. First, plaintiffs have alleged that pharmaceutical companies relayed false information to physicians.[86] Second, and more nefariously, plaintiffs allege that pharmaceutical companies have used physicians to create new, misleading scientific information about the appropriateness of opioid use.[87]

Concerning the relaying of existing false information, plaintiffs have accused pharmaceutical companies of offering information to physicians that systematically overvalues the benefits and undervalues the risks associated with opioids. Plaintiffs specifically accuse pharmaceutical companies of

82. *See*, *e.g.*, *In re* Nat'l Prescription Opiate Litig., No. 1:17-MD-2804, 2019 WL 3917575, at *11–15 (N.D. Ohio Aug. 19, 2019).

83. Rebecca Haffajee and Michelle Mello summarize the high-profile government and class action settlements from 2004 to 2017. Rebecca L. Haffajee & Michelle M. Mello, *Drug Companies' Liability for the Opioid Epidemic*, 377 NEW ENG. J. MED. 2301, 2301–02 (2017).

84. Frequently brought claims include: (1) public nuisance—see, for example, Complaint, *supra* note 59, at 270; Complaint at 1, 4, Wayne Cnty. Comm'n v. Rite Aid of Maryland, Inc., No. 17-01962 (S.D. W. Va. Mar. 21, 2017) [hereinafter, Complaint, *Wayne Cnty. Comm'n*]; (2) Racketeer Influenced and Corrupt Organizations Act ("RICO") violations—see, for example, Complaint, *supra* note 59, at 234; (3) state consumer protections acts claims—see, for example, *id.* at 268; (4) negligence claims—see, for example, *id.* at 272–77; (5) fraud claims—see, for example, Complaint at 96, 115, 119, City of Chicago v. Purdue Pharma L.P., No. 14-04361 (Cir. Ct. Cook Cnty. June 2, 2014) [hereinafter Complaint, *City of Chicago*]; and (6) unjust enrichment claims—see, for example, *id.* at 120; Complaint, *supra* note 59, at 277. While the City of Chicago is no longer part of the MDL, *City of Chicago v. Purdue Pharma L.P.* is informative of the relevant allegations.

85. *See, e.g.*, Complaint, *supra* note 59, at 39, 134; Complaint, *City of Chicago*, *supra* note 84, at 15; Complaint at 38, 132, City of Daytona Beach v. Purdue, No. 19-01103 (M.D. Fla. June 13, 2019).

86. *See, e.g.*, Complaint, *supra* note 59, at 39; Complaint, *City of Chicago*, *supra* note 84, at 15; Complaint, *supra* note 85, at 38.

87. *See, e.g.*, Complaint, *supra* note 69, at 9–10.

misrepresenting (1) the low addiction risk associated with chronic opioid use,[88] (2) the ease with which addiction can be detected and addressed,[89] (3) the risks associated with alternative forms of pain relief,[90] (4) the specific efficacy of particular opioids,[91] and (5) the risks associated with increasing opioid doses.[92] These misrepresentations were intended to "create a series of misperceptions in the medical community."[93]

Concerning the creation of new misleading information, plaintiffs have alleged that pharmaceutical companies perpetuated misleading information by using physicians to create novel, but inaccurate, material about the appropriateness of opioid use, effectively contaminating the existing body of scientific evidence.[94] Pharmaceutical companies are accused of paying physicians that they considered to be "key opinion leaders" to not only present lectures at continuing medical education (CME) events but to develop treatment guidelines that recommend the increased use of opioids.[95] While Russell Portenoy is one of the best known "leaders" recruited by pharmaceutical companies, many other physicians engaged in similar behavior according to plaintiffs.[96]

The provision of existing misleading information and the creation of new misinformation certainly implicates the relationship between pharmaceutical companies and physicians. While this relationship need not always involve the exchange of misleading information, a stronger bond between pharmaceutical companies and prescribers may facilitate the exchange of damaging information or strengthen the effect of this information on prescribers. Accordingly, understanding the nature and extent of this relationship is paramount in the ongoing litigation.

2. Failure to Monitor Supply Chains

The second pattern of behavior alleged by plaintiffs involves the failure of manufacturers and distributors to monitor opioid supply chains.[97] Under the Controlled Substances Act (CSA), manufacturers and distributors have a statutory duty to design and operate a system to identify suspicious orders of controlled substances and notify the Drug Enforcement Administration (DEA)

88. Complaint, *supra* note 59, at 39; Complaint, *supra* note 69, at 9–10; Complaint, *City of Chicago*, *supra* note 84, at 23–27.

89. Complaint, *supra* note 59, at 53.

90. *Id.* at 67; Complaint, *City of Chicago*, *supra* note 84, at 42.

91. Complaint, *supra* note 59, at 70.

92. *Id.* at 59.

93. *Id.* at 38.

94. Complaint, *supra* note 69, at 10.

95. Complaint, *supra* note 59, at 85; Complaint, *City of Chicago*, *supra* note 84, at 53–59.

96. Complaint, *supra* note 59, at 106–12 (listing other key opinion leaders).

97. Complaint at 21, Logan Cnty. Comm'n v. Cardinal Health, No. 17-02296 (S.D. W. Va. Apr. 11, 2017); Complaint, *supra* note 59, at 134; Complaint, *Wayne Cnty. Comm'n*, supra note 84, at 4.

upon the discovery of such an order.[98] The accompanying regulations define as "suspicious" orders of "unusual size, orders deviating substantially from a normal pattern, and orders of unusual frequency."[99] Prior to the current litigation, the extent of this duty to monitor the supply chains remained an open question. Recently, however, the district court handling the MDL determined that the law imposes a duty both to identify and report suspicious orders and not to ship such orders.[100]

In particular, the complaints allege that manufacturers and distributors had a duty, in connection with their general duty to monitor, to notice when physicians excessively prescribed opioids.[101] Indeed, in *In re National Prescription Opiate Litigation*, the court noted that the DEA explicitly stated that "a distributor may not simply rely on the fact that the person placing the suspicious order is a DEA registrant and turn a blind eye to the suspicious circumstances."[102] Accordingly, while physicians retain professional judgment in how they prescribe, manufacturers and distributors have an independent duty to report suspicious orders. Moreover, the plaintiffs have argued that not only did manufacturers fail to recognize these suspicious orders—a form of diversion,[103] according to complaints—manufacturers used their knowledge of which physicians were prescribing unusually large quantities of opioids to *target* these physicians for *even more advertisements*.[104]

Overall, even the allegations concerning pharmaceutical companies' failure to monitor supply chains rest (at least in some cases) on the relationships between these companies and the prescribers of their products. In light of the importance of the prescriber-pharmaceutical company relationship to the current litigation, understanding the current state of this relationship is critical.

98. In particular, a registered entity has a duty to (1) "design and operate a system to identify suspicious orders" for itself, (2) "ensure that the system designed and operated . . . complies with applicable Federal and State privacy laws," and (3) notify the DEA upon discovery of a suspicious order. 21 U.S.C. § 832(a) (2018).

99. 21 C.F.R. § 1301.74(b) (2020).

100. *In re* Nat'l Prescription Opiate Litig., No. 1:17-MD-2804, 2019 WL 3917575, at *7–9 (N.D. Ohio Aug. 19, 2019). This independent legal duty seems to provide the basis for public nuisance and RICO claims. *See* Complaint, *supra* note 69, at 143. Of course, this does not mean that other district courts will agree.

101. *See, e.g.*, Complaint, *supra* note 59, at 134; Complaint, *supra* note 85, at 132.

102. *In re Nat'l Prescription Opiate Litig.*, 2019 WL 3917575, at *5.

103. The DEA describes "diversion" as "the redirection of controlled substances which may have lawful uses into illicit channels," Controlled Substances Quotas, 83 Fed. Reg. 32784, 32784 (July 16, 2018) (to be codified at 21 C.F.R. pt. 1303), and this term encompasses a wide variety of actions. Some complaints have alleged diversion as the actual theft from pharmacies or legitimate patients or the unauthorized use of a legitimate prescription by family members, see Complaint, *supra* note 85, at 154.

104. Complaint, *supra* note 85, at 156 (alleging that the "manufacturers were keenly aware of the doctors who were writing large quantities of opioids. But instead of investigating or reporting those doctors, Defendants were singularly focused on maintaining, capturing, or increasing their sales").

II. THE CONTINUING CONNECTION BETWEEN PHARMACEUTICAL COMPANIES AND PRESCRIBERS

Considering past egregious conduct and the ongoing litigation, this Article focuses its empirical exercise on the current relationship between pharmaceutical companies and providers, as measured by legal, non-research-related payments. Purely illegal transactions—the kind that tend to receive the most attention in plaintiffs' complaints—are essentially unobservable. However, the connection between legal pharmaceutical payments and physician prescription patterns can serve as a proxy for the strength of the relationship between companies and prescribers.

This Subpart provides the theoretical backbone on which the empirical analysis of the relationship between pharmaceutical payments and opioid prescription rates is built. It introduces two potential roles that pharmaceutical promotion to providers may play: a legitimately educational one and a persuasive one. It then distills these potential roles into clear hypotheses that will be tested in the empirical analysis. Although this analysis does not purport to establish any basis of liability for pharmaceutical companies, examining the legal payments from manufacturers to prescribers can provide important and relevant insight into the relationships that underlie allegations of liability in general. Understanding these relationships can also provide insight into legal, but troubling, connections between pharmaceutical companies and prescribers.

A. THE THEORETICAL MECHANISMS FOR PHARMACEUTICAL INFLUENCE

For obvious reasons, pharmaceutical companies do not publicize illegal activities or activities which may subject them to liability. Accordingly, this Article examines the prescriber-manufacturer relationship in the context of documented (and legal) non-research-related payments to physicians from pharmaceutical companies. In order to draw viable (and precise) conclusions from this type of data, certain assumptions underlying this approach are addressed.

(1) Legal, non-research-related payments both represent a legal exchange and serve as a proxy for a pharmaceutical representative's opportunity to spread information.

This is the critical assumption for the following empirical exercise. The observable, legal payments serve not only as a measure of money received by physicians from pharmaceutical companies but also as a useful proxy for pharmaceutical promotion that provides opportunities to inform physicians about the safety and efficacy of a given drug.

While this exercise assumes very little about the effect of documented payments and underlying activity, this analysis requires the following assumption:

(2) The amount of money exchanged is positively correlated with information exchanged.

This argument is justified in one of two ways: (1) more money is correlated with more time to exchange information about the drug, and (2) more money is correlated with higher quality time to exchange information about the drug. In the first sense, more money spent on food and drink is correlated with a higher quantity of promotional visits. In the second sense, more money is spent on a higher quality of visit in the form of higher quality goods and services. Accordingly, the observable payments are proxies for pharmaceutical contact.

Unfortunately, it is impossible to observe what transpires during such contact, particularly the informational content. Therefore, the type of informational content that is exchanged is separated into two categories: "legitimately educational" and "persuasive."[105]

(3) "Legitimately educational" information reflects purely unbiased assessments of opioid risk and benefits.

If pharmaceutical representatives engage in "legitimately educational" promotion, they would merely communicate unbiased information about the safety and efficacy of opioids. Such unbiased information would have to include accurate representations of both the benefits and risks of opioids. An accurate representation of the benefits without an accurate representation of the risks cannot qualify as legitimately educational. No legitimate educational functions of payments from pharmaceutical companies to prescribers should raise red flags or serve as the basis for any liability in the current litigation.

Notably, if the notion that pharmaceutical representatives engage in legitimately educational promotion is believed, recorded payments must be interpreted only as opportunities to present such unbiased education. If interpreted as having independent persuasive value, pharmaceutical representatives would no longer be solely offering legitimately educational conduct.

(4) Information that does not qualify as "legitimately educational" is "persuasive."

Persuasive information exchanged by pharmaceutical representatives encompasses several degrees of misleading information. Persuasive information could merely be the accurate representation of the benefits of opioids without an accurate representation of the risks. It could also include an overoptimistic representation of benefits and risks. Importantly, persuasive information also encompasses entirely false and fraudulent information about risks and benefits.

105. These categories are undoubtedly difficult to differentiate in practice. However, we find this theoretical dichotomy useful, as each provides a clear empirical prediction. The empirical reality will be more mixed, but our average effects will indicate with which type of payment our results are most consistent.

Historically, this type of behavior has led to increased opioid prescription rates,[106] and the continued existence of a strong and positive relationship between opioid-related payments and opioid-prescribing rates deep into the opioid crisis may be cause for continued concern. Indeed, this is one of the central allegations in many of the ongoing suits against opioid manufacturers.[107]

In contrast to a legitimately educational promotion, under a persuasive paradigm, monetary values have a potentially independent effect on opioid prescription rates. That is, while payments could be merely an opportunity for pharmaceutical representatives to persuade physicians, they may also function as independent incentives to prescribe more opioids or reward already-high-prescribing physicians. This leads to a subtle, but important, caveat.

(5) This study does not distinguish between the use of payments to incentivize physicians to prescribe more and the use of payments to reward high-prescribing physicians.

On one hand, manufacturers may encourage physicians to prescribe more opioids by providing incentives in the form of dinners or conferences. On the other hand, the positive association between opioid detailing and prescribing rates may represent less of an incentive-based scheme and more of a reward structure. For example, instead of targeting physicians that may respond to financial incentives or additional education materials, manufacturers may offer something akin to a reward for already high-prescribing physicians. Though not illegal in and of themselves, payments that serve these functions are consistent with various plaintiffs' lawsuits—pharmaceutical companies established relationships with physicians that ultimately led to higher prescription rates.

With these caveats in mind, this Subpart turns to the hypotheses generated from this theoretical model. The empirical analysis searches for evidence of a relationship between opioid-related payments by manufacturers and opioid-prescribing rates by providers. Distinguishing between educational and incentivizing functions is not simple. The different functions of pharmaceutical payments, however, should be associated with different effects on opioid-prescribing rates among providers receiving payments.

If payments serve legitimately educational purposes, then higher levels of payments should only be correlated with more/better education. It is not clear that better education should be correlated with higher levels of prescribing. In some cases, better education may result in more opioids prescribed to patients who need them, but in others, more education may dissuade providers from inappropriately prescribing opioids. Indeed, as the 2016 guidelines on opioid

106. *See supra* Part I.B.
107. *See supra* Part I.C.

prescribing issued by the CDC demonstrate, a better understanding of how to prescribe opioids can often lead to lower prescription rates.[108]

This is not to say that a positive correlation between payments and prescriptions is always inconsistent with legitimate education. If legitimately educational information was targeted mostly to physicians who should be prescribing high levels of opioids (perhaps due to the type of patients they treat), a mechanical correlation between payments and prescriptions might emerge. This would require a very targeted knowledge—not of physician prescription habits, but of the needs of the underlying population the physician serves.

On the other hand, if payments serve primarily to encourage or reward higher prescribing rates, then a straightforward correlation should emerge: the receipt of more payments from pharmaceutical companies should be associated with higher opioid prescription rates.

> *Hypothesis 1a: If there is no significant correlation between pharmaceutical payments and physician prescription, payments do not serve a persuasive function.*
>
> *Hypothesis 1b: If there is a significantly positive correlation between pharmaceutical payments and physician prescription, payments serve either a (1) persuasive function or (2) legitimately educational function directed only to physicians who should be high-volume opioid prescribers.*

By themselves, these hypotheses 1a–1b do not adequately distinguish between a legitimately educational and persuasive function of pharmaceutical payments. Accordingly, to gain better insight into the role of payments from pharmaceutical companies to physicians, changes in state informational laws must be used. As detailed in the next Subpart, these state laws provide the analytical leverage needed to explore more fully the role of payments on opioid prescription rates.

B. CHANGES IN STATE PRESCRIPTION DRUG MONITORING PROGRAM LAWS

Given the severity of the opioid crisis, potential plaintiffs have not been alone in taking action. Policymakers and other stakeholders have come to appreciate the severity of the ongoing epidemic. They have proposed a number of legal, policy, and clinical interventions to forestall the deepening of the crisis. An exhaustive review of these efforts is well beyond the scope of this Article but understanding policies that may play a role in the prescriber-manufacturer relationship provides important context for this empirical analysis.

Although the federal government has taken some steps to mitigate the opioid crisis,[109] states have initiated most policies aimed at this crisis. The most

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108. Deborah Dowell, Tamara M. Haegerich & Roger Chou, *CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016*, 65 MORBIDITY & MORTALITY WKLY. REP. 1, 1–15 (2016).

109. The federal government has passed several funding initiatives aimed at ameliorating the opioid epidemic. In 2016, the CDC issued a guideline on prescribing opioids for chronic pain. *Id.* at 1. This guideline

popular policy option to date has been the use of prescription drug monitoring programs (PDMPs).[110] When implementing these programs, state governments establish a central repository of information on the prescription medications prescribed to individual patients and give providers access to this database.[111] State governments design these programs "to facilitate detection of suspicious prescribing and utilization."[112] The first PDMPs were created in the early 1900s, but modern PDMPs did not emerge until the late 20th and early 21st centuries.[113] These programs employ electronic data transmission to capture information on prescriptions and quickly disseminate that data to relevant stakeholders.[114] Early programs offered only clumsy access to providers or were limited to law enforcement, but later adopting states designed their programs with providers in mind.[115] However, even when providers could access the information contained in PDMPs relatively easily, they often declined to do so: administrative data suggests that only a small proportion of providers chose to obtain patient prescription histories from state PDMPs.[116] Empirical evidence on these types of PDMPs demonstrates that, consistent with few providers accessing them, these programs had little impact on opioid prescriptions.[117]

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was "intended to . . . improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death." *Id.* Evaluating the effectiveness of a national policy of this type is more difficult than evaluating state policies, but several years after the issuance of the CDC's guideline, the opioid crisis did begin to abate. Hedegaard, *supra* note 1, at 1.

110. *See* Thomas C. Buchmueller & Colleen Carey, *The Effect of Prescription Drug Monitoring Programs on Opioid Utilization in Medicare*, 10 AM. ECON. J.: ECON. POL'Y 77, 77 (2018) (noting that "nearly every state has implemented a Prescription Drug Monitoring Program").

111. *Id.* at 77–78.

112. *Id.* at 77.

113. PRESCRIPTION DRUG MONITORING PROGRAM TRAINING & TECH. ASSISTANCE CTR., HISTORY OF PRESCRIPTION DRUG MONITORING PROGRAMS 3–7 (2018), https://www.pdmpassist.org/pdf/PDMP_admin/TAG_History_PDMPs_final_20180314.pdf.

114. *See id.* at 5 ("Taking advantage of emerging technology, Oklahoma (1990), broke the mold of previous PDMPs with its landmark legislation requiring electronic transmission of prescription data from a pharmacy directly to the state.").

115. *Id.* (discussing the evolution of state PDMPs).

116. PRESCRIPTION DRUG MONITORING PROGRAM CTR. OF EXCELLENCE AT BRANDEIS, MANDATING PDMP PARTICIPATION BY MEDICAL PROVIDERS: CURRENT STATUS AND EXPERIENCE IN SELECTED STATES 2 (2014), https://www.ncjrs.gov/pdffiles1/bja/247134.pdf.

117. Ellen Meara, Jill R. Horwitz, Wilson Powell, Lynn McClelland, Weiping Zhou, A. James O'Malley & Nancy E. Morden, *State Legal Restrictions and Prescription-Opioid Use Among Disabled Adults*, 375 NEW ENG. J. MED. 44, 50–52 (2016); Leonard J. Paulozz, Edwin M. Kilbourne & Hema A. Desai, *Prescription Drug Monitoring Programs and Death Rates from Drug Overdose*, 12 PAIN MED. 747, 750–52 (2011); Anupam B. Jena, Dana Goldman, Lesley Weaver & Pinar Karaca-Mandic, *Opioid Prescribing by Multiple Providers in Medicare: Retrospective Observational Study of Insurance Claims*, 348 BRITISH MED. J. 1, 4–5 (2014); Guohua Li, Joanne E. Brady, Barbara H. Lang, James Giglio, Hannah Wunsch & Charles DiMaggio, *Prescription Drug Monitoring and Drug Overdose Mortality*, 1 INJ. EPIDEMIOLOGY 1, 5–6 (2014); Joanne E. Brady, Hannah Wunsch, Charles DiMaggio, Barbara H. Lang, James Giglio & Guohua Li, *Prescription Drug Monitoring and Dispensing of Prescription Opioids*, 129 PUB. HEALTH REP. 139, 142–44 (2014); Tamara M. Haegerich, Leonard J. Paulozzi, Brian J. Manns & Christopher M. Jones, *What We Know, and Don't Know, About the Impact of State Policy and Systems-Level Interventions on Prescription Drug Overdose*, 145 DRUG & ALCOHOL DEPENDENCE 34, 47–48 (2014). *But see* Liza M. Reifler, Danna Droz, J. Elise Bailey, Sidney H. Schnoll, Reginald Fant, Richard C. Dart & Becki Bucher Bartelson, *Do Prescription Monitoring Programs Impact State*

The current evolution of state PDMPs addressed the problem of providers not accessing patients' prescription information.[118] Currently, "[a]ll PDMPs allow access to their data by prescribers and dispensers."[119] And the vast majority of state programs now require providers to query prescription information before writing or dispensing a new prescription to a patient.[120] This mandatory-access nature of PDMPs is relatively recent—only five states had mandated accessing a PDMP prior to prescribing in 2010—and is specifically designed to address the problem of providers not having relevant patient history before writing a new prescription.[121] Research specific to these mandatory PDMPs has revealed consistent evidence that they effectively reduce opioid prescriptions.

For example, Thomas Buchmueller and Colleen Carey examined a series of opioid misuse measures to determine the impact of mandatory PDMPs on patterns of opioid use. They found that "'must access' PDMPs reduce . . . the percentage of Medicare . . . enrollees who obtain prescriptions from five or more prescribers . . . by 8 percent and the percentage of enrollees who obtain prescriptions from five or more pharmacies by more than 15 percent."[122] Their research also revealed a negative relationship between the presence of a PDMP and opioid poisoning incidents.[123] Similar research has "f[ou]nd evidence that mandatory PDMP access laws are effective in reducing [prescription] drug abuse, and in particular opioid abuse."[124] Another study concluded that "[r]obust PDMPs may be able to significantly reduce opioid dosages dispensed, percentages of patients receiving opioids, and high-risk prescribing,"[125] and explained that PDMPs are only effective in reducing prescription rates "if they obligate doctors to check for patient history on the PDMP prior to filling out a

Trends in Opioid Abuse/Misuse?, 13 PAIN MED. 434, 434 (2012) ("Results support an association between PMPs and mitigated opioid abuse and misuse trends.").

118. PRESCRIPTION DRUG MONITORING PROGRAM TRAINING & TECH. ASSISTANCE CTR., *supra* note 113, at 7 ("Building on the experience and knowledge of earlier programs, more recent PDMPs have been implemented faster, employing best practices, and breaking new ground themselves in bringing PDMPs to their full potential.").

119. *Id.*

120. *Id.* ("In 2010, five (5) states (CO, DE, LA, NV and OK) had mandatory query laws, and today 40 states have such requirements.").

121. *Id.*

122. Buchmueller & Carey, *supra* note 110, at 78–79.

123. *Id.* at 78–79.

124. Anca M. Grecu, Dhaval M. Dave & Henry Saffer, *Mandatory Access Prescription Drug Monitoring Programs and Prescription Drug Abuse*, 38 J. POL'Y ANALYSIS & MGMT. 181, 183 (2019).

125. Rebecca L. Haffajee, Michelle M. Mello, Fang Zhang, Alan M. Zaslavsky, Marc R. Larochelle & J. Frank Wharam, *Four States with Robust Prescription Drug Monitoring Programs Reduced Opioid Dosages*, 37 HEALTH AFFS. 964, 964 (2018).

prescription."[126] In general, this evidence supports an important role of mandatory PDMPs in curbing opioid prescriptions and opioid-related harms.[127]

Recent research has investigated the effect of these programs on payments from pharmaceutical companies to prescribers by examining in more detail the role of PDMPs in curbing opioid prescriptions. A team led by Thuy Nguyen found evidence that mandatory access PDMPs reduce the amount companies expend in promoting opioids to prescribers.[128] The researchers explain that their "results are consistent with economic theory, predicting lower promotional activities when return on investment decreases after state prescribing restrictions."[129] This evidence provides important support for the analysis conducted in this Article. By showing that PDMPs can impact the payments received by prescribers from pharmaceutical companies,[130] Nguyen's study highlights the ability of these laws to modulate the prescriber-manufacturer relationship. The following analysis takes the next step, investigating the role of PDMPs in this relationship in greater depth and tying this effect to the ongoing litigation described above.

As a general matter, PDMPs may impact the prescriber-manufacturer relationship in several ways. First, and most importantly, PDMPs can correct misconceptions that physicians have about the undertreatment of pain, particularly misconceptions perpetuated by pharmaceutical detailing. Indeed, the purpose of PDMP laws is to provide more information to physicians so that they prescribe pain treatments more effectively. By providing physicians with an accurate count of the number of opioids their patients receive, physicians may better identify where pharmaceutical claims about the need for opioids deviate from objective evidence for their patients.

Second, PDMP laws may reduce the amount of money pharmaceutical companies are willing to spend on physicians. Nguyen's study found that the adoption of PDMP laws leads to a drop in the amount of pharmaceutical payments in the state.[131] The authors explained that this drop in payments is consistent with pharmaceutical companies decreasing the amount they are willing to spend "when the return on investment decreases."[132]

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126. Ian Ayres & Amen Jalal, *The Impact of Prescription Drug Monitoring Programs on U.S. Opioid Prescriptions*, 46 J. L., MED. & ETHICS 387, 397 (2018).

127. While the existing evidence clearly demonstrates an important role of mandatory PDMPs, recent research has noted that differences in dataset construction may have led to some differences in results across studies. Jill Horwitz, Corey S. Davis, Lynn S. McClelland, Rebecca S. Fordon & Ellen Meara, *The Problem of Data Quality in Analyses of Opioid Regulation: The Case of Prescription Drug Monitoring Programs* 3 (Nat'l Bureau of Econ. Rsch., Working Paper No. 24947, 2018), https://www.nber.org/papers/w24947.

128. Thuy D. Nguyen, W. David Bradford & Kosali I. Simon, *How Do Opioid Prescribing Restrictions Affect Pharmaceutical Promotion? Lessons from the Mandatory Access Prescription Drug Monitoring Programs* 23–37 (Nat'l Bureau of Econ. Rsch., Working Paper No. 26356, 2019), https://www.nber.org/system/files/working_papers/w26356/w26356.pdf.

129. *Id.* at 1.

130. *Id.*

131. *Id.*

132. *Id.*

Third, PDMPs may increase the cost (in the form of more liability) of prescribing more opioids from the perspective of providers. With a PDMP in place, physicians are required to check a patient's prescription history and may be charged with constructive notice of this history.[133] Accordingly, physicians' expected liability may increase because it becomes easier to confirm the occurrence of over-prescription and prove that physicians knowingly overprescribe opioids.

Given these effects of PDMPs, it is possible to leverage the presence of these programs to better understand the role of payments to prescribers. If these payments serve legitimately educational functions, then the presence of a PDMP should have little impact on the relationship between payments and prescribing rates. Consistent with the effects described above, PDMPs could certainly lower prescription rates generally, but this reduction should occur independently of the relationship between opioid payments and prescribing rates. In other words, an additional dollar paid to a prescriber in a state with a PDMP should have the same effect as an additional dollar paid to a prescriber in a state without a PDMP if these payments represent expenditures on legitimate educational opportunities.

On the other hand, if pharmaceutical payments primarily serve a persuasive function, then PDMPs should modulate the effect of these payments on individual prescribers. If, as described above, PDMPs provide prescribers with more accurate information on which patients have received relatively large amounts of opioids, then these programs may correct misconceptions that patients are not over-prescribed opioids. In correcting these misconceptions, PDMPs may decrease the positive impact payments from companies have on opioid prescription rates. Similarly, if, as some research has suggested, companies find it less worthwhile to pay providers when PDMPs are in place, then prescribers may change their response to payments from manufacturers in the presence of a PDMP.[134] Finally, as providers become attuned to their liability in the presence of PDMPs, they may be less willing to respond to the incentives offered by these programs because of the higher liability costs attached to doing so.

Overall, the presence of PDMPs should have little impact on the effect of a payment from a manufacturer to a prescriber if these payments serve legitimate educational functions. However, if these payments primarily serve a persuasive function, then PDMPs should decrease the effectiveness of these payments such that a given payment in a state with a PDMP should increase opioid prescription rates less than in a state without a PDMP. This provides the second testable hypothesis.

> *Hypothesis 2: Conditional on observing a positive correlation between pharmaceutical payments, if payments serve a persuasive function, the*

133. Buchmueller & Carey, *supra* note 110, at 82–86.

134. Nguyen et al., *supra* note 128, at 23–37.

implementation of PDMP laws will mitigate the correlation between payments and prescription rates.

Accordingly, if a significant negative effect of PDMP laws is seen on the impact of pharmaceutical payments on prescriptions, this provides evidence that the original pharmaceutical influence is not legitimately educational but rather persuasive.

Given these clear hypotheses, it is possible to empirically examine the role of payments from pharmaceutical companies to prescribers. The next Part describes the data and methodology used to test these hypotheses in detail.

III. EMPIRICAL ANALYSIS

To examine the prescriber-manufacture relationship in the context of the ongoing opioid crisis, we conduct a groundbreaking empirical analysis. This Part begins by outlining the data and methodology used in that analysis.[135] The analysis itself proceeds in two parts. We first examine the prescriber-manufacturer relationship generally, testing whether payments from manufacturers to prescribers are associated with higher opioid-prescribing rates generally. The second phase of the analysis then examines whether PDMPs impact this relationship. This two-part analysis allows us to empirically test the hypotheses laid out in the previous Part.

A. DATA ON THE PRESCRIBER-MANUFACTURER RELATIONSHIP

As no dataset contains information on both opioid prescription rates and payments to prescribers from pharmaceutical companies, we created one for this study. We focus on the period of 2013–2017.[136] In particular, we synthesized data during this period from three disparate sources, including the Medicare Part D Opioid Prescriber Summary File, the National Plan and Provider Enumeration System (NPPES), and the Open Payments dataset maintained by the Centers for Medicare and Medicaid Services.[137] The Medicare Part D Opioid Prescriber Summary File provides the percent of prescriptions consisting of opioids written by individual providers to Medicare beneficiaries each year between 2013 and

135. We provide a general discussion of our methodology and, in the interest of clarity and readability, reserve the more technical details of our analysis to the footnotes.

136. It bears noting that we are using data from the tail end of the opioid crisis; however, this will bias against finding statistically significant results. In view of the current litigation pressure and scrutiny, we expect that our estimation of the relationship is an underestimate of the historical relationship that existed at the height of the opioid crisis.

137. We examine these years because the Open Payments data begins in 2013, and the Medicare Part D data is only available until 2017 currently. *See Dataset Downloads*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://www.cms.gov/OpenPayments/Explore-the-Data/Dataset-Downloads (last visited Feb. 25, 2021) (showing that available data begins with "Complete 2013 Program Year Open Payments Dataset"); *Medicare Part D Opioid Prescriber Summary File*, CMS DATA, https://data.cms.gov/browse?tags=opioidmap&sortBy=newest (last visited Feb. 25, 2021) (filtering to show datasets for 2013 to 2017).

2017.[138] Though this dataset is limited to Medicare beneficiaries, it has been used in policy evaluations in the past and represents the best available data on opioid prescriptions that can be obtained without triggering important confidentiality problems.[139] The data in this file come from more granular data on Medicare patients but are organized in a way to protect the confidentiality of patients. This dataset identifies individual healthcare providers but does not provide a precise location. To obtain the location of individual providers, which is necessary to determine the applicability of various laws, we rely on the NPPES dataset. After merging these two datasets,[140] we have a new dataset that includes the opioid prescription rates of all providers across the country and the location of each of these providers.[141]

To obtain information on the payments made to these providers by pharmaceutical companies, we rely on the Open Payments dataset maintained by the Centers for Medicare and Medicaid Services. The Affordable Care Act required the creation of this dataset to provide greater transparency in the prescriber-pharmaceutical company relationships.[142] Any time a pharmaceutical or medical device manufacturer "provides a payment or other transfer of value" to a provider, that manufacturer must report, *inter alia*, the name of the provider, the amount of the payment, the date of the payment, and "[a] description of the nature of the payment or other transfer of value."[143] A dataset containing information on all such payments must then be made publicly available. We rely on this "Open Payments" dataset to glean information on legal payments made by pharmaceutical companies to prescribers.

The Open Payments dataset provides rich information on the number of payments received by each provider by name and full address. However, not all of these payments are relevant to opioid prescriptions. Therefore, we filter many of these payments out of the data. First, we only consider general payments, not payments associated with research, in order to capture non-research influence

138. *Medicare Part D Opioid Prescriber Summary File*, *supra* note 137. Because the Medicare prescription data reports opioid claims counts between 1 and 10 as missing, we impute any missing values as 5.5. We then recompute the opioid prescription rate for these providers and impute that for missing values of the opioid prescription rate. We treat reported zeros as true zeros.

139. Ashley C. Bradford & W. David Bradford, *The Impact of Medical Cannabis Legalization on Prescription Medication Use and Costs under Medicare Part D*, 61 J.L. & ECON. 461, 468 (2018).

140. Both the Medicare prescription dataset and NPPES dataset include the national provider identifier ("NPI") number of each provider. *Medicare Part D Opioid Prescriber Summary File*, *supra* note 137; *NPI Files*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://download.cms.gov/nppes/NPI_Files.html (last visited Feb. 25, 2021). We rely on the NPI to accurately match the two datasets.

141. While our sample is limited to Medicare claims, physicians treating Medicare patients also often treat non-Medicare patients. *See* Benjamin J. McMichael, R. Lawrence Van Horn & W. Kip Viscusi, *The Impact of Cannabis Access Laws on Opioid Prescribing*, 69 J. HEALTH ECON. 1, 12 (2020) (examining prescribing patterns that evince physicians treating patients with different types of insurance). Insofar as these treatment patterns are not wholly distinct, our results can be informative of non-Medicare patients. Even if this were not the case, however, Medicare patients constitute a politically-important subgroup and the empirical relationship reflects issues of significant public concern.

142. 42 U.S.C. § 1320a-7h.

143. *Id.* § 1320a-7h(a)(1)(A).

over providers.[144] Second, since we are only interested in the incentive effects of such payments on opioid prescriptions, we only consider payments relating to products considered opioids. To ensure that we only examine payments related to opioids, we use a list of opioid product names maintained by the Centers for Disease Control and Prevention to classify drugs appearing in the Open Payments dataset[145] as opioids.[146] Given the complex structure of the data, we employ a sophisticated algorithm to filter these observations.[147] The result is a dataset that contains detailed information on the non-research-related payments each prescriber received from opioid manufacturers between 2013 and 2017.

Matching the Open Payments data to the Medicare prescribing data is not straightforward,[148] and a key innovation of this Article is merging information on opioid prescription rates from the Medicare dataset to the information on payments from the Open Payments dataset. Because the structure of the datasets differs substantially, we implement sophisticated matching algorithms to match prescription data to pharmaceutical payment data. Though difficult to create and implement, the result of these sophisticated matching programs is a dataset containing information on the payments made by pharmaceutical companies to

144. We take all observations as given and do not make any adjustments based on "Change" status.

145. Each year of Open Payments lists a number of drugs, devices, or supplies associated with the payment; if any of the products are considered opioids, we count the payment as an opioid payment. *See About OpenPayments*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://www.cms.gov/OpenPayments/About/About (last visited Feb. 25, 2021).

146. *CDC Compilation of Benzodiazepines, Muscle Relaxants, Stimulants, Zolpidem, and Opioid Analgesics with Oral Morphine Milligram Equivalent Conversion Factors, 2017 Version*, CDC, https://www.cdc.gov/drugoverdose/data-files/CDC_Oral_Morphine_Milligram_Equivalents_Sept_2017.xlsx (last visited Feb. 25, 2021). We do not consider product names associated with buprenorphine, as it treats addiction to narcotic pain relievers. *See* Christopher Welsh & Adela Valadez-Meltzer, *Buprenorphine: A (Relatively) New Treatment for Opioid Dependence*, 2 PSYCHIATRY 29, 31 (2005).

147. Using the software Python, we construct a set of opioid product names. After extracting the products associated with each payment, the program checks whether there is any overlap between the extracted product names and the set of opioid product names. If there is, we count the payment as an opioid-related payment.

148. The inherent difficulty in matching prescription data to Open Payments lies in the fact that Open Payments data do not include NPI numbers. *See Dataset Downloads*, supra note 136. Accordingly, we must match payments to prescriptions using name and office address. This is not a simple issue of merging data, as random misspellings and inconsistent abbreviations make both names and addresses not uniform. For example, a physician named "John Smith, 1234 Main St., Tallahassee, FL 32306" in the prescription data may be under "John M. Smith, 1234 Main Street, Suite 302, Tallahassee, FL 32306" in the Open Payments data. Moreover, sometimes physicians are associated with multiple addresses or versions of their names in a given dataset. We address these challenges using a combination of data manipulation techniques and string-analysis algorithms. Specifically, we aggregate total payments for opioids by unique provider number provided by Open Payments. (Note that this unique ID number does not correspond to NPI number). While we aggregate total payments for each physician, we associated this aggregate payment with every address the physician is listed by, so that we have a higher likelihood of matching them to whatever address they have listed in the prescription data. We compile all of these payments into a data dictionary. We then use the name and mailing address for each observation in the prescription data to look up the associated payment in the Open Payments data in two steps. We first attempt to use name and the first line of the address to find an exact match in the Open Payments data dictionary. If there is not a perfect match, we look at possible providers in the same state and city as the prescriber and use fuzzy matching on name and first line of the business mailing address to obtain the relevant payment. We do the fuzzy matching using a Python package designed for this purpose.

individual physicians and the opioid prescriptions written by those individual physicians.

This matched dataset is the subject of our empirical analysis detailed below. However, to complete all phases of that analysis, we augment the dataset with several other key pieces of information. First, we construct a variable that indicates whether a provider practiced in a state with a law mandating that providers check the state's PDMP before prescribing controlled substances (which includes all opioids).[149] Second, we construct a variable indicating whether a state had a law authorizing adults to use medical cannabis in a similar fashion.[150] We include information on cannabis access laws because prior work has shown that they can have a significant impact on opioid prescription rates.[151] Thus, controlling for them will better allow us to isolate the role of payments from companies to prescribers.

Our final dataset contains information on opioid prescription rates,[152] pharmaceutical payments, state PDMP laws, and state cannabis access laws. This dataset is organized at the level of the individual provider,[153] providing us with comprehensive and highly accurate information on the relationships between pharmaceutical companies and individual providers. In particular, we can quantify the following relationships: (1) the effect of pharmaceutical payments on opioid prescriptions rates, and (2) how state PDMP laws may mitigate this effect. The following Subpart describes the empirical analysis of these relationships in detail.

149. Information on the dates of adoption of state PDMPs comes from the Prescription Drug Abuse Policy System. Legal Science, *PDMP Reporting and Authorized Use*, PRESCRIPTION DRUG ABUSE POL'Y SYS., http://pdaps.org/datasets/prescription-monitoring-program-laws-1408223416-1502818373 (last visited Feb. 25, 2021). We downloaded the data on December 11, 2019, and used policies indicated as "must-access." We round the policy dates to the nearest year (that is, if date is on or prior to July 1, 1999, the year of enactment is 1999. If the date is after July 1, 1999, the year of enactment is 2000). The policy variable takes the value of one in the enactment year and afterwards.

150. We similarly rely on information provided by the Prescription Drug Abuse Policy System to determine which states allowed access to medical cannabis and the dates on which that access began. Legal Science, *Medical Marijuana Laws for Patients*, PRESCRIPTION DRUG ABUSE POL'Y SYS., http://pdaps.org/datasets/medical-marijuana-patient-related-laws-1501600783 (last visited Feb. 25, 2021).

151. McMichael et al., *supra* note 141, at 1.

152. The opioid prescription rate is defined as the number of opioid claims divided by total claims (by physician), multiplied by 100.

153. During the period analyzed here, only payments to physicians were required to be reported to the Open Payments dataset. Accordingly, we limit our analysis to physicians in this Article. The laws have since been changed and future iterations of the Open Payments dataset (beginning in 2022) will include detailed payment information for other providers, such as nurse practitioners and physician assistants. *Law and Policy*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://www.cms.gov/OpenPayments/About/Law-and-Policy (last visited Feb. 25, 2021).

B. METHODOLOGY

To analyze the connection between pharmaceutical payments and physician opioid prescription rates, we estimate a series of regression models.[154] These models allow us to measure the average effect of pharmaceutical payments on opioid prescription while controlling for other confounding effects. In particular, the estimated models net out the effect of time-invariant differences across states. These differences may include different licensing requirements or the different approaches of medical boards to the opioid crisis. These, and many other factors that differ across states lines, may impact opioid prescription rates. By controlling for these various factors,[155] our models allow us to isolate the effect of payments from manufacturers on opioid prescription rates.

Our models also control for differences across time. In general, the CDC has noted that the opioid crisis has followed a clear trend, and controlling for the various factors within this trend is critical if we are to isolate the role of payments from other factors. Our models include these types of controls.[156] Finally, we allow for differences in prescription rates by different specialties.[157] Controlling for differences across specialties is important because certain specialties prescribe more opioids than others for legitimate medical reasons.[158] By controlling for all of these factors, our models can isolate the variation in opioid prescription rates that is attributable to pharmaceutical payments.[159]

Turning to the details of the models, the outcome we examine throughout our analysis is the opioid prescription rate of individual providers. While this outcome measure is straightforward—we simply examine the percent of prescriptions written that constitute opioid prescriptions[160]—measuring manufacturer payments is less so. In particular, prior research has suggested that

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154. Throughout our analysis, we estimate ordinary least squares regression models with the following general specification: $OpioidRate = PaymentCategory\beta + \partial_y + \gamma_s + \theta_z + \varepsilon$. The dependent variable, *OpioidRate*, is the average number of opioids a physician prescribes across all of his or her patients each year. *PaymentCategory* is a vector of indicator variables that capture the amount of payments received by individual physicians. This series of variables is described in more detail below. All of our regression models also include fixed effects for state (γ_s), year (∂_y), and specialty (θ_z). Standard errors are clustered by state.

155. Specifically, the inclusion of state fixed effects controls for observable and unobservable differences across states.

156. Specifically, the inclusion of year fixed effects control for linear and non-liner temporal trends in opioid prescription rates.

157. We use specialty data reported in Medicare Part D Opioid Prescriber Summary File. *Medicare Part D Opioid Prescriber Summary File*, *supra* note 137.

158. The specialty fixed effects control for differences across specialties.

159. In general, with ordinary lease squares (OLS) regressions, there is always a possibility that an omitted variable that is correlated with pharmaceutical payments is actually impacting opioid prescriptions. This is particularly problematic when a causal relationship is being inferred. However, here, we are not interested in eliciting causality; we are instead interested in how physician prescriptions vary with physician payments.

160. The prescription rate is defined as the number of opioid claims divided by total claims, multiplied by 100. This can be interpreted as the average opioid claims for every 100 claims. While there are potentially other measures we could use for our dependent variable, since our analysis is physician-centric, not patient-centric, the rate per 100 claims seems most reflective of physician behavior.

pharmaceutical payments have a lasting effect on physician prescription decisions.[161] In light of this, we focus not on the amount a physician receives in a given year, but on the cumulative payments they have received over the years in our sample.

For example, in 2013, our cumulative payment variable will include payments from 2013. However, in 2014, the cumulative payment variable will include payments to a given physician from both 2013 and 2014. This allows us to differentiate between one-off payments and longer relationships. Using these cumulative payments, we place prescribers into one of six categories based on the number of payments they have received. The lowest category includes all prescribers who received no opioid-related payments. We then classify all providers who received at least one opioid-related payment from a manufacturer into five separate, equally-sized categories.[162] Physicians with the highest levels of payments appear in the fifth category, those with the next highest levels of payments in the fourth category, and so on.

Based on these categories, we create a series of variables that indicate the category each falls into. These indicator variables capture the relationship between manufacturer payments and opioid prescription rates. For example, the variable indicating the highest category captures the effect of being among the most well-paid providers on opioid prescription rates. The variable indicating the lowest (positive) category captures the effect of receiving some, but not substantial, payments. While this approach is somewhat more complex than simply examining payment rates themselves, it is mathematically preferable because it avoids imposing any assumptions of strict linearity on the effect of payments. We expect that the effect of payments on prescriptions will vary by category, and the nature of this variation will allow us to evaluate the various hypotheses outlined above.

The methodology described so far underlies the first phase of our analysis that investigates the general relationship between payments and opioid prescription rates. We also rely on this methodology in the second phase, but we augment it using information on PDMPs. We describe this augmentation in greater detail in connection with the second phase of our analysis.

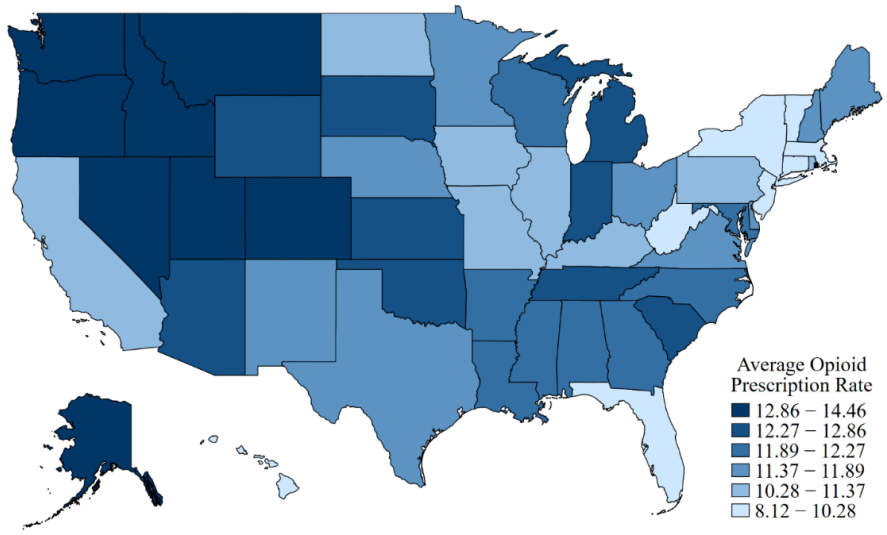
161. Svetlana N. Beilfuss, Pharmaceutical Opioid Marketing and Physician Prescribing Behavior 19 (Oct. 26, 2019) (unpublished manuscript), https://svetlanabeilfuss.com/uploads/1/2/1/5/121526954/jobmarketpaper_svetlananbeilfuss.pdf.

162. These categories are defined for each state and year. Thus, a physician whose cumulative payment is in the highest tier in his state in a given state and year might fall into a different tier in a different state or year. Because pharmaceutical companies separate markets geographically, allowing for different rankings by state is important. As there might be differences in yearly spending by pharmaceutical companies (and to account for the ratcheting effect of using cumulative payments), cumulative payments are only compared to other cumulative payments in a given year.

C. RESULTS FOR THE RELATIONSHIP BETWEEN PHARMACEUTICAL PAYMENTS AND OPIOID PRESCRIPTIONS

We begin our analysis by focusing generally on the relationship between opioid-related payments by manufacturers and opioid prescription rates. Before delving into the details of our empirical models, however, Figures 1 and 2 present an overview of the prevalence of opioid prescriptions and opioid detailing, respectively. These figures are not intended to demonstrate the correlation between opioid prescription and pharmaceutical payments. Indeed, since our empirical analysis measures the relationship between opioid prescription rates and relative payment tiers within states in a given year, the maps necessarily will not preview our empirical results. Instead, these maps present some idea of geographical variation in both payments and prescriptions.

Figure 1. Opioid Prescription Rates Across the United States



As such, Figure 1 reports the average opioid-prescribing rate for physicians in each state across our entire data period. This rate varies from a low of 8.12 opioid prescriptions per 100 prescriptions to a high of 14.46 opioid prescriptions. Interestingly, the regions with the highest-prescribing providers include the Southern, Mountain, and Pacific Northwest states—a group of states that often have little in common with one another. In contrast, states in the Northeast and Midwest generally have lower opioid-prescribing rates.

Figure 2. Opioid-Related Payments Across the United States

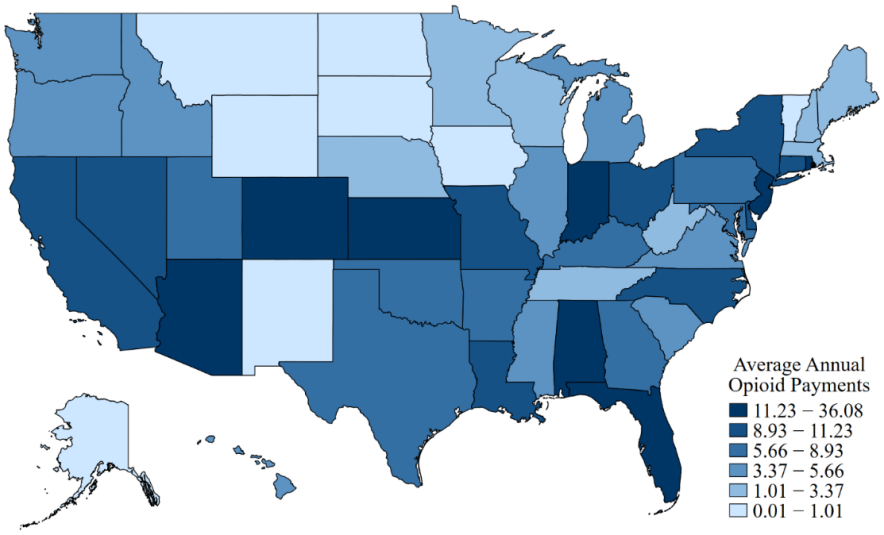


Figure 2 reports the average opioid-related payment rate in each state across our entire data period. As with opioid-prescribing rates, physicians in the southern states and mountain states place higher in the distribution of opioid payments than physicians in other states. While the correlation between states in the highest categories of opioid-prescribing rates and opioid payments is not one-to-one, Figures 1 and 2 demonstrate that states receiving more opioid detailing tend to have higher opioid-prescribing rates.

Figure 3. Opioid Prescriptions by Opioid-Related Payment Category

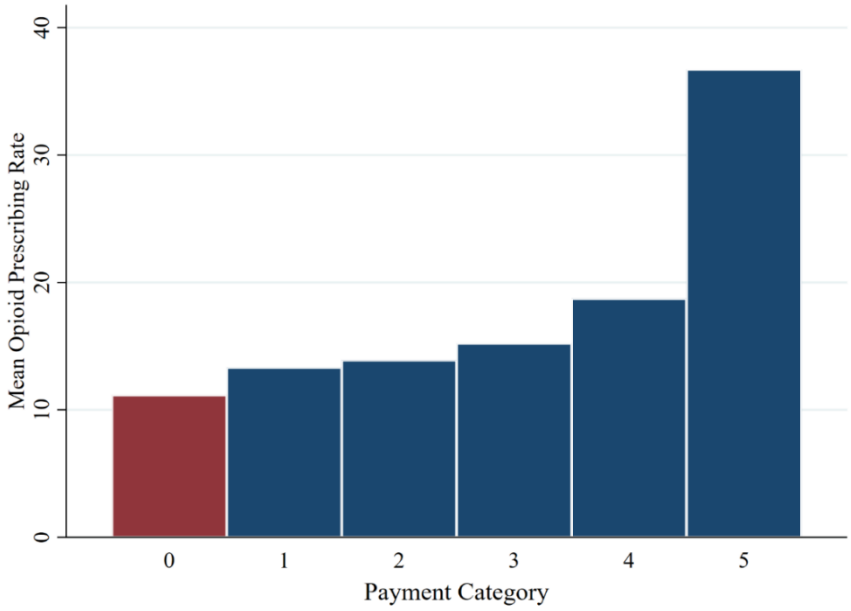


Figure 3 presents more detailed information on the relationship between opioid-related payments and opioid-prescribing rates. In particular, it reports the mean opioid-prescribing rate of physicians who received different amounts of opioid-related payments from pharmaceutical companies. At the lowest end of the payment spectrum are those physicians who received no opioid payments (highlighted in red). These physicians also, on average, had the lowest opioid-prescribing rates. Among the physicians who received some amount of opioid-related payments, Figure 3 divides those physicians into five categories, as described above. Physicians in the first category received the least amount of money, while those in the fifth received the highest amount. As Figure 3 illustrates, the mean opioid-prescribing rate generally increases across the categories. In other words, the more opioid-related payments received by a physician, the more opioids that physician prescribed.

To explore the relationship between opioid payments and prescribing rates further, we estimate a series of regression models. In the interest of succinctness, we report the results graphically. Figure 4[163] reports the results of a model exploring the general relationship between payment levels and prescription rates. The horizontal axis reports the level of payments received by each physician. At the lowest level are those physicians who received no payments from opioid manufacturers. Physicians who received some amount of money

163. The vertical lines indicate 90% confidence intervals, though these coefficients are all significant at the 5% significance levels as well.

from opioid manufacturers are, as before, divided into five categories. The vertical axis tracks the change in physicians' opioid-prescribing rates associated with being in a particular payment category.

Figure 4. Effect of Pharmaceutical Payment on Opioid Prescription Rate

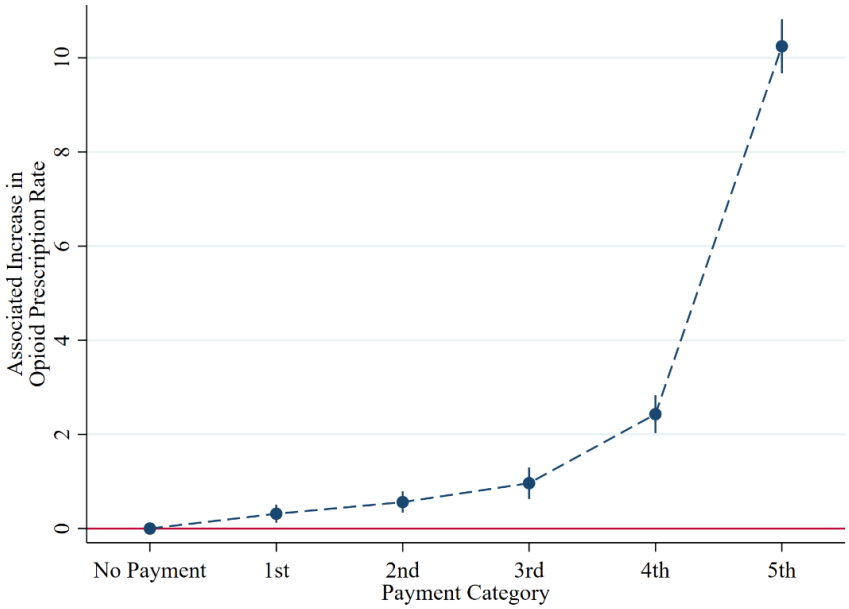


Figure 4 demonstrates an increasing relationship between receiving payments from opioid manufacturers and opioid prescriptions rates. Physicians that received no payments from opioid companies serve as the baseline.[164] Each successive category is associated with a higher opioid prescription rate relative to this baseline. However, much of the effect of opioid detailing is concentrated in the fourth and fifth categories. For example, the first payment category is associated with approximately 0.2 additional opioid prescriptions per 100 prescriptions than the no-payment baseline. However, the fourth category is associated with two additional opioid prescriptions per 100 prescriptions. The fifth payment category is associated with over ten additional opioid prescriptions per 100 prescriptions than the no-payment baseline.

While the associations reported in Figure 4 do not necessarily represent the causal effect of opioid-related payments on opioid-prescribing rates, these

164. This is not to suggest that physicians that receive no payments do not prescribe opioids. They do. The rate at which these physicians prescribe opioids simply serves as the basis of comparison. Each reported effect for the separate payment quintiles represents the change in opioid-prescribing rates relative to physicians who received no payments.

results provide important insight into the hypotheses outlined above. In general, we find no evidence that payments are unrelated to prescribing rates. Instead, we find consistent evidence that the more money prescribers receive from opioid manufacturers, the more opioids they prescribe. This relationship is not linear, and physicians in the highest payment category are much more affected by payments than are physicians in the lowest category. Indeed, the increase of ten opioid prescriptions per 100 prescriptions observed in connection with the highest payment category represents an approximately ninety percent increase from the baseline physicians who received no opioid-related payments.[165]

These results provide clear support for Hypothesis 1b—the hypothesis that higher opioid-related payments are associated with higher opioid-prescription rates. In other words, the results reveal a consistent positive relationship between payments and prescribing rates. As noted before, this positive relationship does not, by itself, demonstrate that opioid-related payments serve a persuasive purpose. The positive correlation may be an artifact of purely educational payments as long as those payments are concentrated only on physicians who should be prescribing high levels of opioids. There are potential reasons for this to be the case—pharmaceutical representatives may have useful information about the type of patient populations each physician serves. If representatives target only physicians whose patients need opioids for unbiased education, the positive relationship observed here could arise absent any kind of deleterious behavior on the part of opioid manufacturers. Of course, as noted in Hypothesis 1b, this positive relationship is also consistent with pharmaceutical payments performing a persuasive role in physician treatment. To discern between these two functions, we extend our analysis to examine the role of PDMPs. The next Subpart discusses that extended analysis.

D. RESULTS FOR THE ROLE OF PRESCRIPTION DRUG MONITORING PROGRAMS

We focus on the role of PDMPs in mitigating the payment-prescribing relationship revealed by the results above. PDMPs were originally designed to provide prescribers with more information about medications patients had previously received.[166] For example, a physician may decline to prescribe opioids if she has credible information that the patient requesting the prescription has already received three other opioid prescriptions from other physicians. In accomplishing this primary purpose, however, PDMPs can also (if unintentionally) affect the ability of opioid manufacturers to influence physician prescription patterns.

If physicians are generally unaware of how prevalent opioid prescription is, the enactment of a PDMP law may reduce prescription rates generally across all tiers of payments. However, if opioid-related payments serve legitimate

165. As indicated in Figure 2, the baseline group of physicians prescribed approximately eleven opioids per 100 prescriptions.

166. Buchmueller & Carey, *supra* note 110, at 82–86.

educational functions, then the presence of a PDMP should have no impact on the relationship between payments and prescribing rates. In this state of the world, manufacturers are not using payments to incentivize over-prescription and are instead disseminating unbiased information about opioid risk and benefits. As such, the informational value that PDMPs add should not cause physicians receiving pharmaceutical payments ("education") to revise their prescription decisions relative to physicians who do not receive payments. Accordingly, there should be no mitigating effect on the relationship between pharmaceutical payments and prescriptions.

On the other hand, if opioid-related payments serve persuasive functions—persuasion which may involve false or misleading advertising—then PDMPs should have a clear effect on the relationship between payments and prescribing rates. In this state of the world, a physician who has received credible information from a PDMP about a patient may be less likely to believe manufacturers' claims about the low risk of addiction associated with chronic opioid use or claims about the undertreatment of pain.[167] Similarly, PDMPs have the potential to expose physicians who prescribe excessively to unwanted attention and even liability. If this is the case, then the additional prescriptions associated with a payment category in states with PDMPs should be smaller than those in states without these programs. In other words, being in the same category of payment in a state with a PDMP should induce a smaller uptick in opioid prescriptions than in a state without a PDMP. Based on Hypothesis 2, we would then expect that the existence of a PDMP law will mitigate the relationship between pharmaceutical payments and prescriptions.

Accordingly, by examining the impact of PDMPs on the relationship between payments and prescription rates, it is possible to understand the nature of these payments better: do they further legitimate goals, or do they simply incentivize more prescriptions? To formally test the impact of PDMPs, we estimate the same regression model that underlies Figure 4, above. Now, however, we include a variable that indicates whether a prescriber practiced in a state that maintained a mandatory-access PDMP. We interact this variable with all of the variables indicating which payment category a physician fell into.[168] By doing so, we can estimate the effect of payments on providers who must access a PDMP relative to those that do not have to access a PDMP under state law.

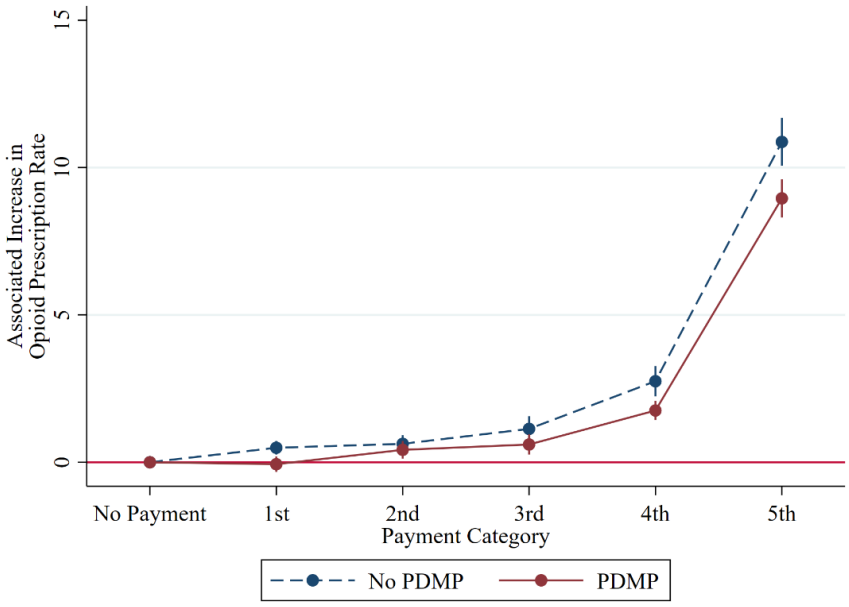
Like Figure 4, Figure 5 graphically reports the changes in prescriptions by pharmaceutical payment category, relative to physicians receiving no payment. Unlike Figure 4, Figure 5 allows this effect to differ between states and years in

167. For a discussion of the allegations made by plaintiffs in connection with these alleged false advertisements, see *supra* Part I.C.

168. Specifically, we estimated the following model: $OpioidRate = PaymentCategory'\beta + \alpha PDMP + PaymentCategoryxPDMP'\delta + \partial_y + \gamma_s + \theta_z + \varepsilon$, with fixed effects for state (γ_s), year (∂_y), and specialty (θ_z). Standard errors are clustered by state. For category i, the plotted treatment effect for the non-PDMP line is β_i, while the plotted effect for the PDMP line is $\beta_i + \delta_i$. The vertical lines indicate 90% confidence intervals.

which a PDMP law is in effect and those in which no PDMP is in effect. If PDMP laws disrupt the existing relationship between pharmaceutical payments and prescriptions, the PDMP line should be significantly lower than the non-PDMP line. Figure 5 indicates that the effect of pharmaceutical payment level is smaller when a PDMP is in place. This effect is statistically significant for all categories except for the second.[169] Thus, not only are PDMP laws generally associated with fewer opioid prescriptions, the reduction is concentrated in physicians receiving pharmaceutical payments. Furthermore, the effect becomes more pronounced in the higher categories of payments, with physicians in the fifth category seeing a bigger effect on the payment-prescription rate relationship than those in lower categories.

Figure 5. Effect of Pharmaceutical Payment on Opioid Prescription Rate, by PDMP Status



In general, the results reported in Figure 5 demonstrate that PDMPs significantly impact the relationship between payments and prescription rates in ways that do not support a legitimately educational function for opioid-related payments. Stated differently, the results provide support for Hypothesis 2. While the results do not clearly indicate the mechanism by which PDMPs have their effect, any effect is consistent with payments serving a persuasive role.

169. The difference in effect is significant at the 10% level for the first, third, fourth, and fifth categories. The difference in effect is also significant at the 5% significance level for the first, fourth, and fifth categories.

Before exploring the implications of this critically important result, we first test its robustness. In particular, we re-estimate the same model reported in Figure 5 but include additional controls for medical cannabis access laws. One relevant set of policies that have proven effective at addressing the harms associated with the opioid crisis has been cannabis access laws, even though these laws were never designed to do so. States that have loosened restrictions on access to cannabis, either through laws legalizing medical cannabis or providing access to cannabis for personal or recreational use, have seen reductions in both opioid use and opioid-related harms.[170] Cannabis access laws accomplish these reductions via a different mechanism than PDMPs, however. Where PDMPs provide prescribers additional information to combat drug-seeking behavior and reduce inappropriate opioid prescriptions, laws facilitating access to cannabis do so by decreasing the demand for opioids as individuals substitute cannabis for opioids.[171]

Insofar as medical cannabis is a substitute for opioid in terms of pain management,[172] the enactment of laws that allow for legal consumption of

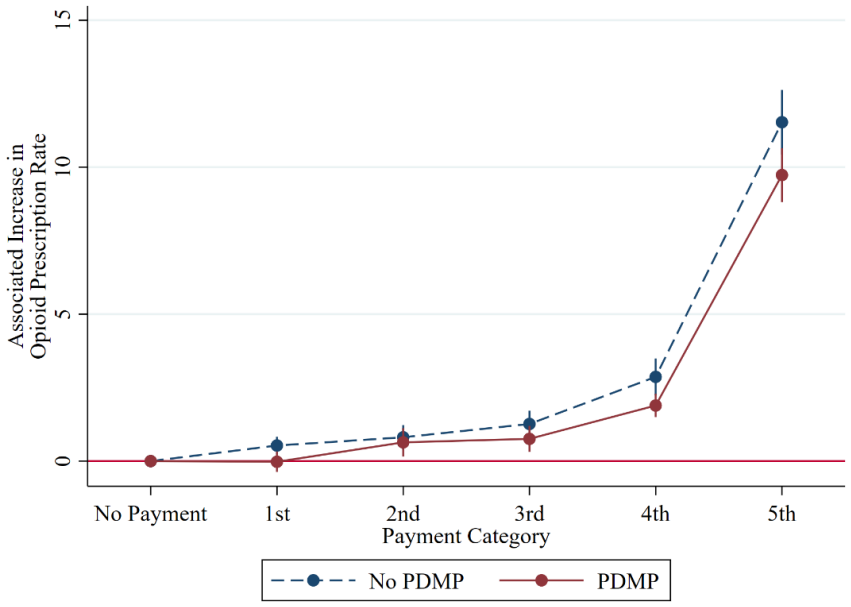
170. McMichael et al., *supra* note 141, at 10; Marcus A. Bachhuber, Brendan Saloner, Chinazo O. Cunningham & Colleen L. Barry, *Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010*, 174 JAMA INTERNAL MED. 1668, 1671 (2014).

171. *See* James M. Corroon Jr., Laurie K. Mischley & Michelle Sexton, *Cannabis as a Substitute for Prescription Drugs—A Cross-Sectional Study*, 10 J. PAIN RSCH. 989, 989 (2017) (finding that nearly 50% of patients substitute cannabis for prescription drugs and that the most commonly substituted drugs are prescription opioids); Michelle Sexton, Carrie Cutler, John S. Finnell & Laurie K. Mischley, *A Cross-Sectional Survey of Medical Cannabis Users: Patterns of Use and Perceived Efficacy*, 1 CANNABIS & CANNABINOID RSCH. 131, 133 (2016) ("In response to the question 'Have you have ever used cannabis as a substitute for prescription drugs?' 59.8% of participants responded yes. When asked which drugs they substitute Cannabis for, over 25% of these participants reported substituting Cannabis for pain medications, including opiates."); Kevin F. Boehnke, Evangelos Litinas & Daniel J. Clauw, *Medical Cannabis Use Is Associated with Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients with Chronic Pain*, 17 J. PAIN 739, 739 (2016) ("Among study participants, medical cannabis use was associated with a 64% decrease in opioid use."); Amanda Reiman, Mark Welty & Perry Solomon, *Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report*, 2 CANNABIS & CANNABINOID RSCH. 160, 162–64 (2017) ("Ninety-two percent of the sample 'strongly agreed/agreed' that they prefer cannabis to opioids for the treatment of their condition and 93% 'strongly agreed/agreed' that they would be more likely to choose cannabis to treat their condition if it were more readily available.").

172. For example, early work demonstrated that medical cannabis laws reduced the use of prescription drugs for which cannabis can serve as a substitute among Medicare and Medicaid beneficiaries. Ashley C. Bradford & W. David Bradford, *Medical Marijuana Laws Reduce Prescription Medication Use in Medicare Part D*, 35 HEALTH AFFS. 1230, 1233–35 (2016); Ashley C. Bradford & W. David Bradford, *Medical Marijuana Laws May Be Associated with a Decline in the Number of Prescriptions for Medicaid Enrollees*, 36 HEALTH AFFS. 945, 948–50 (2017). Later work, which focused more explicitly on opioids, yielded evidence that medical cannabis access laws reduce opioid prescriptions among Medicare beneficiaries by between 8% and 21% across six different types of opioids. Bradford & Bradford, *supra* note 139, at 476–82. Similarly, medical cannabis access laws and adult use cannabis access laws reduced opioid prescriptions among Medicaid beneficiaries by 5.88% and 6.38%, respectively. Hefei Wen & Jason M. Hockenberry, *Association of Medical and Adult-Use Marijuana Laws with Opioid Prescribing for Medicaid Enrollees*, 178 JAMA INTERNAL MED. 673, 673 (2018); *see also* Di Liang, Yuhua Bao, Mark Wallace, Igor Grant & Yuyan Shi, *Medical Cannabis Legalization and Opioid Prescriptions: Evidence on US Medicaid Enrollees During 1993–2014*, 113 ADDICTION 2060, 2063–68 (2018) (finding that medical cannabis access laws reduced opioid prescriptions among the Medicaid population). Focusing on the general population—and not just individuals covered by Medicare or Medicaid, a recent study concluded that recreational cannabis access laws and medical cannabis access laws reduced opioid prescriptions

marijuana might influence the relationship between pharmaceutical payments and prescriptions. To ensure that cannabis access laws do not influence the difference in payment effect for PDMP observations and non-PDMP observations, we control for the enactment of these laws. Figure 6[173] reports the results from models that include controls for medical cannabis access laws. The results are quite similar to those reported in Figure 5. Accordingly, our conclusions about the effect of PDMPs on the relationship between payments and prescription rates are not impacted by the availability of medical cannabis. Given the strength of our results, and the fact that these results demonstrate a persuasive function of opioid-related payments—in technical terms, we find support for both Hypothesis 1b and Hypothesis 2—we explore the implications of these results in the next Part.

Figure 6. Effect of Pharmaceutical Payment on Opioid Prescription Rate, by PDMP Status, Controlling for Cannabis Laws



(as measured in morphine milligram equivalents) by 11.8% and 4.2%, respectively. McMichael et al., *supra* note 141, at 1.

173. The difference in effect is significant at the 10% level for the first, third, fourth, and fifth categories. The difference in effect is also significant at the 5% significance level for the first, fourth, and fifth categories.

IV. IMPLICATIONS OF THE CONNECTION BETWEEN PAYMENTS AND PRESCRIPTIONS

With the explosion of lawsuits against opioid manufacturers in recent years, understanding the relationships between these manufacturers and the healthcare providers who prescribe their products has never been more important. The results of our empirical analysis provide unique insight into these continuing—and troubling—relationships. In this Part, we begin by exploring the nature of these relationships as elucidated by the empirical analysis above and contextualizing our results within the ongoing opioid litigation. We then explore the (unintended) policy implications raised by our results.

A. CONTEXTUALIZING THE EMPIRICAL RESULTS

Given the sheer number of claims that comprise the ongoing opioid litigation, it comes as no surprise that no single theory of liability underlies every claim. However, as discussed above, two theories of liability that permeate many suits are that (1) opioid manufacturers engaged in false or misleading advertising and (2) instead of reporting suspicious orders, opioid manufacturers targeted high-prescribing physicians for additional detailing.[174] The results of our empirical analysis above are generally consistent with both theories of liability. Indeed, even examining data on legal payments demonstrates the continued existence of troubling relationships between manufacturers and prescribers. Moreover, these are the types of relationships that must be present if either of these general theories can support liability on the part of manufacturers. Without a strong connection between manufacturers and prescribers, it would prove exceedingly difficult for manufacturers to offer false or misleading advertisements to prescribers convincingly. Similarly, the types of relationships highlighted by our results are the types that one would expect to see if, instead of monitoring and reporting unusual shipments, opioid manufacturers were targeting prescribers for increased opioid prescriptions.

Importantly, the results of our empirical analysis suggest that not only does a significant relationship exist between pharmaceutical payments and opioid prescription rates, but that this relationship has persisted through the latter part of the opioid crisis.[175] The continuation of this relationship into the later years of the crisis—when drugs such as heroin and fentanyl have played larger roles than prescription opioids—suggests that the behavior of pharmaceutical companies plays an important role in physicians' decisions to prescribe opioids. While the evidence reported above does not necessarily demonstrate any behavior that would subject manufacturers to criminal or civil liability, the

174. *See supra* Part I.C.

175. As previously mentioned, these results are not meant to estimate the causal effect of an additional dollar on prescription rates. Instead, the results document correlations between the prescription rates and payment tiers and describe how these correlations change in the presence of PDMP laws. The implications of these patterns correspond to the predictions of payments serving persuasive functions rather than purely educational ones.

strong and continued relationship between pharmaceutical company payments and physician opioid prescriptions suggests that these companies continue to encourage opioid prescriptions deep into the opioid crisis.

Not only does the association between payments and prescribing rates remain statistically significant despite the presence of illegal alternatives, such as heroin and illicitly manufactured fentanyl, the magnitude of this association increases with the tier of spending. This increase is consistent with the notion that physicians receiving much larger payments from pharmaceutical companies are affected in a qualitatively different way than those receiving minimal amounts.

In general, this pattern of effects may be consistent either with payments serving legitimate educational functions or with payments serving to encourage more opioid prescriptions. The second phase of our analysis, however, demonstrates that the latter is true. The fact that PDMPs have a clear impact on the relationship between payments and prescribing rates demonstrates the persuasive (as opposed to educational) function of payments from opioid manufacturers. While we cannot definitively say that this persuasive role is a function of an incentive structure (with providers targeted to encourage more prescriptions) or a reward structure (with high-prescribing providers receiving payments as rewards), our results indicate the existence of persuasive payments generally.

Though our analysis primarily relied on PDMPs as a mechanism by which to differentiate between persuasive and educational payments, the results of that analysis elucidate an important, if unintended, effect of PDMPs. The next Subpart explores that effect.

B. THE UNINTENDED EFFECTS OF PRESCRIPTION DRUG MONITORING PROGRAMS

In general, the results of this empirical analysis demonstrate that PDMP laws mitigate the association between pharmaceutical payments and opioid prescription rates. States that adopted PMDP laws over time have a weaker association between pharmaceutical payments and opioid prescription rates. This effect persists even after controlling for the emergence of a pain relief alternative, cannabis. While this pattern of results is consistent with pharmaceutical payments serving a persuasive function, it has important implications in and of itself. Chief among these implications is the potential of PDMPs to attenuate the relationships between prescribers and manufacturers.

In general, PDMPs may reduce the effect of pharmaceutical payments on opioid rates via at least three different mechanisms. First, as PDMP laws were established in order to provide healthcare providers with information on what prescriptions their patients were receiving, it is possible that these programs corrected providers' beliefs about their patients' other prescriptions. Our results provide support for this mechanism of effect, as we see a consistently stronger

impact of PDMPs on providers receiving higher levels of payments. This suggests that PDMPs may correct misconceptions among these providers that opioids are under-prescribed—misconceptions that pharmaceutical companies have been accused of perpetuating.

Second, though states did not establish PDMPs to expose providers to greater liability, it is possible that prescribers perceive a greater risk of liability or disciplinary action for over-prescription if a PDMP is in place. In response, physicians receiving payments from pharmaceutical companies may reduce the number of prescriptions they make in order to avoid scrutiny. This would be an unintended "accountability" effect of PDMPs.

Third, as noted above, other researchers have found that companies reduce payments to prescribers following the adoption of a PDMP.[176] Given this finding, our results may stem in part from a general reduction in pharmaceutical payments after the adoption of a PDMP. Because we group payments into tiers by state and year, we do not measure the effect of nominal payments over time; instead, we compare physicians to their in-state peers in a given year. Accordingly, if the pharmaceutical company generally spends less in the year following a PDMP enactment, a physician may receive significantly lower payments in the year following a PDMP enactment but remain in the same tier in both years. Insofar as prescription rates are sensitive to the level of payments, a fascinating corollary presents itself. If pharmaceutical companies reduce payments to physicians after the implementation of a PDMP law, this suggests that they believe that their payments incentivize physicians to prescribe opioids and that PDMP laws might chill this effect. Proving this corollary is beyond the scope of this Article, but these potential explanations confirm the practical importance of these results.

In general, while we cannot isolate the exact mechanism by which PDMPs attenuate the relationship between payments and prescription rates, we can confidently say that PDMPs have this effect overall. Thus, our results suggest that PDMPs have the (likely unintended) effect of reducing the effectiveness of pharmaceutical payments in terms of the ability of these payments to encourage more opioid prescriptions. While this potentially unintended effect may appear rather mundane at first, it has profound implications. At their most basic level, persuasive payments from pharmaceutical companies create important conflicts of interest. Physicians may be induced to prescribe more opioids when these additional prescriptions are not in patients' bests interests. Addressing this type of conflict of interest has proven exceedingly difficult in the past. Indeed, a recent study investigated the role of these conflicts in depth.[177] Disclosure of the

176. Nguyen et al., *supra* note 128, at 23–37.

177. Susannah L. Rose, Sunita Sah, Raed Dweik, Cory Schmidt, MaryBeth Mercer, Ariane Mitchum, Michael Kattan, Matthew Karafa & Christopher Robertson, *Patient Responses to Physician Disclosures of Industry Conflicts of Interest: A Randomized Field Experiment*, ORG. BEHAV. & HUM. DECISION PROCESSES (forthcoming 2021).

underlying conflict is the most recommended method for addressing issues surrounding conflicts of interest. However, a randomized field experiment had little impact on patients' trust of their providers.[178] Thus, to the extent policymakers wish to address conflicts of interest, using PDMPs to reduce the payments that create these conflicts in the first place may be an attractive strategy.

Returning to the central focus of this Article, PDMPs may also be a viable option to undercut the relationships that may support the behavior alleged by plaintiffs in the ongoing opioid litigation. By undermining these relationships—even though the relationships we examine are perfectly legal—PDMPs may undercut the ability of manufacturers to engage in the conduct alleged by plaintiffs. Furthermore, decreasing the prominence and effectiveness of false and misleading advertising by weakening the relationships that facilitate it can only aid patients. Similarly, undermining the ability of manufacturers to target high-prescribing (or potentially high-prescribing) providers can also help patients avoid becoming addicted to opioids in the first instance. Importantly, these potential benefits of PDMPs exist in addition to the already well-documented benefits these programs have in terms of reducing opioid prescriptions generally.[179]

CONCLUSION

Representing the greatest threat to public health of this generation, the opioid crisis has claimed the lives of hundreds of thousands of Americans.[180] Unlike past public health crises, like the HIV epidemic of the 1980s and 1990s, the opioid epidemic arose within the healthcare system itself. While this highlights clear problems within that system, it also means that victims of the current crisis have access to legal redress—something victims of natural epidemics have never had. Thousands of lawsuits seeking this redress have been filed against opioid manufacturers. These claims rely on many different theories of liability, but two important allegations are common to many of these suits: (1) opioid manufacturers produced false and misleading advertising, and (2) manufacturers not only failed to monitor the supply of opioids but targeted certain high-prescribing providers.

These common allegations—along with many others—depend critically on the relationships that exist between manufacturers and the healthcare providers that prescribe their products. Despite the importance of these relationships, however, little empirical evidence on the nature and strength of these

178. *Id.*

179. *See supra* notes 122–127 and accompanying text.

180. *The Drug Overdose Epidemic: Behind the Numbers*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/drugoverdose/data/index.html#:~:text=Overdoses%20involving%20opioids%20killed%20nearly,those%20deaths%20involved%20prescription%20opioids.&text=Learn%20more%20about%20the%20Data,epidemic%20in%20the%20United%20States (last visited Feb. 25, 2021).

relationships exists. This Article fills that gap by providing novel and robust evidence on the association between payments made by pharmaceutical companies and the opioid prescription rates of individual healthcare providers who receive those payments. The results of the analysis reported here demonstrate a positive relationship between payments and prescribing rates, with providers receiving more money from pharmaceutical companies prescribing more opioids.

While the association between payments and prescribing rates may be the result of different activities undertaken by pharmaceutical companies—some more legitimate than others—our analysis demonstrates that these payments primarily serve to incentivize or reward more opioid prescriptions. Our analysis is limited to legal payments and cannot establish any liability on the part of manufacturers. However, it can, and does, clearly establish the existence of troubling relationships—relationships that persist deep into the opioid crisis.

Indeed, the relationships evinced by the data are exactly the type that could facilitate the behavior alleged by plaintiffs in the current opioid litigation. As plaintiffs continue to fight for compensation, this continued contamination may prove a useful foundation on which to build their claims. The persistence of these results through the tail of the opioid crisis cautions against a conclusion that contamination of medical judgment is entirely behind us. Interventions that weaken the impact of this relationship—like state PDMP laws—may be the best defense against the next crisis.

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