ABSTRACT

Title of Dissertation: PHYSICIAN PEER NETWORKS AND PATTERNS OF OPIOID-RELATED BEHAVIOR

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Physicians are known to learn prescribing behavior from peers, although the extent and magnitude of peer influence on opioid prescribing is not well understood. Identifying the role peer networks play on influencing opioid prescribing, or opioid-related behavior, could elicit new understandings on how information in healthcare is spread and, in turn, lead to policy solutions and interventions to modify physician behavior in the direction of evidence-based medicine. The goal of this dissertation was to evaluate physicians prescribing opioids to patients in Medicare, or physicians receiving opioid industry payments, in order to determine if network-level characteristics are associated with patterns in opioid prescribing.

This dissertation has three aims: (1) to determine whether patterns in opioid prescribing exist across physician networks and association with specialties, (2) to empirically demonstrate influence industry can have on clinical decision-making via targeted marketing within provider networks, and (3) to attempt to parse whether certain physicians with greater peer influence result in similar opioid prescribing among network peers.

There are several findings and important implications related to this work. First, I find that primary care physicians who have more peer connections and more peers within a pain management specialty or surgery are more likely to have a higher median opioid prescribing rate across patient-sharing, hospital, and shared group clinic networks. Second, I find physicians who have any opioid payments are associated with three times the likelihood of at least one peer also having an opioid payment compared to physicians who did not have a similar payment. These physicians are more likely to belong to smaller and more interconnected patient-sharing networks. Finally, I perform a novel identification analysis of potential peer influencers to find certain provider-level characteristics that may shape peer prescribing behavior. The implications of this dissertation reveal that peer influence may serve as a potential mechanism for altering prescribing behavior and may be a lower-cost and efficacious way to increase adherence to evidence-based medicine.

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PATTERNS OF OPIOID-RELATED BEHAVIOR

by

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List of Abbreviations

AMA	American Medical Association
CDC	U.S. Centers for Disease Control and Prevention
CME	Continuing Medical Education
CMS	Centers for Medicare and Medicaid Services
CMS-HCC	CMS Hierarchical Condition Category
DEA	U.S. Drug Enforcement Agency
FDA	U.S. Food and Drug Administration
KOL	Key Opinion Leader
MME	Morphine milligram equivalent
NPI	National Provider Identifier
NPPES	National Plan and Provider Enumeration System
PDMP	Prescription drug monitoring program
PUF	CMS Part D Public Use File
SAMHSA	Substance Abuse and Mental Health Services Administration

Chapter 1: Introduction

Introduction

The dissemination of information and technologies within healthcare, while influenced by coverage and payment policies, is motivated to a large extent by the uptake of individual physicians. As such, the majority of healthcare treatment decisions are dictated by physician-specific characteristics and experience leading to large variations in treatment patterns by geography, training, and across organizations (Fisher et al., 2003; Song et al., 2022). Since the locus of healthcare decision-making is on providers and organizations, in 2013 the Institute of Medicine called for removing geography-based indexing payment and quality metrics and, instead, recommended targeting decision-making within provider networks (Committee on Geographic Variation in Health Care Spending and Promotion of High-Value Care et al., 2013; Newhouse & Garber, 2013). As healthcare is inherently hierarchical, identifying the role that physician networks across various levels (hospital, group, patient-sharing) have on clinical behavior could elicit new understandings on how information in healthcare is spread and, in turn, lead to policy solutions and interventions to modify physician behavior in the direction of evidence-based medicine.

To identify network patterns in physician behavior, social network analysis is a particularly useful tool that assess social structures, relationships and/or patterns between two or more nodes (e.g., people, groups, organizations) using graph theory. While data for social network analysis is often collected at the individual-level, the evaluation takes place at the structural level by describing the overall position and distance of nodes, the properties of network subgroups, or the overall patterning of the complete network. Appendix A1 provides additional details on the research methods involved in social network analysis.

Social network analysis is increasingly applied to examine dissemination, adoption, and influence in healthcare settings. Studies have used social network analysis to explore designing healthcare quality improvement teams (Meltzer et al., 2010), increasing electronic health record adoption (Zheng et al., 2010), allocating healthcare worker vaccinations (Polgreen et al., 2010), and evaluating influences on peer prescribing behavior (Donohue et al., 2018; Fattore et al., 2009). Most of this research demonstrates that social networks are important sources of influence within healthcare and can improve effectiveness and efficiency in decision-making and implementation of interventions. For instance, one systematic review found social influence within provider networks is positively related to improved care coordination, achieving quality and safety goals, and improving job satisfaction (Cunningham et al., 2012).

Conversely, some research demonstrates social network-related influence may lead to deviations from evidence-based medicine or result in suboptimal clinical behavior. Winn et al. (2021) find that physicians who share patients may be more likely to accept industry payments if they have multiple peers with payments. Since prior work has shown industry payments often lead to suboptimal prescribing behavior (e.g., prescribing more expensive drugs), the influence of peer acceptance of payment introduces a barrier to achieving goals of evidence-based care (Carey et al., 2020; Yeh et al., 2016; Zezza & Bachhuber, 2018).

Very little research has explored negative consequences of social network-related influence among physicians, especially with regards to opioid prescribing behavior. This is surprising given that more than 263,000 people have died from overdoses involving prescription opioids and it well-known that opioid drugmakers targeted provider networks and peer connections to increase prescribing of their products (*CDC Drug Overdose Statistics*, 2022; *Dreamland*, 2016).

The following chapters examine network relationships between providers across several network types (i.e., patient, hospital, and group clinic levels) and across different physician characteristics and relationships to determine whether patterns exist in opioid prescribing or opioid-related behavior. Determining if these differences exist contains implications for creating, implementing, and maintaining interventions to maximize evidence-based medicine to achieve its full potential of improving patient care.

Study Context

Prior to the COVID-19 pandemic, the opioid epidemic consistently ranked as the nation's top public health emergency. The origins of the opioid epidemic can be traced back to the aggressive marketing campaigns of opioid drugmakers in the mid-1990s leading to rapid increases in the number and dosages of opioids prescribed (i.e., the "first wave" of the epidemic). Prescription opioids, used to treat moderate to severe pain, can cause tolerance, dependence, and addiction, particularly in patients prescribed opioids long-term (National Institute on Drug Abuse, 2021). While the opioid epidemic is now primarily driven by illicit drugs like fentanyl and heroin, around one-tenth of all opioid overdose deaths are still attributable to those received via prescription (National Center for Health Statistic*s*, 2022).

In the 1990s, physicians began to increase prescribing of opioids after drugmakers and prominent physician "thought leaders" claimed the risks of addiction were minimal and that providers should treat pain as a "fifth vital sign" (*Dreamland*, 2016). It is now well established that these early messages promulgated by Purdue Pharma, the manufacturer of OxyContin (time-released oxycodone), were false and misleading. Prescription opioids are effective when used as prescribed and for patients with moderate to severe pain; however, they also have a high potential for addiction and abuse. As a result, many patients prescribed opioids developed dependency or addiction and began seeking out cheaper, more accessible illicit drugs like heroin or fentanyl in what later became known as the “second wave” and “third wave” of the opioid epidemic (*Dreamland*, 2016).

Efforts to curb the impact of the opioid epidemic range from needle exchange programs, expanded access to medication-assisted treatment, and overdose prevention education and treatment. Interventions specific to changing physician behavior include reforming and restraining the ability to prescribe opioids using Prescription Drug Monitoring Programs (PDMPs), task forces that monitor illegal opioid prescribing, creating evidence-based decision-making tools, and shining greater transparency on physician-industry relationships. In addition, efforts have been made to expand physician education on pain management, including additional continuing medical education (CME) courses, and increased academic detailing in which non-industry experts on pain instruct physicians.

In 2016, the Centers for Disease Control and Prevention (CDC) issued guidelines to help providers assess when to initiate opioid drug therapy for chronic pain, how to safely maintain, taper, or discontinue treatment, and how to assess risk in opioid-related harms (Dowell et al., 2016). These guidelines were created for primary care providers making opioid-related decisions about patients 18 years or older with chronic pain outside of those with cancer, or on palliative or end-of-life care. While the guidelines led to a decline in opioid prescribing, they also received intense criticism for being overly strict and for their adoption by physicians outside of primary care (Bohnert et al., 2018; Goldstick et al., 2021). In addition, many providers interpreted the suggested opioid dose and duration limits as strict thresholds leading to abrupt reduction or cessation in pain medications (Busse et al., 2016). Sudden changes or termination of a patient’s opioid prescription can have harmful consequences and is generally not advised unless there are immediate safety concerns. Patients who have abrupt reduction or cessation of opioids often experience withdrawal symptoms, pain, psychological distress, and are at higher risk of suicide or experiencing a substance use related event (e.g., overdose, seeking out illicit opioids) (Oliva et al., 2020).

The CDC subsequently acknowledged the misapplication of the guidelines and updated recommendations in November of 2022 after a public comment period (Dowell et al., 2022). These new guidelines emphasize physician judgment in deciding safe and effective opioid dosages for patients and clarify that they should not be used as “law, regulation or policy that dictates clinical practice.” However, some patients and providers still disagree with the updated guidelines and would like to see more protection in opioid access for chronic pain patients who report a reluctance among providers to address pain (Stone, 2022).

The controversy and confusion surrounding the CDC guidelines highlight the difficult balance regulators, policymakers, and clinicians have in attempting to provide appropriate pain management while accounting for decades of overutilization and abuse of opioids. Furthermore, the CDC guidelines and subsequent debate exposed the lack of training and knowledge that many non-specialized pain providers have regarding appropriate pain management. When physicians are confronted with indecision about how to prescribe, they may turn to clinical peers within their network seeking information or collaboration (Cornelissen et al., 2017; Sacerdote, 2001). Workplace learning from peers has historically been a large source of influence on individual provider behavior- from adoption of new drugs (Donohue et al., 2018; Prosser, 2003), to cancer screening (Pollack et al., 2012, 2017), to overall increased spending and utilization in Medicare (Landon et al., 2012).

This dissertation seeks to exploit potential indecision in opioid prescribing among non-specialized pain physicians as a means of investigating the role that physician peer networks have on influencing prescribing behavior. The aims of this dissertation are to (1) determine whether patterns in opioid prescribing exist across physician networks and association with specialties, (2) empirically demonstrate undue influence that industry can have on clinical decision-making via targeted marketing within provider networks, and (3) attempt to parse whether certain physicians with greater peer influence result in similar opioid prescribing among network peers.

Conceptual Model

Over the last twenty years there has been developing interest in researching social structures within healthcare to understand the role that provider networks have on healthcare performance and outcomes. Most of this work is heavily guided by Everett Rogers's work on the Diffusion of Innovation Theory (Rogers, 2003). Utilizing concepts from communication studies, this theory attempts to understand how an idea, practice, or product (i.e., the innovation) gains momentum and diffuses through a population or a social system. The theory examines factors like the innovation itself, channels where the innovation is communicated, the period over which the diffusion occurs, and the individuals within the social system that the innovation is spreading within. More specifically, the Diffusion of Innovation theory comprises five main steps that are not necessarily consecutive: (1) knowledge (i.e., becoming aware of the innovation); (2) persuasion; (3) decision-making; (4) implementation; (5) and finally, confirmation, wherein the adopter reinforces their decision to use the innovation by affirmation.

Not all innovations will move across these steps at the same rate; whether adoption occurs and at what rate will be determined by both characteristics of the innovation and the population.

Chapter 4 emphasizes this aspect of the theory by utilizing characteristics of the population based on potential rate of adoption. Specifically, this chapter emphasizes what Roger referred to as "Early Adopters," or opinion leaders, who often hold leadership positions, are eager to embrace change, and need very little information to be convinced.

Chapter 2 and Chapter 3 are conceptually motivated by the first four steps of the theory (i.e., knowledge, persuasion, decision-making and implementation) and attempt to exploit the behavior of prescribing (Chapter 2) or accepting payment (Chapter 3) to map out patterns in implementation at the network-level; however, prescribing behavior requires an additional conceptual model to understand how physicians may be evaluating information. Therefore, I also utilize Raisch's Model which provides a concept map for understanding prescribing behavior (Raisch, 1990). Developed by Dennis Raisch, a scholar in the field of Pharmacoeconomics, this popular model draws findings from fields of cognitive behavior, education, and communication studies to evaluate factors that lead to prescribing decision-making. For instance, prescribing may be influenced by individual and practice factors such as patient and provider demographics, patient clinical factors (e.g., diagnosis, treatment history, condition severity, comorbidities), and the organizational structure of the practice site. The remaining types of influence are divided into two groups: direct factors, or structural or administrative programs that restrict or establish standards for prescribing, and indirect factors, or things that change prescribing behavior by altering decision-making involved in the practitioner's thought process. Examples of direct factors include things like drug formularies, prescribing restrictions, and payment models, whereas examples of indirect factors include things like drug advertisements, industry detailing, colleagues, medical school education, and continuing medical education programs.

As outlined in Figure 1, the conceptual model built to support the empirical approach for each chapter blends ideas from the Diffusion of Innovation Theory and Raisch's Model. In addition, this model incorporates modern findings from the literature to update some of the theories underlying the main models which were developed more than 20 years ago. For example, neither model discusses or incorporates the type of healthcare network in which prescribing occurs or innovations transfuse (Donohue et al., 2018; McGettigan et al., 2001; Meltzer et al., 2010). Since this research is guided by assessing several different professional peer networks (e.g., patient-sharing, hospital, group clinic), I have included additional factors that may influence empirical findings.

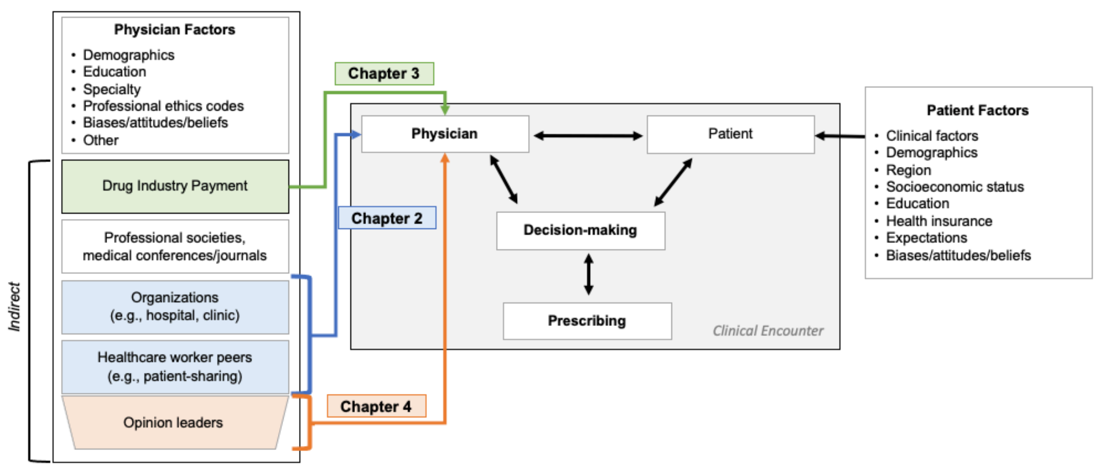

Figure 1: Adapted conceptual model

The resulting conceptual model includes influential physician- and patient-level factors that will influence interactions within the clinical encounter (shaded in gray), such as demographics, race/ethnicity, education level, and other interpersonal processes like expectations, biases, and attitudes. Indirect factors are the focus of this research and include relationships with the drug industry (Chapter 3), interactions within the healthcare system including information learned from peers at the hospital, group, or patient-sharing level (Chapter 2), and interactions with specific influential peer opinion leaders.

Literature Review

A substantial part of the health services literature is dedicated to evaluating area-level variations in utilization, quality, and spending across the United States. While sources of this variation are debated, evidence within the last two decades highlights the influential role that physician- and organizational-level factors have on establishing patterns of utilization. For instance, work by David Cutler and colleagues (2018) demonstrates that the most motivating factor determining variations in healthcare spending is physician beliefs about treatment, regardless of substantiation within clinical evidence or patient demand.

Recently, researchers have begun extending work on provider-level contributions to variations in healthcare to assess how providers within and across networks may construct larger patterns based on peer or organizational learning. For example, researchers find physician networks to be associated with variations in the utilization of cancer treatment (Pollack et al., 2012), adoption of electronic health records (Zheng et al., 2010), and differential patterns of surgery among black and white patients (Hollingsworth et al., 2015). These studies provide new insight into how networks can both enable and obstruct the diffusion of information and behavior patterns (DuGoff, Fernandes-Taylor, et al., 2018).

Though scholarship on the impact of physician networks is recent, researchers have long studied how technologies move through physician communities. In a landmark study, Coleman, Katz, and Menzel (1957) used survey data among Illinois physician communities to examine the diffusion of the antibiotic tetracycline. They find peer interactions influence a physician's decision to begin prescribing tetracycline, and more socially connected physicians adopt tetracycline at faster rates. While the work of Coleman, Katz, and Menzel has received criticism (Burt, 1987; Van den Bulte & Lilien, 2001), the most recent study to re-evaluate their claims validates the existence of peer influence, even after controlling for industry marketing and other systemwide influences (Iyengar et al., 2011).

In the following sections, I review relevant literature describing patterns of network-level prescribing behavior and the effects of industry and opinion leaders on prescribing behavior.

Network-Level Prescribing Behavior

In Chapter 2, I examine physician opioid prescribing patterns across several peer networks, including those at the patient-sharing, hospital-, and group-, network levels. Among the few studies that have examined physician networks and prescribing, most find some effect of peer influence on behavior. For instance, Donohue and colleagues (2018) estimate the effects of peer prescribing of three first-in-class medications on a physician's initiation of prescribing those medications. Using peer networks at the patient, hospital, medical group, and education training level, they find a physician's initiation of prescribing a new drug is heavily influenced by the number of peers who have also adopted those drugs. In addition, they find that a physician's location within their network increases a given social multiplier, or the number of physicians who might adopt a drug following peer adoption of the drug. For example, physicians in the top decile of patient-sharing who have the most connections to other physicians with a new drug adoption have nearly a 2-fold stronger influence on peers to adopt the drug compared to physicians in the top decile of prescribing volume. The magnitude of peer adoption effects is strongest within the patient-sharing network, a finding collaborated by other studies utilizing patient-sharing networks to measure collaboration or coordination (DuGoff, Fernandes-Taylor, et al., 2018).

While there is a paucity of research examining physician networks and prescribing, there are even fewer studies focusing on opioid prescribing behavior within networks. One study by Barnett and colleagues (2017) examines variations in opioid prescribing among physicians in the same emergency department and finds substantial variations in prescribing patterns. After classifying physicians as “low-intensity” or “high-intensity” opioid prescribers, they find the average rates of opioid prescribing to vary by a factor of three within the same hospital; furthermore, they find “high-intensity” prescribers are strongly associated with the likelihood of a patient becoming a longer-term opioid user.

While Barnett and colleagues (2017) evaluate physician opioid prescribing behavior within the same hospital, they do not account for the structural network location and the impact of peer effects. Another study by McClellan et al. (2020), however, does incorporate social network analysis to identify connections between physician network characteristics and potentially inappropriate opioid prescriptions. Using patient-sharing networks and provider usage of the CDC guidelines (e.g., more than 90 days continuous supply of high-dose opioids, overlapping opioid and benzodiazepine prescriptions), they find overall greater provider integration within a network is associated with a decrease in potentially inappropriate prescribing. Integration is defined within this study as a combination of eigenvector and degree centrality, both of which are standardized across each provider community. It is worth noting that they do not find uniform effects across all study outcomes, with provider network location having little to no overall effect on preventing overlapping benzodiazepine and opioid prescriptions.

Concomitant opioids and benzodiazepines use are considered a risky combination since, when combined, they increase the risk of overdose and impairment of cognitive functions. Stein and colleagues (2017) explore the impact of provider networks on co-prescribing opioids and benzodiazepines. They find concomitant prescribing varies substantially across physician patient-sharing networks, with rates in the highest quartile of prescribing over 2.5 times the rate in the lowest prescribing network. They also find the percentage of patients receiving opioids and benzodiazepines within provider networks most likely to prescribe both is over five times greater than similar patients in provider networks at the lowest quartile of prescribing.

While not an exhaustive list, the studies described above highlight associations between physician network characteristics and impacts on prescribing behavior. They also highlight the lack of investigation into how network-level characteristics influence opioid prescribing, particularly across multiple peer networks (e.g., patient, hospital, group clinic) and across different exposures to opioid-related industry payments or influential peer opinion leaders.

Opioid Industry Payments and Prescribing Behavior

Chapter 3 examines relationships between physicians, peer networks, and opioid-related payments from drugmakers. Industry payments often include money or gifts for things like food, travel for conferences, consulting, honoraria, or speaking events. Pharmaceutical companies argue physician-directed payments allow providers to stay up to date, and learn about new drugs, lab tests, and specific diseases; However, the ultimate purpose of these payments is to increase industry market share (L. M. Schwartz & Woloshin, 2019). While physicians often believe payments from pharmaceutical companies will not impact decision-making, research on influence and reciprocity demonstrates the contrary (Austad et al., 2011; Fischer et al., 2009; Sah & Fugh-Berman, 2013; Sah & Loewenstein, 2010; Wazana, 2000). Drugmaker payments can lead to increased health care costs or prescribing contrary to clinical guidelines. For example, many studies have found promotional payments associated with greater prescribing costs per patient and higher rates of brand-name prescribing compared to physicians with no promotional payments (Jones & Ornstein, 2016; Perlis & Perlis, 2016; Sharma et al., 2018; Yeh et al., 2016).

Despite evidence that promotional payments increase prescribing and investigative reports into the duplicitous nature of opioid drugmakers' marketing practices, only a few studies have analyzed relationships between providers and opioid promotional payments. Zezza and Bachuber (2018) find physicians who receive opioid-related payments increase their mean opioid expenditures, daily doses dispensed, and mean expenditures per daily dose compared to physicians who prescribed opioids but never accepted industry payment. These changes are notably larger for physicians who accepted higher total payment amounts. Another study finds industry payments encourage providers to prescribe more patented (and costlier) opioids (Beilfuss, 2019). This study also finds evidence that promotional payments cause spillover prescribing for less safe generic opioids (i.e., not abuse-deterrent formulations). Finally, there is evidence that opioid-related payments are associated with a higher likelihood of exceeding prescribing dosages that are recommended with caution (above 50 mg morphine equivalents per day (MME/day)) and those that should be avoided (above 90 mg MME/day) (Fleischman et al., 2019).

No study has yet to examine the impact of opioid payments and peer influence within provider networks on opioid prescribing; however, a few studies have evaluated opioid payments as they pattern and cluster across specialties. For instance, several studies have consistently found those in anesthesiology, pain management, neurology, and rehabilitation and sports medicine to be the main recipients of opioid-related payments (Hadland et al., 2017, 2018; Hollander et al., 2019; Inoue et al., 2020; Zezza & Bachhuber, 2018). While primary care physicians are among the lowest recipients of opioid-related payments, they are 3.5 times as likely to be in the highest opioid prescribing quartile if they were paid more than $100 from an opioid manufacturer (Hollander et al., 2019). Likewise, psychiatrists and neurologists were seven to thirteen times as likely to be in the highest opioid prescribing quartile if opioid manufacturers paid them more than $100 compared to their colleagues who did not receive payment (Hollander et al., 2019).

Physician Opinion Leaders and Prescribing Behavior

In Chapter 4, I narrow the focus on specific physicians who may have more influence on changing prescribing behavior due to their structural location within a network. In social network analysis, these individuals are often referred to as "opinion leaders" or "peer leaders," and are individuals who typically have somewhat higher social status, are effective communicators, amenable to innovation, and are often at the center of interpersonal communication networks (Rogers, 2003).

In the world of medicine, these individuals are sometimes called "key opinion leaders" (or "KOL"), a term coined by sociologists Paul Lazarsfeld and Elihu Katz who theorized that views or behaviors are changed at the influence of trusted peers within a network rather than advertising efforts (Katz et al., 1955). In the mid-1960s, Katz conducted a study contracted by Pfizer to understand what influences doctors to adopt new drugs. The study, later published in the book "Medical Innovation: a Diffusion Study," asks physicians to list interpersonal connections to understand how peer networks inform new drug adoption (Coleman et al., 1966). The results show that relationships with peers have a strong influence on a physician adopting a new drug, especially if a peer learns about the new drug from a provider who is well-connected.

Today, a "KOL" is usually in reference to physicians who hold relationships with the pharmaceutical industry. Since the 1950s, drug companies have utilized individual-level and prescription data to identify providers most amenable to their products in order to target promotional payments, tailor marketing and sales force efforts, and increase peer-to-peer awareness and adoption of a promoted drug (Fugh-Berman, 2008). Specifically, drug companies look for "KOLs" who are well-respected and able to influence colleagues. For example, Purdue Pharma (manufacturer of OxyContin) hired Dr. Russell Portenoy, Chairman of the Department of Pain and Palliative Care at Beth Israel Hospital in New York, to promote the narrative that opioids are non-addictive and safe (Keefe, 2021). Dr. Portenoy participated in Purdue-funded speaking events, Continuing Medical Education (CME) programs, and authored influential articles claiming opioids are safe at high doses without "serious adverse effects" (Keefe, 2021; Portenoy & Foley, 1986).

Peer opinion leaders in medicine do not always have to be KOLs; in fact, most physicians self-report as opinion leaders within their local peer network since they are representative of their community and face similar work settings and patient populations (Locock et al., 2001). Local opinion leaders can be physician-authors, have academic expertise (e.g., hold additional degrees such as a PhD or MBA), or hold a formal leadership position (e.g., clinical director of medicine).

Physician opinion leaders are known to influence peer adoption of technology or behavior change. Nair and colleagues (2010) found opinion leaders adopting new drug guidelines influenced peer adoption and provided between a 5 to 35 percent return on investment from promotional activities leveed at the opinion leaders. Likewise, Iyengar and colleagues (2015) investigated physician adoption of a risky prescription drug and found that those with high network centrality and high prescription volume are influential in persuading peers to adopt, but only during an initial "trial" period of the drug, and not necessarily on repeat use. They also found physicians are more susceptible to peer leader influence in adopting a risky drug if they have low confidence in their clinical judgment. Finally, Agha and Molitor (2015) found local opinion leaders, especially those who are prominent authors, are associated with patients in their region being 36 percent more likely to receive a new cancer drug. These findings increased drug adoption both within and outside the opinion leader's practice group.

No peer-reviewed studies currently examine physician opinion leaders among providers prescribing opioids to determine if there is a potential impact on prescribing behavior. While pharmaceutical companies no doubt analyze such networks and behavior to determine returns on marketing investments, little is known on what overall effect a physician who is well-connected has on influencing peer prescribing behavior. Part of the challenge in investigating this topic is delineating who is an opinion leader since there is considerable variation in how they are selected and defined. A study by Valente and Pumpuang (2007) assesses ten techniques for finding opinion leaders and reports that some leaders are those whom others turn to for advice (e.g., self-identification or peer nomination methods), while others are identified as those who have inherent leadership ability (e.g., expert identification). An additional challenge is that many strategies rely on survey data to elicit leader identities. Survey data collection presents unique challenges related to significant time and money costs, linkages to administrative claims data, and sensitivity to recall and sampling bias.

To circumvent many of the inherent challenges in opinion leader identification, some studies rely on egocentric network analysis using retrospective data by creating an index for approximating opinion leader status based on certain measures derived from survey data can be approximated from other empirical sources. For instance, one measure of opinion leadership measured in qualitative surveys is related to the level of expertise (Katz, 1957). Expertise relates to technical skills or knowledge in a particular field. As such, authorship, years of experience, and additional academic degrees are appropriate approximations of an otherwise subjective determination. For instance, Agha and Molitor (2015) define opinion leaders in their study on the uptake of cancer drug adoption based on academic citations and clinical trial role. Physicians who were top-cited authors in ten percent of their sample were deemed to have “superstar” influence. Furthermore, Chan (2020) finds decision-making in physician trainee teams is concentrated among a few senior providers lending credence to support that years of experience establishes a stronger influence among providers.

Another measure of opinion leadership relates to traits, or the personality aspects that allow an individual to earn or maintain status as an opinion leader (Katz, 1957). One essential aspect of this determination is an openness to innovation or an individual's ability to become an “early adopter” of technology (Rogers, 2003). Lo-Ciganic (2016) find early adopters of an anticoagulant drug tend to be younger, specialize in relation to the drug, and live in an urban area.

A final common theme of opinion leaders relates to social position. Peer comparison and relative social position, or ranking, play an important role in helping providers become aware of their performance (Navathe & Emanuel, 2016). One dimension of peer comparison is job title; providers who hold greater seniority have greater decision-making authority (Chan, 2020). Another dimension is peer-to-peer comparison within similar demographic groups (e.g., age, sex, race/ethnicity) and/or professional identity groups (e.g., attended the same medical school, residency program, or work in the same specialty). Evidence in education has long demonstrated that peer-to-peer effects have a strong influence over decisions and performance (Secomb, 2008).

Based on findings from the literature, Chapter 4 utilizes a given provider’s network structural location to approximate a potential opinion leader network among providers prescribing opioids.

Specifically, I draw upon a method used by Littero et al. (2017) who use a composite measure of eigenvector centrality and betweenness centrality to estimate individuals within a given population who connect dispersed groups via other highly connected individuals. In addition, I adjust for other relevant and available covariates that may influence an individual's likelihood of being more influential such ash industry payments, years practicing, medical school ranking, and specialty.

Overview

Chapter 2 examines physician opioid prescribers to patients in Medicare and whether prescribing patterns exist across several peer networks, including those at the patient-sharing, hospital-, and group-, network level. This chapter takes a specific focus on network characteristics among primary care providers since these physicians are the most frequent prescribers of opioids and are often not trained in pain medicine during their clinical education. Without specialized knowledge, primary care providers may rely on the expertise of peers with advanced pain training (e.g., pain management physicians, anesthesiologists) when coordinating care for Medicare patients; therefore, I sought to determine if patterns in opioid prescribing emerged by assessing various peer networks and composition of peer specialty groups. I find that primary care physicians do exhibit differences in opioid prescribing depending on peer network characteristics which is likely a reflection of peer specialization, training, and geography.

Chapter 3 describes relationships between physicians, peer networks, and opioid drugmakers. This chapter reviews the history of the opioid epidemic and how payments from drugmakers to physicians initiated the dramatic amount and dosage of opioids beginning in the early 1990s through the present day. Building off previous literature demonstrating the relationship between opioid-related promotional payments and increased prescribing, this chapter examines the association of physician network-level position among peers and the acceptance of opioid-related promotional payments. I find that physicians with opioid payments are significantly more likely to belong to smaller patient-sharing networks and have at least one peer with an opioid payment. This study provides further empirical clarification for how the opioid epidemic ignited and illustrates the susceptibility of physician decision-making to be targeted depending on network.

Chapter 4 explores the types of physicians who may have the most influence within their network based on network structural location. Using a unique combination of network measures that capture both the type of connection and path between connecting providers, I determine if differences in opioid prescribing exist across "potential influencer" physician characteristics and opioid prescribing of their associated network. The results demonstrate a potential new use in combing two social network metrics as a first attempt to identify potential physician influencers. I find that, among potential influencers, there appears to be similar characteristics that may shape peer prescribing behavior.

Chapter 5 summarizes the evidence across all three studies, discusses the policy implications, and provides suggestions for future research.

Chapter 2: Characterizing Physician Network Among Opioid Prescribers

Background

Opioid prescribing rates have fallen over the last decade, but the dosage of opioids prescribed per person is around three times higher than it was in 1999 and there remains significant variation in prescribing behavior from one provider to the next (Guy et al., 2017; Schieber et al., 2019). Variations in these prescribing patterns are not necessarily due to the underlying prevalence of pain within the population (Paulozzi et al., 2014), but rather may be due to provider-level factors such as specialty (Eid et al., 2018), geography (Kuo et al., 2016), education (Schnell & Currie, 2018), as well as a lack of consensus (Larson et al., 2018), or a lack of training (Leventhal et al., 2019), on how to treat patients with pain. Furthermore, this variation may also be due to differences in prescribing practices that vary at the network level among institutional or professional group settings (Barnett et al., 2017; Donohue et al., 2018; Stein et al., 2017).

Confusion about appropriate opioid prescribing is greatest among primary care providers who are often not trained in appropriate opioid prescribing or in managing substance use disorders during their clinical education (Miller et al., 2001; Tong et al., 2017). Research on decision-making in prescribing shows that when uncertainty or a lack of consensus exists, providers may turn to peers or rely on the cultural norms of prescribing within their network (Christakis & Fowler, 2011; Livorsi et al., 2015). For instance, Livorsi and colleagues (2015) find physicians are influenced to prescribe antibiotics, regardless of clinical necessary, if antibiotics are widely prescribed within their institution or by supervising physicians.

Primary care providers may also defer or rely on information learned from peers with specialized pain training (e.g., pain management physicians, anesthesiologists, physiatrists) when coordinating care for patients with pain. Provider coordination is particularly essential when managing care for older adults with an opioid prescription since this population is at an elevated risk for prescription substance abuse and often have co-occurring health conditions (*CDC Guideline for Prescribing Opioids for Chronic Pain*, 2019).

Determining if primary care providers have a pattern of opioid prescribing in accordance with the prescribing of peers within their professional network may indicate the presence of decision-making based on informal social networks. Understanding the composition of provider networks among opioid prescribers is an important step in improving care for patients with pain and for reducing potential prescription opioid-related harms. The goal of this research is to examine network-level patterns among providers prescribing opioids to patients enrolled in Medicare Part D and whether opioid prescribing patterns exist across several peer networks, including those at the patient-sharing, hospital-, and group-, network level.

Methods

Data Sources

I conducted a national cross-sectional study of a sample of providers prescribing opioids in Medicare using the American Medical Association (AMA) Physician Masterfile database and the Centers for Medicare and Medicaid Services (CMS) National Downloadable File. I obtained a commercially available copy of the Masterfile from Redi-Data; the Masterfile is a comprehensive dataset on 1.4 million allopathic and osteopathic physicians practicing in the United States. Data is entered during initial medical licensure and continuously verified by the AMA. The Masterfile contains information on physician characteristics such as age, gender, medical school and residency programs attended, credentials, and specialty. The CMS National Downloadable File contains year-level hospital and practice affiliation associated with providers.

To identify physicians prescribing opioids, I used the 2015 Centers for Medicare and Medicaid Services (CMS) Part D Prescriber Public Use File (PUF) which contains information on approximately 70 percent of all Medicare beneficiaries enrolled in Medicare Part D (*Part D Prescriber Data CY 2015 | CMS*, n.d.). The Part D PUF contains data on the total number of prescriptions written for patients in the given calendar year, total daily doses dispensed for the drug, total expenditures for the medication, and other average patient-level characteristics like gender, race/ethnicity, dual eligibility status, and the average Hierarchical Condition Category (CMS-HCC) risk score. In addition, physician-level characteristics like gender, credentials, primary specialty, practice address, and the number of Medicare patients per physician are also included. The AMA Masterfile was linked to the Part D PUF using the National Provider Identifier (NPI), a unique 10-digit number assigned to a provider for billing purposes.

The list of opioid drugs used for this study come from the CMS Part D Prescriber PUF Drug Category (See Appendix A1). All methadone and buprenorphine products, which are often used for substance abuse treatment, are excluded from the analysis.

Study Sample

Physician specialty was grouped into four categories: (1) primary care physicians (PCPs), or those who self-identify in the AMA Masterfile as having a primary specialty of internal medicine, family medicine, general/preventative medicine, geriatric medicine, and obstetrics and gynecology; (2) pain-related specialties (e.g., pain medicine, anesthesiology, and interventional radiology); (3) surgical specialties (e.g., general surgery, orthopedic surgery); and (4) medical specialties (e.g., emergency medicine, oncologists, urology). I excluded all physicians who were not clinically active, including residents, those in nonclinical roles like teaching, research, or administration, and those who were retired, semiretired, locum tenens, or without classification.

Physician characteristics analyzed include age, gender, specialty, years in practice, practice location, residency program, as well as ranking of medical school attended. Medical school ranking was determined using the 2015 *U.S. News & World Report* and further classified into four categories: schools ranked in the top 20, schools ranked between 21 and 50, schools ranked greater than 50, and schools that were unranked (including foreign medical schools) (*U.S. News & World Report*, 2015). I also included an indicator for whether physicians practiced within a state that had a mandatory access Prescription Drug Monitoring Program (PDMP) in 2015 (n=21 states), as determined from the National Alliance for Model State Drug Laws (*Natonal Alliance for Model State Drug Laws (NAMSDL)*, n.d.). Mandatory access PDMP laws require prescribers check the PDMP database prior to writing an opioid prescription in order to curb inappropriate opioid prescribing.

To adjust for the patient population that each physician cares for, I accounted for the total number of beneficiaries seen by each physician, the average beneficiary age of patients seen per physicians, and the average CMS-HCC risk score for patients seen by each physician. The CMS-HCC score uses demographic information and diagnoses on Medicare Fee-For-Service claims to measure each enrollee's comorbidities, with higher scores going to enrollees with more (or more severe) comorbidities.

Physician Networks

I constructed four physician networks indicative of different types of peer relationships. In the first, I constructed a patient-sharing network using the CMS Referral Data from 2015 (i.e., the most current available data). This publicly available dataset is derived from 100% Medicare claims data and lists the pairs of providers that share at least 11 patients during 30-, 60-, 90-, and 180-day intervals per year. I utilized the 30-day interval data since it most closely measures possible direct communication between providers. Previous studies have utilized similar patient-sharing networks to reflect communication opportunities between providers (Donohue et al., 2018; DuGoff, Cho, et al., 2018). I included only providers who share patients within the same hospital referral region (HRR) since I sought to measure networks around which the primary physician is located.

Using the patient-sharing network as the main sample (n=153,684), I then constructed three additional networks that may be indicative of peer communication. First, I constructed a hospital network by using provider affiliated hospital name and hospital address reported in the National Downloadable File. Second, I created a medical group practice network by using the unique organization identifier variable associated with a group practice reported in the National Downloadable File. Finally, I created a network that included physicians who shared both a hospital and medical group practice affiliation. Each of the four physician networks (i.e., patient sharing, hospital, group, and combined hospital and group network) are analyzed separately as unique networks, however, a given provider may appear in multiple networks. For example, a physician who shares patients with another provider may also share the same hospital affiliation and thus will appear in both patient sharing and hospital networks.

Measures

The primary outcome is a binary variable indicating whether a given physician wrote above the median rate of opioid prescriptions in 2015. The rate of opioid prescriptions is defined as the total number of opioid claims reported per provider divided by the total number of Medicare Part D claims multiplied by 100.

The network measures in the analysis include degree centrality (i.e., the number of shared patients between physicians within a network), betweenness centrality (i.e., the number of times a physician acts as a link along the shortest path between two other physicians, divided by the shortest paths between all the physicians within a network), and transitivity (i.e., the "clustering coefficient," or the number of closed triplets in a physician's network over the total number of closed triplets within the network). Additional information and interpretations for each social network centrality metric used is provided in Appendix A1. Degree centrality is weighted by the average number of shared patients between physicians in order to capture the relative intensity of shared relationships between providers. Physicians are removed if they were linked to another provider in a different HRR (n=17,751). To calculate transitivity, which requires a provider have at least two other ties within the network, I removed anyone with less than three connections (n=14,252).

Additional physician-level covariates include gender, census region (Midwest, Northwest, South, West), number of years practicing, medical school ranking, and the total number of Medicare beneficiaries per provider. Aggregate average patient-level variables per provider include patient age and CMS-HCC risk score.

Statistical Analysis

Summary statistics were conducted across each network. Modified robust Poisson regressions were run to estimate the adjusted incidence rate ratio (aIRR) for the outcome of interest. A modified robust Poisson regression, which combines a log Poisson regression with robust variance estimation, are commonly used to estimate risk ratios for common outcomes when using a logistic regression may overestimate the risk (W. Chen et al., 2018). I adjusted for relevant confounders and clustered standard errors at the HRR level. All social network analyses are performed using R version 1.3 using the igraph package version 1.2.6 (Gabor & Tamas, 2006). All other statistical analyses are run with Stata/MP version 16.1 (*Stata/MP*, 2022).

Sensitivity Analysis

To address differences in provider networks that may arise from utilizing the 30-day CMS Referral dataset, I ran a sensitivity analysis using the same modified robust Poisson regression described above utilizing the 90-day CMS Referral dataset to determine if significant differences in provider networks would alter findings.

Results

Our final patient-sharing sample includes 153,684 physicians, of whom 95% share peers within the same hospital network, 61% share peers within a group clinic, and 59% share peers with the same hospital and group clinic affiliation (Table 1). Opioid prescribers in the sample are predominately men (78%), primary care providers (47%), and physicians in the South (41%).

Table 1: Descriptive characteristics of opioid prescribers in Medicare, 2015

Characteristic	**Patient Network**	**Hospital Network**	**Group Network**	**Hospital + Group**
No. physicians, N (%)	153,684 (100%)	145,884 (95%)	93,633 (61%)	91,167 (59%)
Female, N (%)	33,541 (22%)	31,622 (22%)	23,005 (25%)	22,316 (24%)
Age, mean (SD)	51 (11)	51 (11)	50 (11)	50 (11)
Years practicing, mean (SD)	24 (11)	24 (11)	22 (11)	22 (11)
Mandatory access PDMP, N (%)	50,247 (33%)	47,488 (33%)	29,720 (32%)	28,768 (32%)
U.S. Census Region, N (%)				
Northeast	27,799 (18%)	26,350 (18%)	17,315 (18%)	16,899 (19%)
Midwest	37,357 (24%)	36,172 (25%)	25,987 (28%)	25,641 (28%)
South	63,487 (41%)	60,380 (41%)	36,440 (39%)	35,414 (39%)
West	25,041 (16%)	22,982 (16%)	13,891 (15%)	13,208 (14%)
Medical School Ranking, N (%)				
Top 20	12,334 (8%)	11,582 (8%)	7,685 (8%)	7,477 (8%)
Ranked 21 to 50	28,120 (18%)	26,665 (18%)	18,462 (20%)	17,980 (20%)
Ranked 50+	32,935 (21%)	31,357 (21%)	20,435 (22%)	19,938 (22%)
Unranked or foreign	80,295 (52%)	76,280 (52%)	47,051 (50%)	45,767 (50%)
Specialty, N (%)				
Primary Care	72,378 (47%)	68,491 (47%)	46,313 (49%)	45,032 (49%)
Pain-related specialties	6,298 (4%)	5,443 (4%)	3,178 (3%)	2,832 (3%)
Surgery specialties	24,015 (16%)	23,236 (16%)	12,635 (13%)	12,420 (14%)
Other specialties	50,993 (33%)	48,714 (33%)	31,507 (34%)	30,878 (34%)

Note: Mandatory access prescription drug monitoring programs (PDMPs) is a binary indicator that states whether prescribers are required to check with PDMP for at least some patients;

Beneficiary characteristics have little variability across each network with an average of three (SD: 2) opioid claims per beneficiary per provider, or an opioid prescribing rate of around 14% (SD: 18) (Table 2). Providers prescribe an average of five (SD: 2) long-acting opioids per beneficiary annually, or a prescribing rate of 18% (SD: 12).

Table 2: Medicare beneficiary and prescribing characteristics per provider, 2015

Characteristic	**Patient Network**	**Hospital Network**	**Group Network**	**Hospital + Group**
No. physicians, N (%)	153,684 (100%)	145,884 (95%)	93,633 (61%)	91,162 (59%)
Medicare beneficiary characteristics				
No. beneficiaries[†]*, mean (SD)	306 (253)	306 (254)	295 (254)	294 (254)
Opioid prescription, % (SD)	29 (22)	29 (21)	27 (20)	27 (20)
Female, mean % (SD)	59 (11)	58 (11)	58 (12)	58 (12)
Non-white, mean % (SD)	32 (27)	31 (26)	29 (25)	28 (25)
Age, mean (SD)	71 (4)	71 (4)	71 (4)	71 (4)
HCC, mean (SD)	1.6 (0.7)	1.7 (0.7)	1.7 (0.8)	1.7 (0.8)
Prescribing characteristics				
Opioid claim per beneficiary*				
Mean (SD)	3 (2)	3 (2)	3 (2)	3 (2)
Median (min, max)	2 (1, 33)	2 (1, 33)	2 (1, 33)	2 (1, 33)
Opioid prescribing rate**				
Mean % (SD)	14 (18)	14 (18)	14 (17)	13 (17)
Median %	6	6	6	6
Long-acting opioid claim per beneficiary*				
Mean (SD)	5 (2)	5 (2)	5 (2)	5 (2)
Median (min, max)	5 (1, 27)	5 (1, 27)	5 (1, 27)	5 (1, 27)
Long-acting opioid prescribing rate**				
Mean % (SD)	18 (12)	18 (12)	19 (12)	19 (12)
Median %	15	15	16	16

HCC=hierarchical condition category
[†]refers to the average number of patients per provider across all hospital referral region networks
*observations less than 11 are censored by CMS to protect patient privacy
**prescribing rates refer to the total number of opioid claims per provider divided by the total number of all drug claims multiplied by 100

In terms of characteristics in the main patient-sharing network, most peers are primary care providers (mean: 43%, SD: 28) and prescribe similar opioid claims per beneficiary (mean: 12%, SD: 10) and opioid prescribing rates (between 12% to 13%) (Table 3). Most providers (28%) fall into the top 75% quartile in degree centrality, indicating they have many peers with whom they share patients with; these findings changed across the hospital and group networks with most providers falling into the first quadrant of degree centrality indicating fewer patient-sharing peers. Betweenness centrality was mostly uniform for the patient-sharing, hospital, and combined hospital and group networks; however, physicians in the group clinic were predominately within the first quadrant indicating they do not play a large role in controlling information flow within the network. Finally, physicians in the group clinic network are half as likely to fall within the 75th percentile of transitivity indicating that they belong to more dense networks.

Table 3: Medicare beneficiary characteristics per provider, 2015

Variable	**Patient Network**	**Hospital Network**	**Group Network**	**Hospital + Group**
No. physicians, N (%)	153,684 (100%)	145,884 (95%)	93,633 (61%)	91,162 (59%)
Peers per physician, mean (SD)	15 (18)	15 (17)	7 (8)	13 (14)
HCC score of patients among peers, mean (SD)	1.7 (0.5)	1.8 (0.5)	1.7 (0.7)	1.7 (0.6)
Peer specialties, mean % (SD)				
Primary Care	43 (28)	43 (28)	49 (38)	47 (30)
Pain-related specialties	4 (12)	4 (11)	4 (15)	3 (11)
Surgery specialties	11 (16)	11 (16)	11 (24)	11 (18)
Other specialties	42 (27)	42 (27)	36 (36)	39 (28)
Peer group opioid prescribing rates*, mean % (SD)				
Opioid prescribing	12 (10)	12 (9)	13 (13)	12 (10)
Long-acting opioid	9 (8)	10 (8)	10 (10)	10 (9)
Degree centrality, N (%)				
Q1	33,679 (22%)	39,049 (27%)	34,774 (37%)	25,271 (28%)
Q2	36,738 (24%)	35,783 (25%)	19,140 (20%)	20,773 (23%)
Q3	42,928 (28%)	35,316 (24%)	18,824 (20%)	23,057 (25%)
Q4	40,339 (26%)	35,736 (25%)	20,895 (22%)	22,061 (24%)
Betweenness centrality, N (%)				
Q1	27,093 (18%)	36,472 (25%)	34,126 (36%)	22,791 (25%)
Q2	41,387 (27%)	36,470 (25%)	13,266 (14%)	22,790 (25%)
Q3	42,602 (28%)	36,471 (25%)	22,833 (24%)	22,791 (25%)
Q4	42,602 (28%)	36,471 (25%)	23,408 (25%)	22,790 (25%)

Transitivity centrality, N (%)				
Q1	38,452 (25%)	36,471 (25%)	23,505 (25%)	23,904 (26%)
Q2	38,390 (25%)	36,581 (25%)	24,667 (26%)	21,679 (24%)
Q3	38,435 (25%)	36,368 (25%)	45,461 (49%)	23,260 (26%)
Q4	38,407 (25%)	36,464 (25%)	--	22,319 (24%)

*prescribing rates refer to the total number of opioid claims per provider divided by the total number of all drug claims multiplied by 100

I assessed whether physicians prescribe above the median opioid prescribing rate defined as the total number of opioid claims divided by the total number of claims for all other drugs associated with a given provider (Table 4). Across all networks, primary care providers are much less likely to be above the median opioid prescribing rate (aIRR: 0.57, 95% CI: 0.54, 0.60 for the patient-sharing network) compared to all other specialists. In the patient-sharing network, having a higher opioid prescribing rate varies by the composition of peer specialty groups with those having predominately pain-related or surgery peers prescribing higher than the median (aIRR: 1.12, 95% CI: 1.08, 1.16 and 1.28, 95% CI: 1.24, 1.32, respectively) while providers who are less likely to prescribe at rates above the median predominately have peers in other specialties (aIRR: 0.81, 95% CI: 0.78, 0.83).

In the patient-sharing network, primary care providers were more likely to be over the median opioid prescribing rate if they were in the third quartile for degree centrality (i.e., top quartile compared to the third quartile aIRR: 1.07, 95% CI: 1.04, 1.10), more likely to belong to more dense networks (i.e., top quartile compared to the third quartile for betweenness centrality aIRR: 1.07, 95% CI: 1.05, 1.10), and more likely to belong to highly clustered networks (i.e., top quartile compared to the first quartile for transitivity centrality aIRR: 1.17, 95% CI: 1.14, 1.19), however, the magnitude of these associations is small. In the group and combined hospital and group networks, a similar but stronger association was found with providers being much more likely to prescribe over the median opioid prescribing rate if they fell within the top quadrant of degree centrality (i.e., top quartile compared to the first quartile aIRR: 1.16, 95% CI: 1.11, 1.22 and 1.13, 95% CI: 1.08, 1.17, respectively). In the hospital and group networks, providers in the top half of transitivity centrality were much more likely to prescribe over the median opioid prescribing rate (i.e., top quartile compared to the third quartile aIRR: 1.16, 95% CI: 1.14, 1.19 and 1.16, 95% CI: 1.12, 1.21, respectively).

I replicated the main analysis described above in a sensitivity analysis using the 90-day CMS Referral dataset from 2015 to determine if significant differences in provider networks would alter findings based on the 30-day referral networks. Of the providers appearing in the 30-day referral dataset, around 72% also appeared in the 90-day referral dataset (n=110,065). While additional providers were added to the analysis, the magnitude and direction of the coefficients were not found to be meaningfully different between 30- or 90-day networks (Table 5).

Table 4: Results of modified Poisson regression assessing whether physicians prescribed above the median prescribing rate, 2015

Variables	**Model 1:** Patient network (n=153,684)		**Model 2:** Hospital network (n=145,884)		**Model 3:** Group network (n=93,633)		**Model 4:** Hospital + group network (n=91,162)	
	IRR	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
Specialty (ref=non-primary care specialties)								
Primary Care	0.57***	(0.54, 0.60)	0.57***	(0.54, 0.60)	0.63***	(0.60, 0.66)	0.62***	(0.59, 0.65)
Peers in primary care, % of total peer network (ref= no peers)								
≤10%	0.85***	(0.80, 0.90)	0.85***	(0.80, 0.91)	0.82**	(0.73, 0.93)	0.89***	(0.83, 0.97)
11% to 50%	0.90***	(0.88, 0.92)	0.92***	(0.89, 0.94)	0.88***	(0.85, 0.91)	0.88***	(0.85, 0.91)
50%+	0.92***	(0.90. 0.95)	0.94***	(0.91, 0.97)	0.86***	(0.83, 0.90)	0.88***	(0.85, 0.92)
Peers in pain-related specialties, % of total peer network (ref=no peers)								
≤10%	0.92***	(0.90, 0.94)	0.92***	(0.89, 0.94)	0.83***	(0.79, 0.88)	0.90***	(0.87, 0.94)
11% to 50%	1.12***	(1.09, 1.14)	1.12***	(1.10, 1.14)	1.11***	(1.08, 1.14)	1.14***	(1.10, 1.17)
50%+	1.12***	(1.08, 1.16)	1.14***	(1.09, 1.19)	1.24***	(1.17, 1.30)	1.19***	(1.13, 1.25)
Peers in surgery specialties, % of total peer network (ref=no peers)								
≤10%	1.01	(0.99, 1.04)	1.01	(0.98, 1.03)	0.96	(0.91, 1.00)	0.99	(0.96, 1.02)
11% to 50%	1.07***	(1.04, 1.09)	1.06***	(1.03, 1.08)	1.02	(0.99, 1.06)	1.07***	(1.04, 1.09)
51%+	1.28***	(1.24, 1.32)	1.28***	(1.24, 1.32)	1.41***	(1.35, 1.48)	1.39***	(1.34, 1.45)
Peers in other specialties, % of total peer network (ref=no peers)								
≤10%	1.06**	(1.02, 1.10)	1.03	(0.99, 1.07)	1.16***	(1.08, 1.23)	1.08***	(1.03, 1.13)
11% to 50%	0.91***	(0.89, 0.93)	0.91***	(0.89, 0.93)	0.99	(0.97, 1.02)	0.95***	(0.92, 0.98)
50%+	0.81***	(0.78, 0.83)	0.81***	(0.79, 0.83)	0.84***	(0.81, 0.88)	0.87***	(0.84, 0.90)
Degree (ref= Q1)								
Q2	1.02*	(1.00, 1.04)	1.03***	(1.01, 1.04)	1.03**	(1.01, 1.06)	1.05***	(1.02, 1.07)
Q3	1.07***	(1.04, 1.10)	1.09***	(1.07, 1.12)	1.08***	(1.05, 1.11)	1.14***	(1.10, 1.17)
Q4	1.04*	(1.01, 1.08)	1.04**	(1.01, 1.08)	1.16***	(1.11, 1.22)	1.13***	(1.08, 1.17)
Betweenness (ref=Q1)								
Q2	1.07***	(1.05, 1.09)	1.05***	(1.07, 1.11)	1.12***	(1.08, 1.15)	1.09***	(1.05, 1.12)
Q3	1.07***	(1.05, 1.10)	1.04***	(1.14, 1.19)	1.17***	(1.13, 1.22)	1.09***	(1.05, 1.14)
Q4	0.99	(0.96, 1.02)	0.95***	(1.12, 1.17)	1.17***	(1.11, 1.23)	1.03	(0.98, 1.08)
Transitivity (ref=Q1)								

Q2	1.11***	(1.09, 1.13)	1.09***	(1.07, 1.11)	1.07***	(1.04, 1.09)	1.08***	(1.05, 1.10)
Q3	1.18***	(1.16, 1.21)	1.16***	(1.14, 1.19)	1.16***	(1.12, 1.21)	1.13***	(1.10, 1.16)
Q4	1.17***	(1.14, 1.19)	1.14***	(1.12, 1.17)	--	--	1.14***	(1.09, 1.18)

Note: All models adjust for specialty, gender, tenure, metropolitan practice, region, specialty, average age among beneficiaries, average HCC score among beneficiaries, and HRR; **p-value<0.05; **p-value<0.01; ***p-value<0.001*

Table 5: Results of sensitivity analysis utilizing the 90-day CMS Referral dataset, 2015

Variables	**Model 1:** Patient network (n=153,753)		**Model 2:** Hospital network (n=113,352)		**Model 3:** Group network (n=86,793)		**Model 4:** Hospital + group network (n=75,733)	
	IRR	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
Specialty (ref=non-primary care specialties)								
Primary Care	0.45***	(0.43, 0.48)	0.48***	(0.45, 0.51)	0.48***	(0.45, 0.50)	0.45***	(0.43, 0.48)
Peers in primary care, % of total peer network (ref= no peers)								
≤10%	0.84***	(0.80, 0.89)	0.85***	(0.80, 0.90)	0.94	(0.84, 1.05)	0.82***	(0.76, 0.88)
11% to 50%	0.90***	(0.89, 0.92)	0.97**	(0.94, 0.99)	0.92***	(0.89, 0.95)	0.90***	(0.88, 0.93)
50%+	0.92***	(0.89, 0.94)	0.98	(0.95, 1.01)	0.87***	(0.83, 0.91)	0.90***	(0.87, 0.94)
Peers in pain-related specialties, % of total peer network (ref=no peers)								
≤10%	0.94***	(0.91, 0.96)	0.94***	(0.92, 0.96)	0.87***	(0.82, 0.92)	0.91***	(0.88, 0.94)
11% to 50%	1.05***	(1.03, 1.07)	1.06***	(1.03, 1.08)	1.05***	(1.02, 1.08)	1.07***	(1.04, 1.10)
50%+	1.08***	(1.04, 1.11)	1.15***	(1.11, 1.20)	1.17***	(1.12, 1.22)	1.13***	(1.08, 1.18)
Peers in surgery specialties, % of total peer network (ref=no peers)								
≤10%	1.02*	(1.00, 1.05)	1.02	(1.00, 1.05)	1.01	(0.96, 1.07)	1.03	(1.00, 1.06)
11% to 50%	1.05***	(1.02, 1.07)	1.04***	(1.02, 1.06)	1.05**	(1.02, 1.08)	1.05***	(1.03, 1.07)
51%+	1.16***	(1.12, 1.21)	1.21***	(1.17, 1.26)	1.28***	(1.23, 1.34)	1.22***	(1.18, 1.27)
Peers in other specialties, % of total peer network (ref=no peers)								
≤10%	1.11***	(1.06, 1.16)	1.13***	(1.07, 1.19)	0.96	(0.87, 1.07)	1.05	(1.00, 1.12)
11% to 50%	0.94***	(0.92, 0.96)	0.95***	(0.93, 0.97)	0.91***	(0.89, 0.94)	0.90***	(0.88, 0.93)
50%+	0.85***	(0.82, 0.87)	0.88***	(0.85, 0.91)	0.87***	(0.82, 0.91)	0.86***	(0.83, 0.89)
Degree (ref= Q1)								
Q2	1.03	(1.01, 1.05)	1.04***	(1.02, 1.07)	0.99	(0.96, 1.02)	1.08***	(1.05, 1.11)
Q3	1.09	(1.05, 1.12)	1.08***	(1.05, 1.11)	1.04*	(1.00, 1.08)	1.16***	(1.12, 1.20)

Q4	1.06	(1.02, 1.10)	1.04	(1.00, 1.08)	1.13***	(1.08, 1.18)	1.12***	(1.07, 1.17)
Betweenness (ref=Q1)								
Q2	1.04	(1.02, 1.06)	1.03	(1.01, 1.05)	--	--	1.04**	(1.01, 1.07)
Q3	1.05	(1.03, 1.07)	1.02	(1.00, 1.05)	1.03**	(1.01, 1.05)	1.07***	(1.04, 1.11)
Q4	0.96	(0.93, 0.98)	0.95**	(0.92, 0.98)	1.04**	(1.01, 1.07)	0.99	(0.96, 1.02)
Transitivity (ref=Q1)								
Q2	1.05	(1.03, 1.07)	1.06***	(1.04, 1.08)	0.96*	(0.93, 1.00)	1.07***	(1.04, 1.09)
Q3	1.11	(1.09, 1.13)	1.11***	(1.09, 1.14)	1.06***	(1.03, 1.10)	1.14***	(1.11, 1.17)
Q4	1.10	(1.08, 1.12)	1.09***	(1.07, 1.11)	--	--	1.14***	(1.11, 1.17)

Note: All models adjust for specialty, gender, tenure, metropolitan practice, region, specialty, average age among beneficiaries, average HCC score among beneficiaries, and HRR; **p-value<0.05; **p-value<0.01; ***p-value<0.001*

Discussion

I found primary care providers who have more connections (i.e., higher degree centrality) and more peers within a pain management specialty or surgery are more likely to have a higher median opioid prescribing rate across all networks after controlling for various physician and patient-level confounders. The magnitude of the associations between network centrality and opioid prescribing rate are small and suggest future research is needed to better understand what impact network connections have on guiding opioid prescribing behavior based on prescribing guidelines.

These findings are likely due to the intrinsic nature of the network themselves; in other words, primary care physicians share more patients with a pain-related specialist or surgeon may prescribe more opioids since they are more likely to be indicated for patients who have just received surgery or have a pain-related diagnosis. The findings for betweenness (i.e., measure of distance) and transitivity centrality (i.e., measure of clustering) are more challenging to interpret since the findings demonstrate physicians in each network have similar distribution across quadrants with only marginal increases in opioid prescribing. When replicating our results using a longer-term referral network (i.e., the 90-day referral dataset), we found no meaningful difference in prescribing, peer composition, or network centrality metrics.

Similar to these findings, Donohue and colleagues (2018) utilized comparable network construction and find patient-sharing physicians in the top ten percent degree centrality were nearly twice as likely to influence peer adoption to uptake a new drug compared to physicians in the top percentiles of prescribing volume. Results for networks created at the hospital and group clinic level were found to be not significant or unclear (Donohue et al., 2018). Other studies have also supported similar findings in terms of providers who are more integrated being less likely to over-prescribe opioids; for instance, McClelland and colleagues (2020) analyzed shared-patient networks in Medicaid to find subsequent prescribing of high-dose opioids for chronic pain or overlapping opioid prescriptions were reduced when providers were more integrated. However, it is suggested that less integrated providers (i.e., who share fewer patients) have higher rates of potentially inappropriate prescriptions.

Prescribing behavior that varies at the network-level has implications for influencing providers to adhere to clinical guidelines or, conversely, may indicate avenues of undue or sub-optional prescribing behavior. For example, adherence to clinical guidelines or uptake of a new medication is increased when respected colleagues adopt or exhibit the practice to their peers (Agha & Molitor, 2015). On the other hand, physicians may be influenced by peers to engage in prescribing behavior incentivized by industry promotional payments, rather than clinical necessity or cost-effectiveness (Agha & Zeltzer, 2019). The extent of this influence, whether optimal or sub-optimal, is dependent on network characteristics such as the number of peers within a given provider's network (i.e., degree centrality), the "closeness" of those peers, (i.e., betweenness centrality), and whether connections between providers are "dense" (i.e., transitivity centrality). While I attempted to parse out the influence of these network characteristics among opioid prescribers, future research should explore to what extent other indirect factors like provider beliefs and training inform prescribing decisions.

This study has several limitations. First, I relied on information within the publicly available Part D PUF which contains information aggregated at the yearly level. This precludes adjusting for temporal confounding, or in other words, determining whether peer influence within a given network occurred in the days or months before or after an opioid prescription was written. Second, the data does not contain clinical or diagnosis data and therefore, I cannot make any determinations about the appropriateness of an opioid prescription. Third, the sample includes only physicians who prescribe to patients enrolled in Medicare Part D which is not generalizable to the prescribing behavior of all physicians in the United States. It is worth noting, however, that less than one percent of physicians have opted out of Medicare (Boccuti et al., 2013). In addition, since I only focus on patients enrolled in Medicare Part D, I do not capture a representative sample of a physician's entire prescribing behavior that likely includes non-Medicare patients. In addition, there is a possibility for unmeasured confounding related to individual-level aspects of providers not captured in the data such as personality, opinions about opioid prescribing, and adherence to clinical evidence and guidelines.

Conclusion

This study demonstrates that primary care physicians with more peer connections to physicians in specialized pain fields may have higher opioid prescribing rates. This study highlights the often overlooked influence of peer network composition on variability in opioid prescribing behavior.

Chapter 3: Association of Physician Networks with Receipt of Opioid-Related Promotional Payments

Background

Opioid-related payments to providers are known to increase prescribing of the promoted opioid product and can lead to subsequent elevated mortality from opioid-related overdoses (Hadland et al., 2019). Payments include compensation for consulting, gifts, food, travel, education, grants, research, ownership, licenses, royalties, speaker honoraria and charitable contributions, among others. Since 2013, all manufacturers are required to report payments made to physicians under the Physician Payments Sunshine Act; however, financial relationships between industry and physicians started decades earlier. In the 1990s, pharmaceutical companies like Purdue Pharma initiated aggressive marketing campaigns to increase prescribing of opioids for non-cancer pain. As a result, these marketing activities have been linked to igniting the first wave of the opioid epidemic, the rapid increase in prescription opioids (Alpert et al., 2021). Years later, opioid promotional payments among physicians remain common with around 1 in 12 physicians receiving an opioid-related payment between 2013 to 2015, and around 1 in 5 among family physicians (Hadland et al., 2017).

The majority of prior research on promotional payment influence focuses on individual provider behavior and ignores network-level factors, such as the physician's position among peers and whether peer receipt of payment influences individual receptivity to accepting a payment. There are several potential intersecting pathways in which peers may influence provider behavior or vice versa. First, colleagues may communicate information relating to work, but also may share opinions, advice, and whether they hold industry relationships. While parsing communication related to industry relationships is difficult, structural effects like the number of peers with payments and network position of a provider may serve as a proxy for industry communication (Stuart & Ding, 2006). For instance, prior work utilizes similar indicators to show individuals within academia are more likely to become entrepreneurs or patent holders if they have peers engaging in related commercial activity (Azoulay et al., 2005; Stuart & Ding, 2006).

A second pathway of peer-to-peer influence is the cultural norm of accepting industry payments within a network. Research has shown that higher peer acceptance of general industry payments is associated with individual acceptance of payments (Winn et al., 2021). In other words, multiple peer relationships with industry can lower the barrier for a given physician to also be receptive to industry payments as they may perceive the relationship as an accepted practice within their workplace. The amplifying effect that a norm of industry relationships sets can have a large return on investment for drugmakers. In fact, one study finds promotional payments went disproportionately to physicians with multiple peers and these peers increased usage of promoted drugs by two percent on average (Agha & Zeltzer, 2019).

Finally, certain peers within a network may have a disproportionate amount of influence on other peers. These peers have been referred to as "key opinion leaders" or those who are well-connected within a network with greater sway over colleagues due to social or professional ranking. Models on behavior and influence suggest that these influential individuals can increase adoption and momentum of an innovation if they are first to subscribe to the product, idea, or behavior (Raisch, 1990). Among physician opinion leaders who are clinical investigators and top-cited authors, local peers have been found to increase prescribing of new cancer drugs (Agha & Molitor, 2015).

I examined the association of physician network-level position among peers and the acceptance of opioid-related promotional payments using national publicly available datasets from 2015. First, I created a social network analysis by constructing networks based on physicians who share patients. Second, I assessed the proportion of a physician's peers who received opioid payments alongside other network characteristics including the overall number of shared peers, how central the physician is within the network, and how dense the network is. Third, among providers with opioid-related payments, I determined the influence of the number and dollar amount of payments on network-level characteristics.

Methods

Data Sources

To establish patient-sharing networks, I use the CMS Referral Data from 2015. As previously described in Chapter 2, this publicly available dataset is derived from 100% Medicare claims data and lists pairs of providers that share at least 11 patients during 30-, 60-, 90-, and 180-day intervals per year. I utilized the 30-day interval data since it most closely measures possible direct communication between providers.

I identified physicians with opioid-related promotional payments using the 2015 general payment files within the Sunshine Act's Open Payments data from Centers for Medicare and Medicaid Services (CMS) (*CMS Open Payments*, n.d.). Open Payment data provide legally mandated information on the amount of industry payments made to physicians, the drug name associated with payment, and date of payment. The list of opioid drugs used to subset the Open Payment dataset comes from the CMS Part D Prescriber PUF Drug List Summary which contains an opioid flag variable (see Appendix Figure A2).

I merged additional physician characteristics within the American Medical Association (AMA) Masterfile and the CMS National Downloadable File to the Open Payment data using the national provider identifier (NPI), a unique 10-digit number assigned to each healthcare provider. The Masterfile contains information on physician characteristics such as age, gender, medical school and residency programs attended, credentials, and specialty. The National Downloadable File contains physician characteristics such as physician-hospital affiliation.

Physician specialties were grouped into four categories including general medicine (internal medicine, family medicine, general practice, pediatric medicine, obstetrics/gynecology, hospitalists, geriatric medicine, and preventive medicine), surgery, pain-related specialties (pain management, physiatrists, anesthesiology, and interventional radiology), and other specialists (e.g., cardiology, oncology, emergency medicine, psychiatry). To determine medical school ranking, I used the 2015 *U.S. News & World Report* to create four categories: schools ranked in the top 20, schools ranked between 21 and 50, schools ranked greater than 50, and unranked schools (including foreign medical schools) (*U.S. News & World Report*, 2015). I identified teaching hospitals from the CMS Open Payment Teaching Hospital list from 2015 and matched to physician-hospital affiliation listed within the National Downloadable File.

Measures

The main dependent variable is a binary indicator for whether a physician received at least one opioid payment (*0=no, 1=yes*). Previous work shows physicians who receive a greater number of payments or higher value payments increase prescribing costs per patient (Perlis & Perlis, 2016); as such, these providers may differ from peers with no payments or very few payments by having stronger industry relationships. Therefore, I also examine, among those who have payments, the number who have more than two payments (i.e., above the median number of payments in the sample; *0=no, 1=yes*), and those who received $100 or more in payments within the year (*0=no, 1=yes*). I chose $100 as a rounded threshold close to the median number of payments within the sample.

The network measures in the analysis include degree centrality (i.e., the number of shared patients between physicians within a network), betweenness centrality (i.e., the number of times a physician acts as a link along the shortest path between two other physicians, divided by the shortest paths between all the physicians within a network), and transitivity (i.e., the "clustering coefficient," or the number of closed triplets in a physician's neighborhood over the total number of closed triplets within the neighborhood). Additional information on social network centrality metrics is provided in Appendix A1. Degree centrality is weighted by the average number of shared patients between physicians in order to capture the relative intensity of shared relationships between providers. Since HRR's are indicative of unique healthcare markets where providers practice, I created quartiles of each social network metric within a physician's respective HRR. I removed physicians linked to another provider in a different HRR (n=95,317). To calculate transitivity, which requires a provider have at least two other ties within the network, I dropped anyone who had less than three connections (n=46,133).

Additional physician-level covariates include gender, number of years practicing, metropolitan practice, region, HRR, medical school ranking, teaching hospital affiliation, specialty, and number of peers with payments.

Statistical Analysis

Summary statistics were generated across providers who received opioid payments and those who did not. Modified Poisson regressions with standard errors clustered at the HRR level were used to estimate the adjusted incidence rate ratio (IRR) for social network position (i.e., degree, betweenness, and transitivity) and number of peers with payments as a function of individual receipt of opioid payments within each network (n=150,871). Among those with payments (n=24,424), I ran additional modified Poisson models to examine those who have more than two payments and those who have $100 or more in payments. A modified robust Poisson regression, which combines a log Poisson regression with robust variance estimation, are commonly used to estimate risk ratios for common outcomes when using a logistic regression may overestimate the risk (W. Chen et al., 2018). All social network analyses were performed using R version 1.3 using the igraph package version 1.2.6 (Gabor & Tamas, 2006). All other statistical analyses were run with Stata/MP version 16.1 (2022).

Sensitivity Analysis

A fundamental challenge in estimating peer effects is endogeneity, or the "reflection problem", which arises in assessing endogenous influences on an individual's behavior compared to the average behavior of the individuals comprising the peer group (Manski, 1993). In other words, it is possible that the index physician is influencing the behavior of peers to accept opioid payments, rather than peers influencing the index physician. It is convention to employ lagged instruments to assess identification and model specification in the peer effects literature, with the assumption that average prior-year influence of a peer group is unconnected to the current-year behavior of an individual physician of interest (Winn et al., 2021). I therefore conducted a sensitivity analysis by lagging opioid payments received in the previous year (i.e., 2014) among peers as a proxy for current year acceptance of payments among index physicians. That is, average payments to peers in 2014 would likely still influence the 2015 behavior of the index physician, however, payments made to the index physician in 2015 could not influence the behavior of peers to accept payments in 2014. It may be the case that index physicians influence peers to accept payments in 2014 as well; however, since most physicians receive payments from year-to-year (~63% between 2014 to 2015), narrowing the sample to only providers who have 2015 payments, but not 2014 payments and vice versa with their respective peers creates a substantially smaller sample to test our main analysis and is not reflective of real-world payment behavior. Therefore, to account for these spillover concerns, we include a control variable for 2014 payment acceptance among index physicians.

Additional sensitivity analyses were conducted to evaluate whether heterogeneity of physician specialty groups and opioid drug type associated with payments alters the relationships between peer receipt of payment and network position. A modified Poisson regression with standard errors clustered at the HRR level was run for each additional analysis and then predicted probabilities using marginal standardization were used.

Results

Our final sample included 351,103 physicians sharing patients with at least two other physicians in 2015, of whom 7% received at least one opioid-related payment (Table 6). On average, physicians received 5 payments (SD: 12) or an average of $439 (SD: $4,692). Physicians with opioid-related payments had a higher percentage of peers with similar payments compared to physicians with no opioid payments (69% versus 41%). Overall, physicians with payments are less likely to be within the top 25th percentile of each network metric compared to those without payments indicating they may have fewer connections, may not be as influential (based on betweenness centrality), and may belong to less dense networks (based on transitivity centrality).

Table 6: Descriptive characteristics by recipient of opioid-related payments, 2015

	Physicians with opioid-related payments	**Physicians with no opioid-related payments**

	N= 24,424 (7%)	N= 326,679 (93%)
Physician Characteristics		
Male, N (%)	19,541 (80%)	246,621 (75%)
Years practicing, mean (SD)	25 (10)	24 (11)
Metropolitan practice, N (%)	21,406 (88%)	297,351 (91%)
U.S. Census Region, N (%)		
Northeast	4,416 (18%)	71,021 (22%)
Midwest	5,372 (22%)	74,451 (23%)
South	10,503 (43%)	119,450 (37%)
West	4,133 (17%)	61,757 (19%)
Medical School Ranking, N (%)		
Top 20	1,433 (6%)	35,549 (11%)
Ranked 21 to 50	3,758 (15%)	66,057 (20%)
Ranked 50+	5,533 (23%)	68,690 (21%)
Unranked	13,700 (56%)	156,383 (48%)
Teaching Hospital, N (%)	1,322 (5%)	27,603 (8%)
Specialty, N (%)		
General Medicine	13,477 (55%)	99,041 (30%)
Surgery	1,560 (6%)	36,849 (11%)
Pain Specialties	3,229 (13%)	22,875 (7%)
Other specialties	6,158 (25%)	167,914 (51%)
Payment Characteristics		
Number of payments, total	134,121	0
Mean (SD)	5 (12)	0
Median (min, max)	2 (1, 291)	0
Payment amount, total $	$10,724,341	$0
Mean (SD)	$439 ($4,692)	$0
Median (min, max)	$29 ($0.7, $241,969)	$0
Payment Characteristics Among Network		
Peers with payments, N (%)	16,786 (69%)	134,085 (41%)
Peers with payments within provider network, mean % (SD)	12 (17)	4 (8)
Number of payments, total within networks		
Mean (SD)	19 (33)	22 (40)
Median (min, max)	8 (1-415)	7 (1-1068)
Payment amount, total $ within networks		
Mean (SD)	$1,465 ($8,913)	$1,469 ($8,378)
Median (min, max)	$112 ($1-$183,364)	$118 ($0.5-$242,076)
Network Characteristics		
Number peers in network, mean (SD)	26 (31)	39 (56)
Degree centrality, (%)		
Q1	21%	21%

Q2	32%	27%
Q3	30%	25%
Q4	17%	27%
Betweenness centrality, (%)		
Q1	21%	21%
Q2	30%	26%
Q3	27%	26%
Q4	22%	26%
Transitivity, (%)		
Q1	21%	25%
Q2	29%	25%
Q3	27%	25%
Q4	23%	25%

*observations <11 are censored by CMS to protect patient privacy; NA=Not applicable

After adjustment, I find that physicians are more likely to accept opioid payments if they have peers with opioid payments (Model 1, Table 7). For instance, physicians are 3.3 times as likely to accept payment if they have one peer in their network with an opioid payment, and 8.4 times as likely if they have between six to nine peers with opioid payments. In terms of network characteristics, physicians with opioid payments are less likely to be well-connected by having fewer shared patients (i.e., IRR top quartile compared to the first quartile for degree centrality: 0.18, 95% CI: 0.16, 0.20), but are more likely to have more cohesive networks (i.e., IRR top quartile compared to the first quartile for betweenness centrality: 1.18, 95% CI: 1.12, 1.23), and belong to more dense networks (i.e., IRR top quartile compared to the first quartile for transitivity centrality: 1.13, 95% CI: 1.06, 1.19). Receiving above the median number of payments (Model 2) or more than $100 in payments (Model 3) appears to have little variation in overall magnitude of effect compared to physicians accepting any payment (Model 1). Notably, however, pain-related specialties are much more likely to accept frequent payments and higher payment value (IRR: 1.86, 95% CI: 1.76, 1.96 for Model 2 and 4.74, 95% CI: 4.30, 5.22 for Model 3) compared to peers in general medicine. Physician with more payments and higher payment value are also likely to have a greater number of peers (i.e., 10 or more) accepting opioid payments, although at a smaller magnitude than those accepting any payment (Model 2, IRR: 1.47, 95% CI: 1.36, 1.69; Model 3, IRR: 1.41, 95% CI: 1.19, 1.67).

Table 7: GLM Poisson regression modeling the relationship between physician payment and peer acceptance of payment, 2015

	Model 1- Any Payments (n= 351,103)		**Model 2- 2+ payments** (n=24,424)		**Model 3- $100+ payments** (n=24,424)	
Variables	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
Female	0.78***	(0.75, 0.81)	0.79***	(0.76, 0.83)	0.71***	(0.66, 0.77)
Tenure (ref = ≤10 years)						
11 to 20 years	1.31***	(1.24, 1.39)	0.95	(0.89, 1.01)	0.83***	(0.76, 0.92)
21+ years	1.40***	(1.32, 1.49)	0.96	(0.91, 1.02)	0.83***	(0.75, 0.91)
Metropolitan	1.18***	(1.12, 1.25)	1.17***	(1.08, 1.28)	1.27***	(1.12, 1.44)
U.S Census Region (ref=Northeast)						
Midwest	1.09	(0.97, 1.23)	0.88	(0.64, 1.19)	0.68	(0.35, 1.30)
South	0.96	(0.85, 1.08)	0.83	(0.62, 1.09)	0.73	(0.41, 1.27)
West	0.95	(0.71, 1.28)	0.86	(0.61, 1.20)	0.52*	(0.28, 0.94)
Teaching hospital	0.86**	(0.76, 0.95)	0.91*	(0.83, 0.99)	0.74***	(0.64, 0.85)
Specialty (ref= general medicine)						
Surgical	0.29***	(0.27, 0.31)	0.53***	(0.47, 0.60)	0.80*	(0.66, 0.96)
Pain specialists	0.97	(0.91, 1.04)	1.86***	(1.76, 1.96)	4.74***	(4.30, 5.22)
Other specialists	0.30***	(0.28, 0.32)	1.04	(0.98, 1.10)	1.84***	(1.68, 2.02)
Peers with payment (ref=none)						
One peer	3.33***	(3.16, 3.53)	1.11***	(1.09, 1.19)	1.00	(0.94, 1.07)
2 to 5 peers	5.65***	(5.28, 6.05)	1.21***	(1.18, 1.30)	0.99	(0.92, 1.07)
6 to 9 peers	8.43***	(7.63, 9.31)	1.39***	(1.32, 1.53)	1.22***	(1.09, 1.37)
10+ peers	6.72***	(5.73, 7.90)	1.47***	(1.36, 1.69)	1.41***	(1.19, 1.67)
Degree (ref=Q1)						
Q2	0.77***	(0.74, 0.81)	0.94*	(0.90, 0.99)	0.95	(0.87, 1.04)
Q3	0.46***	(0.43, 0.49)	0.87***	(0.83, 0.93)	0.85**	(0.76, 0.95)
Q4	0.18***	(0.16, 0.20)	0.70***	(0.65, 0.76)	0.61***	(0.53, 0.70)
Betweenness (ref=Q1)						
Q2	1.05*	(1.00, 1.09)	1.05	(1.00, 1.10)	1.03	(0.95, 1.11)
Q3	1.09***	(1.04, 1.14)	1.10**	(1.03, 1.16)	1.17**	(1.07, 1.29)
Q4	1.18***	(1.12, 1.23)	1.12**	(1.03, 1.17)	1.18**	(1.07, 1.31)
Transitivity (ref=Q1)						
Q2	1.23***	(1.18, 1.28)	0.98	(0.94, 1.03)	1.00	(0.93, 1.07)
Q3	1.17***	(1.11, 1.23)	0.98	(0.92, 1.03)	0.96	(0.89, 1.04)
Q4	1.13***	(1.06, 1.19)	1.00	(0.95, 1.06)	1.01	(0.92, 1.11)

Note: All models include dummy variables for HRR
**p-value<0.05; **p-value<0.01; ***p-value<0.001*

In the sensitivity analysis, I examined lagged opioid payments made to peers in 2014 and whether this influenced whether the index physicians received an opioid payment in 2015 (Table 8). I find similar results to the base-case model with smaller overall magnitude in associations across peers with payments and slightly more concentration of physicians with more peer connections (i.e., IRR top quartile compared to the first quartile for degree centrality: 0.24, 95% CI: 0.22, 0.26 in Model 1 sensitivity analysis versus 0.18, 95% CI: 0.16, 0.20 in Model 1 base-case).

Table 8: GLM Poisson regression sensitivity analysis using peers with lagged payments, 2015

	Model 1- Any Payments (n=351,103)		**Model 2- 5+ payments** (n=24,424)		**Model 3- $100+ payments** (n=24,424)	
Variables	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
Peers with payment (ref=none)						
One peer	2.38***	(2.25, 2.51)	1.18***	(1.12, 1.24)	1.05	(0.98, 1.13)
2 to 5 peers	3.78***	(3.53, 4.05)	1.29***	(1.23, 1.35)	1.17***	(1.09, 1.26)
6 to 9 peers	4.84***	(4.35, 5.39)	1.31***	(1.19, 1.45)	1.37***	(1.21, 1.56)
10+ peers	3.58***	(3.07, 4.18)	1.41***	(1.23, 1.61)	1.63***	(1.36, 1.96)
Degree (ref=Q1)						
Q2	0.84***	(0.79, 0.88)	0.93**	(0.89, 0.98)	0.93	(0.85, 1.02)
Q3	0.55***	(0.51, 0.59)	0.86***	(0.81, 0.92)	0.81***	(0.72, 0.91)
Q4	0.24***	(0.22, 0.26)	0.71***	(0.65, 0.78)	0.57***	(0.49, 0.65)
Betweenness (ref=Q1)						
Q2	1.05*	(1.01, 1.10)	1.06*	(1.00, 1.11)	1.04	(0.96, 1.13)
Q3	1.11***	(1.06, 1.16)	1.11**	(1.04, 1.18)	1.19***	(1.08, 1.30)
Q4	1.20***	(1.13, 1.28)	1.12**	(1.05, 1.19)	1.19**	(1.08, 1.32)
Transitivity (ref=Q1)						
Q2	1.22***	(1.17, 1.27)	0.98	(0.94, 1.02)	1.00	(0.93, 1.08)
Q3	1.14***	(1.08, 1.20)	0.97	(0.92, 1.03)	0.97	(0.90, 1.05)
Q4	1.05	(0.99, 1.12)	1.00	(0.95, 1.06)	1.04	(0.94, 1.15)

Note: All models adjust for specialty, gender, tenure, urbanicity, region, teaching hospital affiliation, and HRR; **p-value<0.05; **p-value<0.01; ***p-value<0.001*

I also assessed heterogeneity of physician specialties across network and peer metrics. Pain-related specialists, followed by generalists, are the most likely to accept payment conditional on the growing number of peers within their network who have similar opioid payments (Figure 2). For instance, the marginal predicted IRR of a physician accepting any opioid payments conditional on having ten or more peers with similar payments is 0.86 (95% CI: 0.66, 1.07) if they are a pain-related specialist and 0.42 (95% CI: 0.37, 0.47) if they are a generalist.

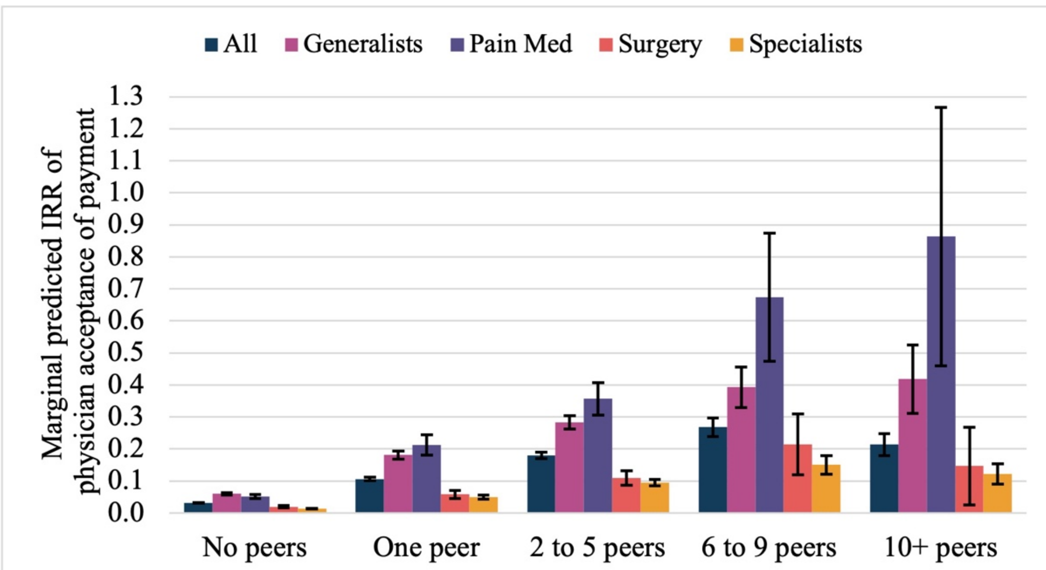

Figure 2: Sensitivity analysis results demonstrating marginal predicted IRR of physician specialties accepting a payment based on the number of peers within their respective network who have an opioid payment

Pain-related specialists and generalists are also most likely to accept an opioid payment if they have fewer peer connections (i.e., quadrant one in degree centrality, marginal predicted IRR: 0.27, 95%: CI: 0.25, 0.30 and 0.19, 95% CI: 0.18, 0.20, respectively), but more cohesive networks (i.e., quadrant four in betweenness centrality, marginal predicted IRR: 0.19, 95% CI: 0.17, 0.20, and 0.13, 95% CI: 0.12, 0.14, respectively) (Figure 3).

Finally, I examined the top four opioid drugs associated with payments to assess if the presence of a drug-specific payment was associated with the likelihood of a peer having a

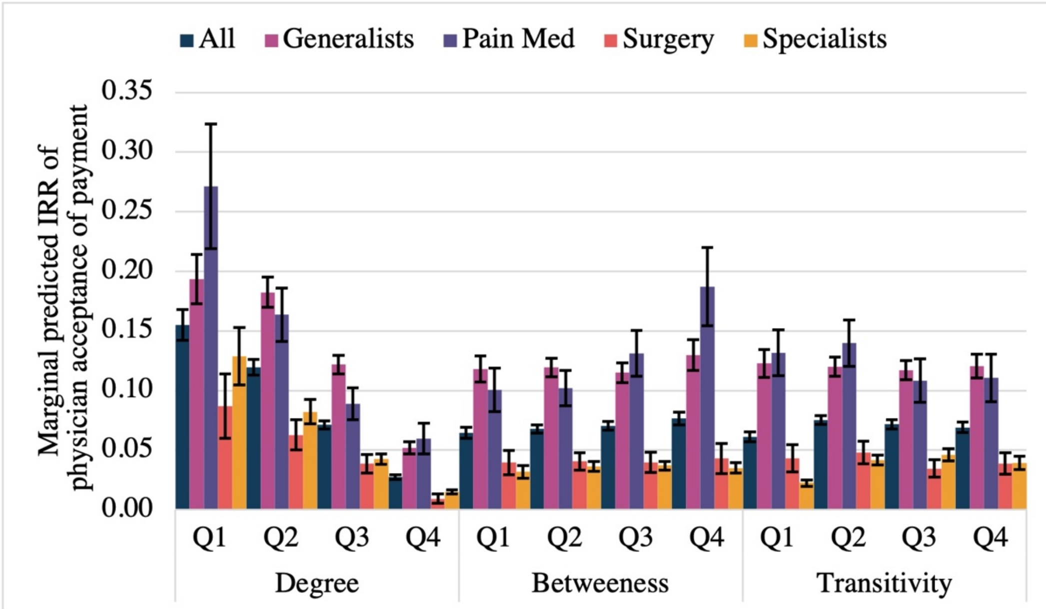

Figure 3: Sensitivity analysis results demonstrating the marginal predicted IRR of physician specialties accepting a payment based on their associated social network metric location

payment for the same drug. OxyContin (oxycodone) and Embeda (morphine/naltrexone) are the most frequently promoted drug in 2015 among networks and both appear to increase the marginal predicted IRR of a physician accepting payment with additional peers accepting similar payments (Figure 4). Physicians with lower degree centrality appear more likely to accept a payment regardless of drug-type, although OxyContin and Embeda have the largest marginal predicted IRR indicating that less connected physicians are more likely to accept payments for these drugs (Figure 5). Similar to findings from the base-case model, I also observe physicians having more cohesive networks across all top-promoted drug types (i.e., betweenness centrality) and fewer dense connections (i.e., transitivity centrality) with the majority falling into the bottom 50^{th} percentile.

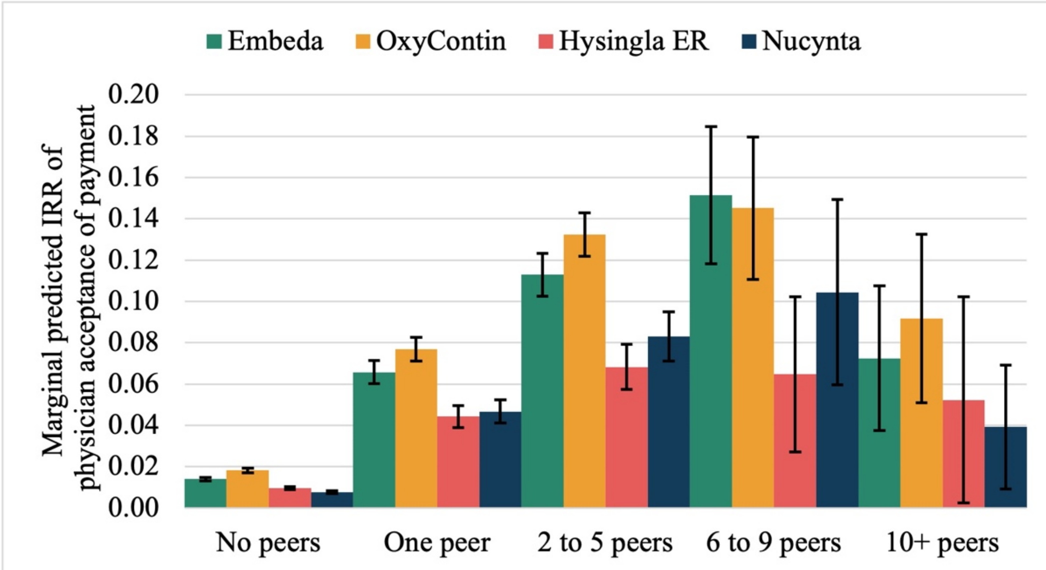

Figure 4: Sensitivity analysis results demonstrating the marginal predicted IRR of a physician accepting a payment based on the number of peers within their respective network who have the same opioid-drug-type payment

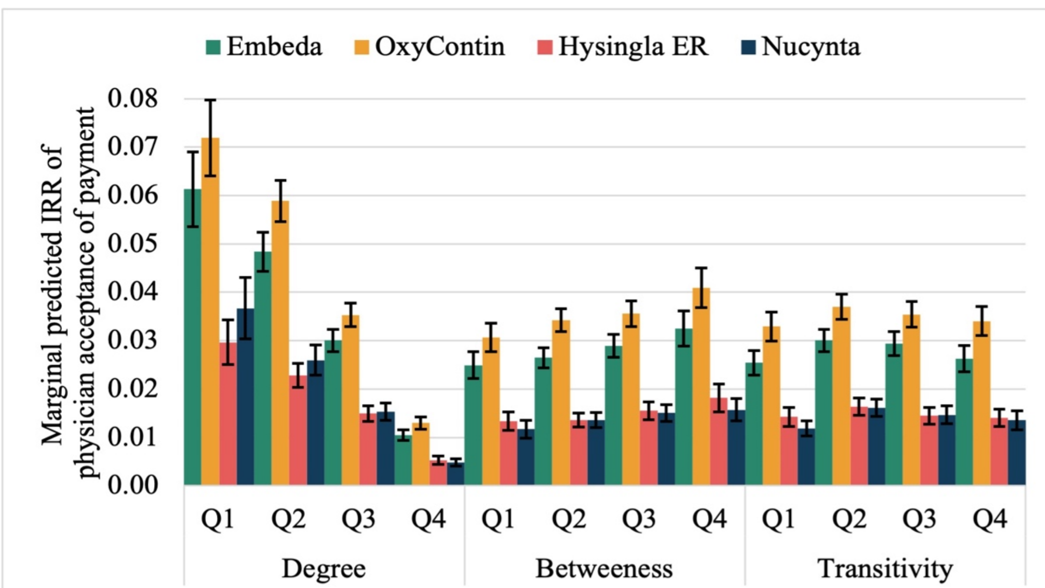

Figure 5: Sensitivity analysis results demonstrating the marginal predicted IRR of physician specialties accepting a payment based on their associated social network metric location

Discussion

This study is the first to quantify the extent and effect of network-level relationships on acceptance of opioid-related payments. I find network characteristics like the number of shared peers and number of peers with a payment may play a role in a given physician's likelihood or receptivity to accepting an opioid payment. For instance, physicians with any opioid payment in 2015 were found to be associated with three times the likelihood of at least one peer also having an opioid payment compared to physicians who did not have a similar payment. These physicians are more likely to belong to smaller and more interconnected patient-sharing networks.

Several factors may explain these findings in network patterns. First, physicians with payments may be geographically isolated (e.g., in rural or suburban practices) or may have other connections to peers with reduced clinical time (e.g., physician researchers). There is evidence to suggest that providers in more rural areas tend to have higher patient populations with chronic pain (e.g., mining communities in Appalachia) and that these communities received more concentrated marketing from opioid drugmakers compared to states with more rigorous prescription drug monitoring programs (Alpert et al., 2021). Furthermore, some physician "thought leaders" targeted for promotions by opioid drugmakers did not always hold full-time clinical positions and instead served as pharmaceutical executives or academic researchers (Hadland et al., 2019; Joseph, 2019b; Nguyen et al., 2019).

Variation was also found among specialties accepting payment, with generalists the most likely to have any opioid payment and pain specialists the most likely to have accepted higher payment counts and payment amounts. These findings may reflect the fact that generalists and pain medicine physicians prescribe more opioids to their patients than other specialty providers and therefore, may be more likely to receive industry marketing (Levy et al., 2015). In addition, it is likely that pain physicians may be receiving higher opioid payment amounts if they are selected to speak at conferences, give promotional symposiums, or serve as consultants.

These findings align with previous work analyzing physician acceptance of payment and peer acceptance of payment. For instance, Winn et al. (2021) analyzed general promotional payments for drugs and devices and found receipt of payment strongly associated with the likelihood that peers within the focal physician's network also received a payment (Winn et al., 2021). The authors also found an inverse relationship between strong network clustering and receipt of payment. However, in contrast to these findings, they found more central physicians were more likely to have payments. Likewise, Agha and Zeltzer (2019) found physicians more likely to be targeted for anticoagulant payments if they were highly connected within their network (Agha & Zeltzer, 2019). Since I found the opposite to be true for physicians with opioid-related payments, this suggests there may be unique factors associated with opioid drugs that may cause physicians to distinguish them from other drug payments. For instance, media attention towards the opioid epidemic and the role that drugmakers and physicians played in contributing to its initiation and perpetuation may have led to hesitancy among well-connected providers to accept opioid payments out of concern for reputation. In addition, medical schools, centers, and associations may have restricted promotional activity via conflict-of-interest policies which may directly curtail the likelihood of a physician with a larger professional network from accepting payment (Carlat et al., 2016; Larkin et al., 2017; Rothman, 2016).

As policymakers grapple with strategies to change physician behavior, especially with respect to curbing inappropriate or unnecessary prescribing of opioids, understanding the role that physician network and peer characteristics play is important. Future work should investigate how opioid-related payments made within physician networks impact opioid prescribing, whether status-conferring characteristics among physicians (e.g., publication count, leadership position) increase their propensity to influence peer behavior and examine physician attitudes towards opioid promotional payments.

This study has several limitations. First, this study is cross-sectional and therefore does not capture payments received over time which may influence the results if prior payments from years before 2015 influenced network dynamics in a way that predisposed relationships between physicians, peers, and industry. However, previous work has shown that post-payment effects on prescribing behavior are seen within the first year (Carey et al., 2020). Given the assessment of patient-sharing networks within a 30-day interval, it is likely I am still capturing subsequent impacts that receipt of an opioid payment among peers has on an individual provider. Second, the patient-sharing networks originated from Medicare data; therefore, I cannot account for non-Medicare provider patient-sharing relationships. Third, there are additional physician characteristics that may influence provider or network-level acceptance of promotional payments that I am unable to control for. These include a physician's prestige within a network, friendships, personal beliefs, morals, ethics, as well as policies on acceptance of promotional payments at affiliated institutions. I also do not include additional networks that may influence a physician's acceptance of a promotional payment like those at the group practice level, hospital level, or training level. However, prior work has shown that patient-sharing relationships tend to be the most meaningful in terms of influencing behavior (Donohue et al., 2018). Finally, I do not account for opioid prescribing within the sample and therefore cannot state the impact that payments may have had on influencing prescribing behavior.

Conclusion

Physicians who accept opioid-related payments may be more likely to have peers with a similar likelihood or receptivity to accepting opioid payments. This work highlights the importance of peer networks on physician behavior and the potential amplifying effect of promotional activities.

Chapter 4: Physician Network Characteristics and Prescribing Behavior

Background

Relationships between physicians are an integral part of the healthcare system; physicians rely on each other for referrals, care coordination, teaching, advice, and networking. Within these networks, certain physicians may have a stronger influence on peers than others due to expertise, job title, or prominence within their field. For example, Nair and colleagues (2010) find peers significantly alter prescribing behavior to align with prescribing of research-active physician specialists within their network, or peer-defined "opinion leaders." These opinion leaders are often at the center of interpersonal communication networks and play an important role in the rate and extent of disseminating information (Rogers, 2003).

Opinion leaders can change network behavior across various settings and can be used to promote evidence-based practices (Flodgren et al., 2007). For instance, Lomas et al. (1991) find that after local opinion leaders, defined as those physicians nominated by peers to be "educationally influential," encourage compliance with cesarean section guidelines, physicians are more likely to adhere to recommendations than other educational interventions. Adherence to evidence-based guidelines within physician networks may be particularly relevant for older adults prescribed opioids since this population has higher rates of comorbidities and, as a result, requires greater amount of care coordination across providers. However, very little is known about whether patterns of opioid prescribing among Medicare patients differ depending on whether a physician is more well-connected within their professional social network.

Social network analysis is increasingly used in health services research to examine the organizational context of healthcare delivery and the diffusion of technologies within systems

(DuGoff, Fernandes-Taylor, et al., 2018). Furthermore, social network analysis can provide important insights concerning what components of a network can be targeted to reduce unwanted outcomes and encourage adherence to evidence-based care. Since previous work suggests that structural location of an individual within a network is a good indicator of opinion leadership, I utilize a composite measure of two social network metrics to detect physicians who may have greater access to peers, and thus, a greater likelihood of influencing behavior (Litterio et al., 2017; Van Der Merwe & Van Heerden, 2009). The aim of this study is to use social network analysis to examine physician characteristics, opioid prescribing, and physician network location among select providers who fall into the upper strata of potential influencers using an experimental method; the goal is to determine if these select few physicians with the greatest influence potential are categorically different in characteristics compared to peers.

Methods

Data Sources

I conducted a national cross-sectional study of a sample of providers prescribing opioids in Medicare between 2013 to 2015 using the Centers for Medicare and Medicaid Services (CMS) Part D Prescriber Public Use File (PUF) which contains information on approximately 70 percent of all Medicare beneficiaries (*Centers for Medicare & Medicaid Services Data*, 2015). The Part D PUF contains data on the total number of prescriptions written for patients in the given calendar year, total daily doses dispensed for the drug, total expenditures for the medication, opioid prescribing rate, and other patient-level characteristics like gender and the average Hierarchical Condition Category (CMS-HCC) risk score. The list of opioid drugs used for this study came from the CMS Part D Prescriber PUF Drug Category. All methadone and buprenorphine products, which are often used for substance abuse treatment, were excluded from the analysis.

The Part D PUF was linked to the American Medical Association (AMA) Physician Masterfile using the National Provider Identifier (NPI), a unique 10-digit number assigned to a provider for billing purposes. I obtained a commercially available copy of the Masterfile from Redi-Data; the Masterfile is a comprehensive dataset on 1.4 million allopathic and osteopathic physicians practicing in the United States. Data is entered during initial medical licensure and continuously verified by the AMA. The Masterfile contains information on physician characteristics such as age, gender, medical school and residency programs attended, credentials, and specialty. To determine medical school ranking, I used the 2015 *U.S. News & World Report* to create four categories: schools ranked in the top 20, schools ranked between 21 and 50, schools ranked greater than 50, and unranked schools (including foreign medical schools) (*U.S. News & World Report*, 2015).

Previous work describes how industry often targets "key opinion leaders" to receive payments in hopes of creating a multiplier effect among those physician peers to adopt the promoted product (Sismondo, 2013). Therefore, I included information on physician acceptance of general industry payments (e.g., payment for food and beverage, travel, speaking, consulting, etc.) and opioid-related payments from the 2013 to 2015 CMS Open Payments database. Data are transformed to the provider-payment level using the aggregate count and value of general payments received by each physician per year and the count and value of all opioid-related payments. Collapsed Open Payments data are merged to the Part D PUF and AMA Masterfile using NPI. To determine if payments are concentrated among a few physicians, I calculated the Gini index, a commonly used measure of income dispersion to examine aggregate payments across physician network categories. The Gini index ranges from 0, indicating that everyone receives an equal number of payments, to a Gini index of 1, indicating that only one person receives all the payments. I also attempt to characterize physicians on the highest end of the payment spectrum by categorizing those who received more than $10,000 in payments across all three years. Finally, I included the type of payment (e.g., food and beverage, consulting, speaker, etc.) received by each physician for general payments.

Physician Networks

The patient-sharing network includes all physicians with at least one record of opioid prescribing recorded in the Part D PUF sharing at least 11 Medicare patients with another provider. I established patient-sharing networks using the 2013 to 2015 CMS Referral Data. As described previously in Chapter 2, the CMS Referral Data is derived from 100% Medicare claims data and lists the pairs of providers that share at least 11 patients during 30-, 60-, 90-, and 180-day intervals per year. I utilized the 180-day interval data since these measure longer-term provider interactions. Since I sought to measure direct referral networks, I only include providers sharing patients within the same hospital referral region (HRR).

Classifying Physicians Based on Network Location

Using social network analysis, I calculated three metrics highlighting an individual's unique position within a network to be influential depending on their location. These include:

- **Degree centrality:** Assess the number of connections (i.e., shared patients) a physician has with other physicians within a network. The higher the degree centrality, the more well-connected the physician is. I weight degree centrality by the average number of patients shared between physicians.

- **Eigenvector centrality:** Measures the influence of each physician by calculating a score dependent on the number of connections that a particular physician has to all other physicians within the network. The score is proportional to the sum of scores of all other connected physicians. In other words, a physician who has many connections may still have a low eigenvector score if those connections are linked to other low-scoring physicians. In addition, even if a physician has a high betweenness score (i.e., the extent to which physicians are distanced from each other), they may still have a low eigenvector score if they are some measure of distance away from the center of the network. A high eigenvector score indicates that the physician is connected to many other physicians who also have high scores.
- **Betweenness centrality:** Measures the number of times a physician acts as a link along the shortest path between two other physicians, divided by the shortest paths between all the physicians within a network. Physicians with high betweenness centrality act as bridges connecting other physicians and thus may be more influential. Physicians with lower betweenness centrality have fewer links to other providers and therefore may be less influential or have less of a role in diffusing information.

Betweenness and eigenvector centrality, when combined, simultaneously provide valuable information on influence potential since they pinpoint individuals who connect dispersed groups via other highly connected individuals. Therefore, I implement a method by Litterio et al. (2017) to utilize both betweenness and eigenvector to identify physicians within the sample who may have the highest potential to be influenced. In this method, a network is categorized into five groups depending on an individual's betweenness and eigenvector centrality score:

(1) “Well-connected” physicians are within the top 5% of betweenness and eigenvector centrality. In other words, “well-connected” are those physicians who have connections to popular physicians, but also serve as a bridge to less well-connected physicians. Physicians within this category may have the highest potential to influence peers given their unique peer-centered network location and are thus the main focus of the analysis.

(2) “Brokers,” or physicians within the top 5% of betweenness and the bottom 95% of eigenvector centrality. A “broker” is a physician with a high betweenness centrality meaning they strategically connect physicians to each other, but a low eigenvector score indicating they are not as well connected with other influential physicians.

(3) “Physicians with important connections” are physicians within the top 5% of eigenvector and the bottom 95% of betweenness centrality. These physicians have multiple connections to well-connected peers but limited outreach to other less-connected peers.

(4) “Secondary actors” are in the bottom 95% of betweenness and eigenvector centrality and are physicians who make up most of the sample.

(5) “Dispersed actors” are physicians who fall within the bottom 5% of eigenvector and betweenness centrality. In other words, these physicians are the least likely to be connected to peers overall, and less likely to be connected to peers who are potentially influential or well-connected.

Figure 6 demonstrates each group in relation to each other and their respective defining thresholds. These selection criteria are advantageous in that they group physicians into unique groups based on specific network location and thus, allow for cross-comparisons between providers who fall within extreme values of eigenvector and betweenness centrality.

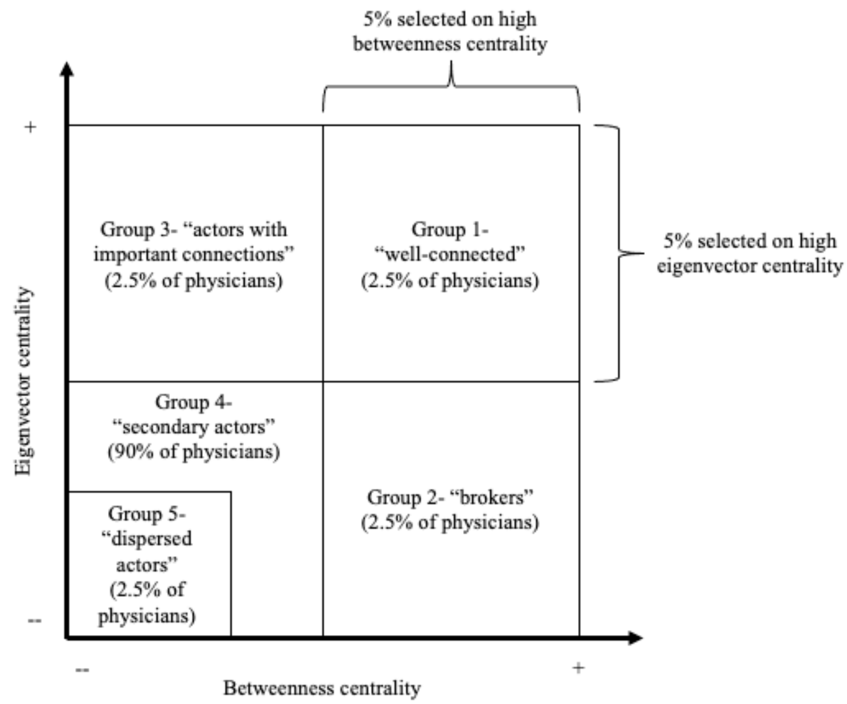

Figure 6. Adapted figure from Littero et al. (2017) demonstrating group classifications based on eigenvector and betweenness centrality thresholds

Measures

The primary outcome is whether a physician is “well-connected” (group 1) across all three years of available data. The main independent variable is each physician’s yearly average opioid prescribing rate (i.e., percent of total claims represented by the number of opioid claims) grouped into quartiles. Additional physician-level covariates include gender, number of years practicing, medical school ranking, specialty, and receipt of opioid payment. Patient-level covariates include the average HCC risk score among beneficiaries for a given provider. HCC scores incorporate health risk of beneficiaries by using age, sex, eligibility for Medicaid, and diagnosis, among others. Beneficiaries with lower HCC scores are considered relatively healthy and those with higher scores are considered relatively less healthy and may require additional healthcare resources.

Statistical Analysis

A social network analysis was run to determine degree, eigenvector, and betweenness centrality for each physician sharing patients within respective HRR networks. Using a composite measure of eigenvector and betweenness centrality, physicians were grouped into five categories demarking physician structural location using thresholds described in Figure 2. Next, I retained only physicians who fell consistently into the same five categories between 2013 to 2015 to ascertain longer-term consistency in network position (n=62,858 physicians removed).

Multinomial logistic regression (MLR) modeled the relationship between network categorization (0="well-connected" (group 1), 1="brokers" (group 2), 2="actors with important connections" (group 3), 3="secondary actors" (group 4), 4="dispersed actors" (group 5)) and opioid prescribing rate quartile. The "well-connected" (group 1) was selected as the base category and the relative risk ratio (RRR) was reported. The MLR adjusted for relevant physician- and patient-level confounders and included an interaction term between opioid prescribing rate quartile and physician specialty. All social network analyses are performed using R version 1.3 using the igraph package version 1.2.6 (Gabor & Tamas, 2006). All other statistical analyses are run with Stata/MP version 16.1 (*Stata/MP*, 2022).

<u>Results</u>

Among the 162,073 physicians sharing patients and prescribing opioids to patients in Medicare Part D, 0.5% of them are "well-connected," 1% of them are "brokers," 1% of them are "actors with connections," 96% of them are "secondary actors," and 1% of them are "dispersed actors" (Table 9). Among "well-connected" physicians, the majority are specialists (69%), while the majority of "dispersed actors" are in primary care (68%). The opioid prescribing rate varies across each network category, with "well-connected" physicians having the lowest prescribing rate (10, SD: 14) and “secondary actors” having the highest prescribing rate (16, SD: 19). Although beneficiary characteristics appear similar across all categories, “well-connected” physicians have Medicare Part D patients with the highest average HCC scores (2, SD: 0.8).

Among general industry payments, “well-connected” physicians have the highest percentage of acceptance (77%) compared to other network categories and are more likely to be paid for serving as faculty, speaker, or consultant (Table 10). Among opioid industry payments, “secondary actors” are most likely to have any payment followed by “dispersed actors” who had an average of $2,152 (SD: $19,759) opioid-related payments. The Gini index for general industry payments ranges from 0.87 (“important connections”) to 0.93 (“dispersed actors”), indicating industry payments across each category are highly skewed, with only a few physicians receiving a disproportionate share of the total value of payments.

After adjustment, “well-connected” physicians (group 1) are less likely to be among the top 25th percentile of opioid prescribers relative to “brokers” (group 2), “actors with important connections” (group 3), and “dispersed actors” (group 4), although findings are not statistically significant (Table 11). Compared to peers in primary care, specialty physicians have a higher probability of having opioid prescribing rates in the top 25th percentile if they are “actors with important connections” (group 3, RRR: 3.32, 95% CI: 1.4, 7.9), “secondary actors” (group 4, RRR: 8.25, 95% CI: 3.8, 18.1), or “dispersed actors” (group 5, RRR: 12.43, 95% CI: 5.0, 31.1).

Table 9. Descriptive characteristics among physicians prescribing opioids and sharing patients in Medicare based on network location category, 2013 to 2015

Characteristics	**Overall**	***"Well-connected" (group 1)***	***"Brokers" (group 2)***	***"Important connections" (group 3)***	***"Secondary actors" (group 4)***	***"Dispersed actors" (group 5)***
Sample size, N (%)	162,073 (100)	883 (0.5)	1,989 (1)	2,286 (1)	155,221 (96)	1,694 (1)
Network Characteristics						
Degree, mean (SD)	34 (34)	251 (142)	94 (49)	116 (45)	29 (25)	1 (1)
Eigenvector, mean (SD)	0.12 (0.19)	0.88 (0.10)	0.12 (0.13)	0.82 (0.08)	0.1 (0.13)	0 (0)
Betweenness, mean (SD)	1418 (9274)	43555 (116001)	34607 (41524)	881 (1067)	629 (946)	0 (0)
Physician Characteristics						
Female, N (%)	38,087 (24)	54 (6)	224 (10)	354 (12)	36,724 (24)	731 (43)
Age, mean (SD)	52 (10)	53 (9)	53 (10)	51 (9)	52 (10)	49 (11)
Tenure, mean (SD)	25 (11)	26 (10)	26 (10)	24 (10)	25 (11)	21 (11)
Medical School Ranking, N (%)						
Top 20	13,824 (9)	63 (10)	227 (12)	193 (7)	13,183 (9)	158 (10)
Ranked 21 to 50	31,389 (19)	160 (17)	397 (20)	425 (18)	30,070 (19)	337 (24)
Ranked 50+	36,030 (22)	182 (22)	361 (17)	513 (22)	34,650 (22)	324 (18)
Unraked or foreign	80,830 (50)	478 (51)	1,004 (51)	1,155 (54)	77,318 (50)	875 (48)
Region, N (%)						
Northeast	28,900 (18)	108 (12)	407 (20)	434 (19)	27,632 (18)	319 (19)
Midwest	38,924 (24)	238 (27)	475 (24)	603 (26)	37,236 (24)	372 (22)
South	64,872 (40)	421 (48)	708 (36)	856 (37)	62,333 (40)	554 (33)
West	29,377 (18)	116 (13)	399 (20)	393 (17)	28,020 (18)	449 (27)
Specialty, N (%)						
Primary care	83,836 (52)	176 (20)	468 (24)	747 (33)	81,296 (52)	1,149 (68)
Internal medicine	38,893 (24)	147 (17)	354 (18)	56 (2)	37,472 (24)	359 (21)
Family medicine	40,956 (2)	24 (3)	101 (5)	166 (7)	39,956 (26)	709 (42)
Other	3,987 (2)	5 (1)	13 (1)	20 (1)	3,868 (2)	81 (5)
Surgery	25,565 (16)	94 (11)	193 (10)	192 (8)	24,983 (16)	103 (6)

General surgery	8,134 (5)	9 (1)	29 (1)	61 (3)	8,006 (5)	29 (2)
Orthopedics	11,442 (7)	5 (1)	60 (3)	72 (3)	11,264 (7)	41 (2)
Other	5,989 (4)	80 (9)	104 (5)	59 (3)	5,713 (4)	33 (2)
Specialists	52,672 (33)	613 (69)	1,328 (67)	1,347 (59)	48,942 (32)	442 (26)
Anesthesiology	1,984 (1)	6 (1)	29 (1)	24 (1)	1,898 (1)	27 (2)
Cardiology	2,323 (1)	229 (26)	273 (14)	67 (3)	1,746 (1)	9 (1)
Critical care	806 (0.5)	23 (3)	32 (2)	30 (1)	712 (0.5)	9 (1)
Emergency medicine	12,722 (8)	51 (6)	244 (12)	562 (25)	11,651 (8)	214 (13)
Gastroenterology	1,403 (0.9)	8 (1)	26 (1)	30 (1)	1,336 (1)	3 (0.2)
Oncology	6,985 (4)	40 (5)	92 (5)	128 (6)	6,696 (4)	29 (2)
Infectious Disease	818 (0.5)	4 (0.5)	8 (0.4)	27 (1)	772 (0.5)	7 (0.4)
Nephrology	2,257 (1)	61 (7)	121 (3)	109 (5)	1,962 (1)	4 (0.2)
Neurology	2,995 (2)	41 (5)	62 (3)	70 (3)	2,808 (2)	14 (1)
Ophthalmology	691 (0.4)	8 (1)	65 (3)	3 (0.1)	610 (0.4)	5 (0.3)
Otolaryngology	2,516 (2)	0 (0)	21 (1)	23 (1)	2,465 (2)	7 (0.4)
Pain medicine	451 (0.3)	1 (0.1)	9 (0.5)	2 (0.1)	437 (0.3)	2 (0.1)
Physiatry	2,646 (2)	35 (4)	60 (3)	46 (2)	2,486 (2)	19 (1)
Rheumatology	2,267 (1)	5 (0.6)	28 (1)	13 (1)	2,206 (1)	15 (1)
Sports medicine	2,090 (1)	2 (0.2)	11 (1)	14 (1)	2,046 (1)	17 (1)
Urology	4,120 (3)	32 (4)	105 (5)	108 (5)	3,871 (2)	4 (0.2)
Other	5,598 (3)	67 (8)	142 (7)	91 (4)	5,240 (3)	58 (3)
Beneficiary Characteristics						
No. of opioid claims per beneficiary						
Mean (SD) per physician	3 (2)	3 (2)	3 (2)	2 (2)	3 (2)	3 (2)
Median (IQR) per physician	3 (1, 33)	2 (1, 8)	2 (1, 33)	1 (1, 13)	3 (1, 26)	3 (1, 15)
Opioid prescribing rate, mean (SD)**	16 (19)	10 (14)	12 (16)	15 (16)	16 (19)	13 (15)
No. of Medicare beneficiaries with an opioid prescription						
Mean (SD) per physician	71 (71)	107 (171)	85 (114)	93 (124)	70 (66)	48 (40)
Median (IQR) per physician	51 (58)	42 (73)	50 (71)	58 (77)	51 (58)	36 (38)
Medicare beneficiary characteristics						

Female (%), mean (SD)	60 (11)	55 (9)	56 (11)	58 (9)	60 (11)	62 (11)
Age, mean (SD)	70 (5)	72 (4)	71 (5)	70 (4)	70 (5)	69 (5)
HCC score, mean (SD)	1.4 (0.6)	2 (0.8)	2 (1)	1.8 (0.8)	1.4 (0.5)	1.3 (0.5)

IQR=interquartile range
*Sample size corresponds to physicians with at least 11 patients since CMS suppresses observations ≤10 for patient confidentiality
**refers to the percent of the total claims represented by the number of opioid claims

Table 10. Industry payment characteristics among physician prescribing opioids in Medicare, 2013 to 2015

	Overall N=162,073 (100%)	***"Well-connected" (group 1)*** n=883 (0.5%)	***"Brokers" (group 2)*** n=1,989 (1%)	***"Important connections" (group 3)*** n=2,286 (1%)	***"Secondary actors" (group 4)*** n=155,221 (96%)	***"Dispersed actors" (group 5)*** n= 1,694 (1%)
General industry payment, N (%)	92,157 (57)	680 (77)	1,245 (63)	1,176 (51)	88,391 (57)	665 (39)
No. of payments	3,489,977	28,712	276,304	397,603	9,719,396	52,403
Mean (SD)	22 (40)	36 (56)	27 (48)	23 (41)	21 (39)	13 (34)
Median (IQR)	5 (24)	15 (43)	7 (32)	4 (28)	5 (23)	1 (10)
Value ($) of payments	1,172,675,584	4,948,965	49,344,672	32,377,356	1,078,767,744	7,236,927
Mean (SD)	7,235 (121262)	18,398 (76687)	14,496 (11800)	5,664 (31215)	7,126 (123938)	5,550 (49146)
Median (IQR)	431 (2060)	1,391 (4898)	691 (3508)	357 (2215)	433 (2038)	62 (753)
No. who received ≥$10,000	9,636 (6)	50 (19)	439 (13)	424 (7)	8,666 (6)	57 (4)
Gini index	--	0.88	0.90	0.87	0.90	0.93
Opioid industry payment, N (%)	6,446 (4)	29 (3)	57 (3)	70 (3)	6,222 (4)	68 (4)
No. of payments	234,468	365	3,863	6,732	221,074	2,434
Mean (SD)	7 (20)	12 (21)	9 (19)	8 (23)	7 (19)	14 (41)
Median (IQR)	2 (5)	5 (7)	3 (7)	3 (5)	2 (5)	3 (7)
Value ($) of payments	18,763,374	24,010	270,616	366,277	17,719,386	383,086
Mean (SD)	578 (8256)	800 (3574)	658 (4863)	462 (7268)	571 (8207)	2152 (19759)
Median (IQR)	37 (77)	56 (131)	51 (114)	39 (84)	37 (76)	50 (116)
Gini index	--	0.90	0.91	0.92	0.94	0.97
Payment types, N (%)*						
Food and beverage	117,611 (73)	784 (89)	1,514 (76)	1,533 (67)	112,823 (73)	957 (56)
Compensation**	7,766 (4)	147 (17)	221 (11)	125 (5)	7,215 (5)	58 (3)
Consulting fee	10,371 (6)	115 (13)	197 (10)	116 (5)	9,872 (6)	71 (4)
Ownership†	1,260 (0.8)	6 (1)	21 (1)	20 (1)	1,207 (1)	6 (0.4)
Speaker at CME‡	782 (0.5)	16 (2)	22 (1)	11 (0.5)	728 (0.5)	5 (0.3)
Travel and lodging	20,941 (13)	258 (29)	375 (19)	262 (11)	19,926 (13)	120 (7)
Other§	48,046 (30)	421 (48)	741 (37)	649 (28)	45,930 (30)	305 (18)

Year, N (%)						
2013	103,331 (64)	720 (82)	1,369 (69)	1,353 (59)	99,116 (64)	773 (46)
2014	115,956 (72)	777 (88)	1,505 (76)	1,484 (65)	111,252 (72)	938 (55)
2015	118,261 (73)	775 (88)	1,516 (76)	1,562 (68)	113,413 (73)	995 (59)

IQR=interquartile range
*Categories not mutually exclusive and refer only to general payments
**Compensation for services other than consulting, including serving as faculty or as a speaker at a venue other than a continuing education program
†Includes current or prospective ownership or investment interests and royalty or license
‡Includes compensation for serving as faculty or as a speaker for non-accredited and non-certified continuing education program and compensation for serving as a faculty or speaker for an accredited or certified continuing education program
§Includes grants, gifts, honoraria, entertainment, charitable contributions

Table 11. Multinomial logistic regression results modeling the relationship between network category and opioid prescribing rate quartile, 2013 to 2015

Variables	**Group 1 vs. Group 2** (n=3,673)		**Group 1 vs. Group 3** (n=5,985)		**Group 1 vs. Group 4** (n=151,649)		**Group 1 vs. Group 5** (n=1,573)	
	RRR	**95% CI**	**RRR**	**95% CI**	**RRR**	**95% CI**	**RRR**	**95% CI**
Opioid prescribing quadrant (ref=Q1)								
Q2	0.87	(0.6, 1.3)	1.23	(0.8, 1.8)	0.97	(0.7, 1.4)	0.95	(0.6, 1.4)
Q3	1.34	(0.8, 2.1)	2.02**	(1.3, 3.2)	1.20	(0.8, 1.8)	1.51	(1.0, 2.3)
Q4	1.54	(0.7, 3.6)	1.89	(0.8, 4.2)	0.66	(0.3, 1.4)	1.32	(0.6, 3.0)
Specialty category (ref=Primary Care)								
Surgeons	4.01	(0.5, 32.5)	0.35	(0.1, 5.7)	0.79	(0.1, 5.7)	0.49	(0.02, 8)
Specialists	0.68*	(0.5, 1.0)	0.34***	(0.2, 0.5)	0.09***	(0.1, 0.1)	0.04***	(0.01, 0.1)
Opioid prescribing quadrant x Specialty category (ref=Q1 x Primary Care)								
Q2 x Surgeons	0.38	(0.01, 5.3)	0.81	(0.1, 24.6)	0.84	(0.1, 9.7)	0.00	(0.0, 0.0)
Q2 x Specialists	1.94*	(1.1, 3.3)	1.70*	(1.0, 2.9)	3.79***	(2.4, 5.9)	6.17***	(3.3, 11.6)
Q3 x Surgeons	0.11*	(0.01, 0.9)	0.42	(0.1, 7.2)	0.27	(0.01, 2.1)	0.20	(0, 3.5)
Q3 x Specialists	1.08	(0.6, 1.9)	1.59	(0.9, 2.7)	3.59***	(2.3, 5.7)	6.19***	(3.4, 11.3)
Q4 x Surgeons	0.16	(0.1, 1.5)	1.64	(0.1, 30)	2.19	(0.3, 18.3)	0.64	(0.01, 11.8)
Q4 x Specialists	1.47	(0.6, 3.6)	3.34**	(1.4, 7.9)	8.25***	(3.8, 18.1)	12.43***	(5, 31.1)

Note: model also controls for physician gender, years practicing, medical school ranking, industry payment from opioid manufacturer, the average beneficiary HCC risk score among patients, and hospital referral region; RRR= relative risk ratio; **p-value*<0.05; ***p-value*<0.01; ****p-value*<0.0001

Discussion

My results suggest there may be differences in opioid prescribing behavior depending on physician network category and specialty. For example, "well-connected" physicians appear to be more likely to have general industry relationships and are more likely to be specialists or surgeons. In terms of prescribing, "well-connected" physicians appear less likely to fall within the top 25th percentile of opioid prescribing rates, indicating physicians who are highly connected at the intersection of eigenvector and betweennesses centrality are most likely highly referred specialists coordinating care across several physician peers and prescribing opioids at lower rates.

These findings align with what we may expect to find in traditional physician referral networks, with primary care providers writing the largest total number of opioid prescriptions compared to all other specialties (J. H. Chen et al., 2016). Previous research also demonstrates wide variation in opioid prescribing across specialties, especially those within a primary care field (e.g., family medicine, internal medicine, general practice). These differences are likely due to variations in education, training, patient characteristics, or the number of pain-specialized peers a provider is connected to which may vary by network and region.

This novel approach to identifying physicians with differential potential to diffuse or access information from peers relies on a simplified metric compiled from data on physicians' network location alone. While this approach presents an accessible and feasible identification method, it is an atypical process in social network analysis which classically relies on peer nomination to ascertain opinion leaders. For instance, Nair and colleagues (2010) identify physician opinion leaders as those nominated by peers via survey and supplemented with individual-level data on prescribing behavior used by drugmakers to target industry payments. Using this identification method, they found opinion leaders adopting new drug guidelines impacted the decisions of their peers significantly and provided between a 5 to 35 percent return on investment from promotional activities leveed at opinion leaders. Iyengar et al. (2011) find evidence of social contagion in new drug adoption among providers who are well-connected (i.e., identified from drugmaker data on prescribing behavior) and not just those who have high prescribing volume. Finally, Agha and Molitor (2015) found local opinion leaders, defined as those who are prominent authors, are associated with patients in their region being 36 percent more likely to receive a new cancer drug.

This study contributes to the evolving research applying social network analysis in healthcare by offering a potential first step in identifying influential physicians based on structural location within a network. Specifically, this approach assists in potentially identifying local physicians who may have greater potential or access to diffuse or gain information from peers. Since previous work suggests that the structural location of an individual within their network is a good indicator of opinion leadership, this research contributes to the potential first-level identification of physician peers who may be more important targets for peer-level behavior interventions (Van Der Merwe & Van Heerden, 2009). Future work should validate this approach using different patient-sharing networks or networks at the hospital or group clinic level and combine peer survey data that confirms identification or more explicitly outlines the role that a potential influencer has on actually influencing provider behavior.

Limitations

There are several limitations to this analysis. First, this study should be evaluated as a first-pass quantitative method to identify potential influential physicians based on network structure alone, and not as a sole approach to define opinion leaders. Qualitative data utilizing peer nominations of influencers relays more information on the content of social relations within the larger network structure. Therefore, a mixed-methods approach provides a deeper understanding of network relationships (Valente, 2010). Second, this study is cross-sectional and therefore does not capture the effect or consistency of influencers over time. Third, the patient-sharing networks originated from Medicare data; therefore, I cannot account for non-Medicare provider patient-sharing relationships and the results do not span the full range of a given provider's opioid prescribing behavior. Fourth, there are additional physician characteristics that may determine an individual's propensity for influence within a network that I am unable to control for. These include physician leadership positions, scholarship, friendships, and social media presence, among others. Finally, the influence categorization is based on a method proposed by Litterio et al. (2017) for detecting significant actors based on online social communities. The extent to which this method reliably translates into physician networks has not been tested and may not adequately convey real-life influence among physician peers. However, previous work has established the strength of eigenvector and betweenness metrics in detecting prominent actors (Van Der Merwe & Van Heerden, 2009); therefore, while the technique is simplified, it is also advantageous in its versatility when the availability of information on physician networks is limited and challenging to obtain. Future work incorporating survey data on physicians' beliefs about peer influence would provide additional insight into the strength of this method to detect influencers.

Conclusion

This study suggests there may be differences in opioid prescribing behavior depending on physician network category and specialty. This work contributes to the developing field of identifying potential prescribing variations based on physician location within professional networks.

Chapter 5: Conclusion

Summary

Physician networks and their characteristics and overall structure are important indicators of care coordination and patient-outcomes (DuGoff, Fernandes-Taylor, et al., 2018). The goal of this dissertation was to combine a novel nation-wide dataset on physician characteristics and prescribing behavior among providers serving Medicare patients to determine if patterns in either opioid prescribing or opioid-related payments exist across various network types or provider types. My hypothesis was that physicians would demonstrate patterns in opioid prescribing or acceptance of opioid-related payments based on larger network-level attributes such as composition of specialty among peers, or position within the overall network.

The evidence presented in Chapter 2 demonstrates that primary care physicians exhibit differences in opioid prescribing depending on peer network characteristics which is likely a reflection of peer specialization, training, and geography. Specifically, I find primary care providers who have more connections and more peers within a pain management specialty or surgery are more likely to have a higher median opioid prescribing rate in patient-, hospital-, group-, and hospital/group-networks. These results highlight the role that peer connections have on influencing prescribing behavior, although future work is needed to understand, outside direct patient-related clinical needs, what role provider-level beliefs and institutional training inform prescribing.

In Chapter 3, I find physicians who accept opioid-related payments may be more likely to have peers with a similar likelihood or receptivity to accepting opioid payments. For instance, physicians with any opioid payments had around three times the likelihood of at least one peer within their patient-sharing network who also had an opioid payment compared to physicians without any opioid payments. These physicians are more likely to belong to smaller and more interconnected patient-sharing networks. This study highlights the importance that peer networks have on influencing physician behavior and the potential amplifying effect of promotional activities. Future work should examine how opioid payments within networks impact changes in opioid prescribing.

Finally, in Chapter 4, I explored a subset of physicians who may have the most influence within a network based on structural location. The results demonstrated a potential new use in combing two social network metrics as a first attempt to identify potential physician influencers. The results suggest there may be differences in opioid prescribing depending on physician network category and specialty. For instance, “well-connected” physicians appear to be more likely to have general industry relationships and are more likely to be specialists or surgeons. In terms of prescribing, “well-connected” physicians appear less likely to fall within the top 25 percent of opioid prescribing rates, indicating physicians who are highly connected are most likely highly referred specialists coordinating care across several physician peers and prescribing opioids at lower rates. These findings align with what we may expect to find in physician referral networks, with primary care providers writing the largest total number of opioid prescriptions compared to all other specialties. Future work should utilize mixed-methods research to affirm the use and appropriateness of utilizing eigenvector and betweenness centrality to locate potentially well-connected physicians.

Policy Implications and Future Research

Exploiting information pathways within physician networks is increasingly employed as a strategy to increase the uptake of evidence-based decision-making and improve patient care. Overall, the evidence presented within this dissertation support the utilization of network-based interventions since it appears physicians may, in part, be using information learned from informal network sources to guide prescribing decisions or acceptance of industry payments.

Various interventions and policies could utilize provider networks to increase adherence to appropriate pain management, or utilization of the updated CDC opioid guidelines. One such intervention could be peer comparison letters that notify physicians, usually high prescribers, that their prescribing behavior is outside the norm of their colleagues and reiterate guideline recommendations. Several studies have found these interventions effective at reducing unnecessary prescriptions (Sacarny et al., 2019; K. L. Schwartz et al., 2021). Likewise, network-level interventions could be leveled within specific areas that have a reduced pain management workforce and/or cluster of providers with potentially inappropriate prescriptions. Within these networks, additional CME courses could be offered to educate physicians on current practices in evidence-based pain management. A simplified electronic clinical decision support (CDS) system within electronic health records could “nudge” providers towards guideline-concordant prescribing and may be useful in reducing provider indecision and workload (Ancker et al., 2021). Relatedly, work being done to assess an interoperable CDS tool for shared decision-making among primary care physicians prescribing opioids may also lead to reduced provider indecision and concordance with guidelines (Salloum et al., 2022). Collaborative care models that emphasize partnering with pharmacists, nurses, or behavioral health care specialists, to deliver multimodal pain care also offer a promising path for reducing pain management uncertainty among primary care providers (Alford et al., 2011; Lagisetty et al., 2020). Finally, reimbursement policies could be realigned such that clinically- and cost-effective nonopioid pain therapies (e.g., physical therapy, cognitive behavioral therapy, massage, yoga) are covered which may reduce provider concerns about prescribing opioids since many multimodal non-drug treatments do not have the adverse side effects and complications that opioids have.

Provider and healthcare worker networks could also be utilized to increase access for medication assisted treatment (MAT) for opioid use disorder such as methadone and buprenorphine. Despite evidence that MAT is the best treatment modality for reducing opioid overdose, use, and mortality, many primary care providers who are waivered to provide MAT do not always offer treatment to patients who need it (Huhn & Dunn, 2017). Physicians report similar reasons for under prescribing MAT as they do for not prescribing opioids- namely, that they are uncertain about the treatment and their ability to care for patients who require it (Huhn & Dunn, 2017). One initiative to increase MAT access is the hub-and-spoke model wherein a substance use disorder specialty clinic (the hub) works with a network (the spokes) of physicians, nurses, and behavioral health specialists to provide fully integrated substance use disorder treatment and general healthcare and wellness services. Another model is the Physician Clinical Support System-Buprenorphine (PCSS-B), a federally funded program that pairs physician mentors with expertise in buprenorphine with a physician peer to provide a range of services and support (Egan et al., 2010). Collaborative network models like this have shown promising results including an increase in the number of physicians obtaining a US Drug Enforcement Administration (DEA) waiver to prescribe buprenorphine, and demonstrate the ability of provider networks to increase access for MAT via peer collaborations across specialties and professions (Brooklyn & Sigmon, 2017; Mohlman et al., 2016).

Finally, this dissertation discusses and reveals potential ways in which provider networks may have been exploited to increase inappropriate or unnecessary opioid prescribing in the early 1990s leading to the first wave of the opioid epidemic. In Chapter 4, I find that potential physician influences may hold characteristics within their network that predispose them to transmit information faster or more efficiently to peers than those who are on the fringes of the network. Evidence from court documents and investigative reporting detail how opioid drugmakers like Purdue Pharma exploited the network positions of well-connected physicians, or “key opinion leaders” (KOLs), who could spread information further and influence peers (Joseph, 2019a; Keefe, 2021). These KOLs were often given scripted promotional presentations devised by former tobacco company consultants to assuage physician peer concerns about the harms caused by opioids (Keefe, 2021). In addition, opioid drug makers targeted sales force efforts on providers with small networks practicing in rural areas known to have higher populations of patients with pain (e.g., mining-based communities in Appalachia). Court documents find physicians who met with opioid drug representative were ten times more likely to have prescribed opioids to patients who later died of an opioid-related overdose compared to physicians who prescribed opioids without having met with a company sales representative (Joseph, 2019a).

Future work should incorporate informative and influential patient-level factors (e.g., diagnosis, opioid dosage and duration) to evaluate the extent of opioid prescribing appropriateness among physician networks and whether network-level factors translate into differential patient outcomes. Research on physician network-level patterns in opioid prescribing could also benefit from the incorporation of qualitative data that may reveal contextual complexities underlying physician relationships within a network that quantitative data alone cannot address. For instance, Kierkegaard and Owen-Smith (2021) use semi-structured interviews, document analysis, and ethnographic field observations to reveal reasons underlying a physician’s decision to collaborate across different networks. These include, among others, a desire to establish personal relationships with physicians in different specialties, to increase reputation, and to collaborate on research.

Appendices

Table A1: Explanations and examples of social network attributes and centrality measures

Network Attributes	**Definition**	
Node	Actors (e.g., individuals or groups) that make up a network.	
Edge	Connections or relationships between edges. Edges can be either "directed," meaning information flows in a certain direction from one node to another, or "undirected," meaning the information flow or influence between two nodes is assumed to be the same.	
Centrality Measure	**Definition**	**Interpretation**
Degree centrality	Assesses the number of connections (i.e., shared patients) that a physician has with other physicians within a network.	A physician with a high degree centrality is one that has a higher number of connections within the network. Physicians with lower degree centrality have less connections to other physicians within the network.
Betweenness centrality	Measures the number of times a physician acts as a link along the shortest path between two other physicians, divided by the shortest paths between all the physicians within a network.	Physicians with high betweenness centrality act as central hubs connecting other physicians and thus play a role in network cohesiveness and may be considered more influential. Physicians with lower betweenness centrality have fewer links to other providers and therefore may be less influential.
Transitivity centrality (also known as the clustering coefficient)	Measures the number of closed triplets (i.e., three physician connections) in a physician's neighborhood over the total number of closed triplets within the neighborhood. In other words, transitivity centrality measures cliques within a network by assuming the following pattern: if physician A and physician B are friends (A—B), and physician B and physician C are friends (A—B), then physician A and physician C are also friends (A—C).	Higher transitivity within a network indicates dense connections and the possibility of greater physician communication. Lower transitivity within a network indicates less dense connections and may indicate less overall communication between providers.
Eigenvector centrality	Measures the influence of each physician by calculating a score dependent on the number of connections that a particular physician has to all other physicians within the network. The score is proportional to the sum of scores of all other connected physicians. In other words, a physician who has many connections may still have a low eigenvector score if those	A high eigenvector score indicates that the physician is connected to many other physicians who also have high scores. Lower eigenvector scores indicate the physician is not well-connected to other

	connections are linked to other low-scoring physicians. In addition, even if a physician has a high betweenness score (i.e., the extent to which physicians are distanced from each other), they may still have a low eigenvector score if they are some measure of distance away from the center of the network.	potentially influential physicians.

Network example:

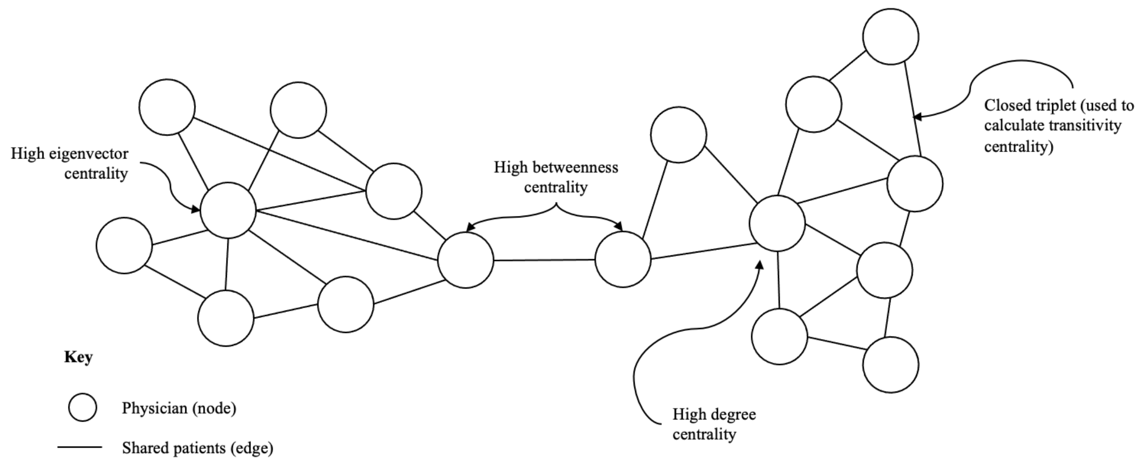

Figure A2: list of opioid drugs included, sourced from CMS Part D Prescriber PUF Drug List Summary opioid flag variable
Abstral (fentanyl citrate)
Acetamin-Caff-Dihydrocodeine (acetaminophen/caff/dihydrocode)
Acetaminoph-Caff-Dihydrocodeine (dhcodeine bt/acetaminophn/caff)
Acetaminophen-Codeine (acetaminophen with codeine)
Actiq (fentanyl citrate)
Arymo ER (morphine sulfate)
Asa-Butalb-Caffeine-Codeine (codeine/butalbital/asa/caffein)
Ascomp With Codeine (codeine/butalbital/asa/caffein)
Aspirin-Caffeine-Dihydrocodeine (aspirin/caffein/dihydrocodeine)
Aspirin-Caffeine-Dihydrocodeine (dihydrocodeine/aspirin/caffein)
Avinza (morphine sulfate)
Butalb-Acetaminoph-Caff-Codeine (butalbit/acetamin/caff/codeine)
Butalb-Caff-Acetaminoph-Codeine (butalbit/acetamin/caff/codeine)
Butalbital Compound-Codeine (codeine/butalbital/asa/caffein)
Butorphanol Tartrate (butorphanol tartrate)
Capital W-Codeine (acetaminophen with codeine)
Carisoprodol Compound-Codeine (carisoprodol/aspirin/codeine)
Carisoprodol Compound-Codeine (codeine/carisoprodol/aspirin)
Carisoprodol-Aspirin-Codeine (carisoprodol/aspirin/codeine)
Carisoprodol-Aspirin-Codeine (codeine/carisoprodol/aspirin)
Co-Gesic (hydrocodone/acetaminophen)
Codeine Sulfate (codeine sulfate)
Conzip (tramadol HCL)
Demerol (meperidine HCL)
Dihydrocodeine-Acetaminoph-Caff (acetaminophen/caff/dihydrocod)
Dihydrocodeine-Acetaminoph-Caff (dhcodeine bt/acetaminophn/caff)
Dilaudid (hydromorphone HCL)
Duragesic (fentanyl)
Embeda (morphine sulfate/naltrexone)
Endocet (oxycodone HCL /acetaminophen)
Endodan (oxycodone HCL /aspirin)
Exalgo (hydromorphone HCL)
Fentanyl (fentanyl)
Fentanyl Citrate (fentanyl citrate)
Fentora (fentanyl citrate)
Fioricet with Codeine (butalbit/acetamin/caff/codeine)
Fiorinal with Codeine #3 (codeine/butalbital/asa/caffein)
Hycet (hydrocodone/acetaminophen)
Hydrocodone Bit-Ibuprofen (hydrocodone/ibuprofen)
Hydrocodone-Acetaminophen (hydrocodone/acetaminophen)
Hydrocodone-Ibuprofen (hydrocodone/ibuprofen)
Hydromorphone ER (hydromorphone HCL)
Hydromorphone HCL (hydromorphone HCL)
Hysingla ER (hydrocodone bitartrate)
Ibudone (hydrocodone/ibuprofen)
Kadian (morphine sulfate)

Lazanda (fentanyl citrate)
Levorphanol Tartrate (levorphanol tartrate)
Lorcet (hydrocodone/acetaminophen)
Lorcet HD (hydrocodone/acetaminophen)
Lorcet Plus (hydrocodone/acetaminophen)
Lortab (hydrocodone/acetaminophen)
Meperidine HCL (meperidine HCL)
Meperitab (meperidine HCL)
Morphabond ER (morphine sulfate)
Morphine Sulfate (morphine sulfate)
Morphine Sulfate ER (morphine sulfate)
MS Contin (morphine sulfate)
Norco (hydrocodone/acetaminophen)
Nucynta (tapentadol HCL)
Nucynta ER (tapentadol HCL)
Opana (oxymorphone HCL)
Opana ER (oxymorphone HCL)
Oxaydo (oxycodone HCL)
Oxecta (oxycodone HCL)
Oxycodone HCL (oxycodone HCL)
Oxycodone HCL ER (oxycodone HCL)
Oxycodone HCL-Acetaminophen (oxycodone HCL/acetaminophen)
Oxycodone HCL-Aspirin (oxycodone HCL/aspirin)
Oxycodone HCL-Ibuprofen (ibuprofen/oxycodone HCL)
Oxycodone-Acetaminophen (oxycodone HCL/acetaminophen)
Oxycodone-Aspirin (oxycodone HCL/oxycodon ter/asa)
Oxycodone HCL-Acetaminophen (oxycodone HCL/acetaminophen)
Oxycodone HCL-Aspirin (oxycodone HCL/aspirin)
Oxycodone HCL-Ibuprofen (ibuprofen/oxycodone HCL)
Oxycodone-Acetaminophen (oxycodone HCL/acetaminophen)
Oxycodone-Aspirin (oxycodone HCL/oxycodon ter/asa)
OxyContin (oxycodone HCL)
Oxymorphone HCL (oxymorphone HCL)
Oxymorphone HCL ER (oxymorphone HCL)
Pentazocine-Acetaminophen (pentazocine HCL/acetaminophen)
Percocet (oxycodone HCL/acetaminophen)
Percodan (oxycodone HCL/aspirin)
Primlev (oxycodone HCL/acetaminophen)
Reprexain (hydrocodone/ibuprofen)
Roxicet (oxycodone HCL/acetaminophen)
Roxicodone (oxycodone HCL)
Rybix ODT (tramadol HCL)
Subsys (fentanyl)
Synalgos-DC (aspirin/caffein/dihydrocodeine)
Tramadol HCL (tramadol HCL)
Tramadol HCL ER (tramadol HCL)
Tramadol HCL-Acetaminophen (tramadol HCL/acetaminophen)
Tylenol-Codeine (acetaminophen with codeine)

Tylox (oxycodone HCL/acetaminophen)
Ultracet (tramadol HCL/acetaminophen)
Ultram (tramadol HCL)
Ultram ER (tramadol HCL)
Vicodin (hydrocodone/acetaminophen)
Vicodin ES (hydrocodone/acetaminophen)
Vicodin HP (hydrocodone/acetaminophen)
Vicoprofen (hydrocodone/ibuprofen)
Xartemis XR (oxycodone HCL/acetaminophen)
Xodol (hydrocodone/acetaminophen)
Xtampza ER (oxycodone myristate)
Xylon 10 (hydrocodone/ibuprofen)
Zamicet (hydrocodone/acetaminophen)
Zohydro ER (hydrocodone bitartrate)
Zolvit (hydrocodone/acetaminophen)
Zydone (hydrocodone/acetaminophen)

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