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Buprenorphine dispensing in an epicenter of the U.S. opioid epidemic: A case study of the rural risk environment in Appalachian Kentucky

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Abstract

Background—Buprenorphine is a cornerstone to curbing opioid epidemics, but emerging data suggest that rural pharmacists in the US sometimes refuse to dispense this medication. We conducted a case study to explore buprenorphine dispensing practices in 12 rural Appalachian Kentucky counties, and analyze whether and how they were shaped by features of the rural risk environment.

Methods—In this case study, we conducted one-on-one semi-structured interviews with 14 pharmacists operating 15 pharmacies in these counties to explore buprenorphine dispensing practices and perceived influences on these practices. Thematic analyses of the resulting transcripts revealed three features of the rural risk environment that shaped dispensing. To explore these three risk environment features, we analyzed policy documents (e.g., Attorney General lawsuits) and administrative databases (e.g., incarceration data). Textual documents were analyzed using thematic analyses and administrative data were analyzed using descriptive statistics; memos explored relationships among risk environment features and dispensing practices.

Results—Twelve of the 15 pharmacies limited dispensing, by refusing to serve new patients; limiting dispensing to known patients or prescribers; or refusing to dispense buprenorphine altogether. Concerns about exceeding a “Drug Enforcement Administration (DEA) cap” on opioid dispensing stifled dispensing. A legacy of aggressive and fraudulent marketing of opioid analgesics (OAs) by pharmaceutical companies and physician OA overprescribing undermined pharmacist trust in buprenorphine and in its prescribers. The escalating local war on drugs may have undermined dispensing by reinforcing stigma against people who use drugs.

Conclusions—Initiatives to increase buprenorphine *prescribing* must be accompanied by policy changes to increase *dispensing*. Specifically, buprenorphine should be removed from opioid monitoring systems; efforts to de-escalate the war on drugs should be extended to encompass rural

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areas; initiatives to dismantle aggressive OA marketing should be strengthened; and efforts to rebuild pharmacist trust in physicians are needed.

Keywords

Buprenorphine; rural areas; risk environment; pharmacists; implementation chasm

Introduction

Epidemics of opioid use disorder (OUD) and related harms have been expanding into rural areas in Australia and North America in recent years.(Belzak & Halverson, 2018; King, Fraser, Boikos, Richardson, & Harper, 2014; Rintoul, Dobbin, Drummer, & Ozanne-Smith, 2011) In the US, rates of opioid overdose deaths in rural areas have been as high as or higher than rates in cities for the past decade,(Hedegaard, Miniño, & Warner, 2019) and rates of neonatal opioid withdrawal syndrome are higher in rural areas than they are in cities. (Rintoul et al., 2011; Villapiano, Winkelman, Kozhimannil, Davis, & Patrick, 2017) A recent “vulnerability analysis” conducted by the US Centers for Disease Control and Prevention (CDC) concluded that the counties most vulnerable to imminent HIV and HCV outbreaks among people who use drugs are “overwhelmingly rural,”(Van Handel et al., 2016) and rural young adults now bear the highest incidence of hepatitis C virus (HCV) of all US subpopulations.(Zibbell et al., 2015).

In rural areas, the implementation chasm – defined as the gap between scientific advances and their implementation – is wide for harm reduction services, including for buprenorphine and other medications to treat OUD (MOUDs). MOUDs effectively treat OUD when dosed appropriately,(Office of the US Surgeon General, 2018) and reduce the incidence of overdoses, HIV, and HCV. (Norton et al., 2017; Tsui, Evans, Lum, Hahn, & Page, 2014; Volkow, Frieden, Hyde, & Cha, 2014) Spatial access to MOUD and other harm reduction services is fundamental to their utilization.(Amiri et al., 2018; Cooper et al., 2011) Spatial access to MOUD is poor in rural areas: 30% of rural residents live in a county without a buprenorphine provider, compared with only 2.2% of urban residents, (Andrilla, Moore, Patterson, & Larson, 2019) and the average drive time to methadone programs is 6.3 times greater in rural areas than in large metropolitan areas (49.1 minutes vs. 7.8 minutes). (Joudrey, Edelman, & Wang, 2019).

Federal and state governments in the US have launched multiple initiatives to close the MOUD chasm. In 2016, for example, Congress passed the Comprehensive Addiction and Recovery Act (CARA), which expanded the categories of health professionals permitted to prescribe buprenorphine to temporarily include nurse practitioners and physician assistants. Because of the geographic distribution of these healthcare professionals, CARA increased the number of buprenorphine prescribers in rural areas: between 2012 to 2017, per capita waived providers (i.e., individuals trained to prescribe buprenorphine) doubled in rural counties.(Pew Charitable Trust, 2019) In 2018, Congress passed the SUPPORT for Patients and Communities Act, which made these expansions permanent, and increased the number of patients to whom each provider could prescribe buprenorphine.

These initiatives focus on prescribers, and assume that pharmacists will dispense the buprenorphine that is prescribed by the ever-growing number and type of providers. This assumption may not, however, hold in US rural areas. Data from several countries where pharmacists have dispensed MOUD for decades suggest that they remain ambivalent about dispensing, and may refuse to dispense methadone, buprenorphine, and other MOUD.(Chaar et al., 2013; Irwin, Laing, & Mearns, 2012; Sheridan, Manning, Ridge, Mayet, & Strang, 2007) Identified barriers to dispensing include stigma, lack of financial support, and concerns about other customers' reactions and about poor alignment of MOUD dispensing with the pharmacist's role.(Chaar et al., 2013; Matheson, Thiruvethiyur, Robertson, & Bond, 2016; Uosukainen et al., 2013) Buprenorphine is the first MOUD that US pharmacists have been charged with dispensing widely, and emerging evidence suggests that pharmacists in rural areas are refusing to do so. One survey found that 46% of pharmacists in West Virginia, a predominately rural state, did not stock buprenorphine and 25% did not stock buprenorphine/naloxone. (Thornton, Lyvers, Scott, & Dwibedi, 2017) During qualitative interviews with physicians in Tennessee, another predominately rural state, physicians expressed frustration with pharmacists who refused to dispense the buprenorphine prescriptions that they wrote.(Ventricelli et al., 2019) Notably, a large body of research on buprenorphine access exists for US urban areas, and none has identified dispensing as a barrier.(Allen & Harocopos, 2016; Fox, Chamberlain, Sohler, Frost, & Cunningham, 2015; Gryczynski et al., 2013) In the midst of overlapping opioid-related crises, pharmacists may be stymying federal and state initiatives to increase the flow of MOUD into rural communities.

Purpose and Risk Environment Model

The present case study investigates pharmacists' dispensing practices in 12 Appalachian Kentucky counties at the heart of the US opioid epidemic, and explores the formation of these practices within the local rural risk environment. The original formulation of the Risk Environment Model (REM) posited that features of the political, social, economic, and physical environments interact with one another across levels to shape vulnerability and resilience to drug-related harms. (Rhodes, 2002; Rhodes & Simic, 2005) REM has supported a flourishing of research into the relationships between features of these environments and drug-related harms.(Strathdee et al., 2010) Cooper and colleagues added a fifth influence to capture healthcare and criminal justice interventions to support US-based work.(Cooper et al., 2012; Cooper, Linton, et al., 2016) Originally, REM had included the healthcare service/criminal justice environment as features of the social, political, and physical environments; gathering them into their own influence type was important in the US context, where a war on drugs has raged since the 1980s,(Alexander, 2020) and harm reduction access is low.(Des Jarlais et al., 2015; Tempalski, Cleland, Williams, Cooper, & Friedman, 2018).

The present analysis is nested within and seeks to strengthen two ongoing evolutions in REM: (1) a *post-structuralist* turn, and (2) deepening engagement with the *mesolevel*. REM-guided research has been criticized for often applying a structuralist approach to conceptualizing and studying the impact of macrolevel features on health.(Duff, 2007; Rhodes, 2009) Treating these features as "forever 'outside' the contextual field, originating elsewhere and powered by unfamiliar and seemingly incomprehensible historical processes,"

(Duff, 2007, p 505–506) structuralist approaches assume that macrolevel features are universal and deterministic. Accordingly, structuralist analyses obscure heterogeneous local risk environments, and the processes through which they are formed. A *post*-structuralist approach, in contrast, is contingent and local.(Duff, 2007; Rhodes, 2009) It analyzes the formation of local risk environments through interactions of macrolevel features, with potent agents acting within and across levels.(Duff, 2007; Rhodes, 2009) Here, we follow a post-structuralist approach to describe one feature of the local rural healthcare service/criminal justice environment – pharmacist buprenorphine dispensing practices in 12 Appalachian Kentucky counties – and analyze its formation through particular local interplays of select salient features of the macrolevel, mesolevel, and microlevel environment in this rural area. Consistent with a post-structuralist approach, we recognize and analyze pharmacist agency, and view pharmacists’ buprenorphine dispensing practices as simultaneously shaped by and constitutive of this particular local rural risk environment.

Guided by REM’s emphasis on interplays across levels,(Rhodes, 2002, 2009) we describe and analyze the formation of a vital feature of the *mesolevel* local rural risk environment. The mesolevel has had a precarious presence in REM, flickering in and out of REM’s theoretical writings. It is absent from Rhodes’ earliest writings, which delineate just two levels, the macrolevel and the microlevel.(Rhodes, 2002; Rhodes et al., 1999) It appears in Rhodes et al’s 2005 paper on the social structural production of HIV among people who use drugs, where it is defined as including “perceived group ‘norms’ ... and institutional or organisational responses.”(Rhodes, Singer, Bourgois, Friedman, & Strathdee, 2005, p 1027) It then disappears from several subsequent landmark REM papers.(e.g., Strathdee et al., 2010) Despite inattention to the mesolevel in REM’s theoretical work, several empirical studies guided by REM have explored mesolevel features of the risk environment over the past decade. McNeil and colleagues, for example, have explored how policies within safe consumption sites undermined the utility of these facilities for people living with disabilities; (McNeil, Small, Lampkin, Shannon, & Kerr, 2014) Knight found that women who lived in single-room occupancy hotels with trauma-informed policies felt safer and less anxious than women living in hotels that were more chaotic and crowded.(Knight et al., 2014) The present REM-guided analysis centers one feature of the healthcare service/criminal justice environment operating within the mesolevel, exploring the formation of buprenorphine dispensing practices within rural pharmacies.

We view these two REM evolutions as complementary, and particularly generative for exploring the formation of pharmacists’ buprenorphine dispensing practices in a rural area. Pharmacist reluctance to dispense MOUD is well documented internationally;(Chaar et al., 2013; Irwin et al., 2012; Matheson et al., 2016; Sheridan et al., 2007; Uosukainen, Turunen, Ilomäki, & Bell, 2014) in the US, reports of restrictive dispensing practices are originating exclusively in rural areas. (Thornton et al., 2017; Ventricelli et al., 2019) With its emphasis on the formation of heterogeneous local risk environments, a post-structuralist analysis allows us to explore risk environment features that may give rise to restrictive buprenorphine dispensing practices in a particular US rural area. A post-structuralist analysis that centers the *mesolevel* illuminates the ways in which pharmacists serve as one of multiple agents that influence how macrolevel features move from being “‘outside’ the contextual field” to manifesting locally, as pharmacists craft dispensing practices by interpreting, transforming,

amplifying, and resisting multiple features of their risk environment, including seemingly monolithic features of the macrolevel environment.

Methods

Overview

We employed a case study approach to describe pharmacists' buprenorphine dispensing practices, conceptualized as a feature of the mesolevel healthcare service/criminal justice environment, and to describe the formation of these practices within one local rural risk environment.(Quinn Patton, 2002) The case study was conducted in 12 Appalachian Kentucky counties that collectively formed our unit of analysis. These counties have a high level of social, economic, and healthcare service integration. We have been working with residents, community-based organizations, and government agencies and leaders in these counties for over three years, and have learned through these partnerships that many people live in one of these counties and work, learn, socialize, shop, or worship in another; were raised in one and later moved to another; or have family scattered across the 12 counties. Residents share a common identity as living in Appalachian Kentucky. These counties also suffer high rates of drug-related harms, and all but two were ranked in the top 5th percentile of the CDC's vulnerability assessment, mentioned above.(Van Handel et al., 2016) These counties are served by two health districts, and services often have to be shared across counties to be sustainable.

This case study draws on two strengths of qualitative research: discovery and flexibility. It is embedded within a broader study of the risk environment for OUD, HIV, HCV, and overdose in these counties. As a part of this study, we conducted qualitative interviews with local pharmacists to understand their harm reduction attitudes and practices, viewing these pharmacists as vital actors in the mesolevel healthcare/criminal justice environment. We did not anticipate discovering barriers to buprenorphine dispensing. When these barriers surfaced in early interviews, we altered the project in two ways:

1. We revised the qualitative interview guide to support detailed explorations of dispensing practices. Interviews explored pharmacists' insights into buprenorphine's purpose and impacts, advantages and disadvantages, and features of the micro-, meso-, and macrolevel risk environment that they engaged with as they crafted these practices.

Preliminary and ongoing analyses of qualitative transcripts identified three especially salient features of the rural healthcare service/criminal justice environment that pharmacists considered when dispensing: a perceived "DEA cap" on dispensing; pharmaceutical companies' OA marketing strategies and consequent physician overprescribing of OAs; and the local war on drugs and interpersonal stigma. Interviews thus focused on these features in detail, exploring pharmacist interpretations of and responses to the "DEA cap" (e.g., resistance, acquiescence), OA prescribing, and criminal justice vs. public health responses to the opioid epidemic.

2. Given the prominence of these features of the healthcare service/criminal justice environment in interviews, we sought out additional existing data to quantify the manifestation of these features locally, and conducted a policy review of the “DEA cap” and other features of the buprenorphine dispensing regulatory context.

Data Sources and Analytic Methods

Qualitative interviews with pharmacists in the 12-county area—We applied purposive sampling methods to create a sample of pharmacists who represented all 12 counties, and who represented enough independent pharmacies and enough chain pharmacies to support comparisons of dispensing practices and salient risk environment features across these two pharmacy types. Interviews were conducted from February 2018–January 2019.

After pharmacists consented, trained interviewers conducted inperson, semi-structured interviews in a private location inside each pharmacy. As noted, interviews covered perceptions of the local opioid epidemic; buprenorphine dispensing and other harm reduction practices; and features of the micro-, meso-, and macrolevel environment in which these dispensing practices were embedded. (*NB:* We did not query experiences with the “DEA cap” with four pharmacists because (1) they reported that they did not dispense buprenorphine; and/or (2) their interviews [N=2] preceded the study team’s knowledge of this perceived cap.) Interviews lasted one hour on average, and pharmacists received a modest honorarium (\$10).

Interviews were audiotaped and transcribed verbatim. Transcripts were analyzed using thematic analysis methods. Following Braun and Clarke, (Braun & Clarke, 2006) codes were generated based on concepts in the transcripts and REM-guided research. Using memos and team discussion, codes were then grouped into themes that were internally coherent and mutually exclusive. We conducted multiple focused readings of the transcripts to apply REM. One reading identified and coded dispensing practices and salient features of the risk environment; features typically became themes. We also conducted focused readings dedicated to exploring the interplay of dispensing practices with these features, including tracing how risk environment features that might seem “outside” of the local environment materialized in these 12 counties (e.g., resistance to the perceived DEA cap); coded these interplays; and described emerging findings in memos. Consistent with a post-structuralist approach, in these readings we conceptualized pharmacists as potent agents who might (or might not) challenge risk environment features manifesting locally, perhaps transforming, acquiescing to, or resisting them.

One pharmacist operated two pharmacies; dispensing practices differed across these two pharmacies, and so we treated this pharmacist as two participants with diverging practices. A licensed pharmacist who directs the Center for Advancement of Pharmacy Practice at the University of Kentucky (PF) was invited to join the team during the analysis phase to guide analyses and help interpret findings. Negative cases were sought to enhance validity.

Policy review of the perceived “DEA cap” and other dispensing regulations—

We conceptualized the perceived “DEA cap” as a feature of the macrolevel healthcare service/criminal justice environment because it was perceived as a policy that governed access to a therapeutic medication, and was promulgated by a potent federal agency in the US War on Drugs.(Beletsky & Goulka, 2018) We conducted a policy review to explore the possibility that the DEA capped buprenorphine dispensing, and to learn about the broader regulatory environment governing buprenorphine dispensing. We used Westlaw and internet searches to identify Kentucky and federal statutes and regulations, case law, and secondary sources that shaped or described the legal landscape governing pharmacists’ duties for preventing buprenorphine diversion. We also reviewed grey literature and media to gain insights into how enforcement of federal regulations against wholesalers and pharmaceutical companies, nationally and in Kentucky specifically, may be influencing buprenorphine dispensing.

OA Marketing strategies and physician overprescribing—We conceptualized pharmaceutical companies’ OA marketing strategies as part of the macrolevel healthcare service/criminal justice environment because they pertained to the marketing of a therapeutic medication by multinational corporations. We analyzed these strategies using two data sources: (1) lawsuits filed by Kentucky’s Office of the Attorney General (OAG) against pharmaceutical companies for their Kentucky-based opioid marketing practices; and (2) Hadland et al’s analysis of Centers for Medicare and Medicaid Services (CMS) data on county-level opioid-analgesic marketing expenditures by pharmaceutical companies, aggregated across 2013–2015 (see Table 1 for details). (Hadland, Rivera-Aguirre, Marshall, & Cerdá, 2019) Four OAG lawsuits were selected for analysis because they were current and thus likely reflected recent practices; one (against Purdue) was initiated in 2007 and was selected because of the magnitude of concern expressed in interviews about Oxycontin prescribing. Note that all OAG documents analyzed here describe allegations, and so have not been proven. We used thematic analysis methods to identify dominant marketing strategies that the OAG’s investigation concluded were especially prominent and damaging in the state.

We conceptualized physician OA overprescribing as a feature of the mesolevel healthcare service/criminal justice environment because it pertained to organizational-level (i.e., clinic) distribution of a therapeutic medication. We assessed this risk environment feature using annual CDC county-level data on dispensed opioid analgesics (Table 1). (Centers for Disease Control and Prevention, 2017).

War on Drugs—The War on Drugs was conceptualized as a feature of the macrolevel healthcare service/criminal justice environment that intertwines recursively with multilevel stigma against people who use drugs. The War on Drugs is characterized by punitive, militaristic approaches to particular drug-related activities that often undermine human rights and public health.(Cooper & Fullilove, 2020) Here, we explore its manifestation at the mesolevel in these 12 counties, where local law enforcement agencies, prosecutors, courts, and corrections may deploy punitive approaches to curtailing drug-related activities. We analyzed Vera Institute of Justice data to track rates of jail-based detention and jail and

prison population size over time (Table 1). To contextualize findings for our 12-county area, we analyzed parallel data for the 12 most populous counties in the US.

We also drew on responses to items querying self-reported experiences with incarceration and interpersonal stigma (anticipated and enacted) in the “Gateway2Health” survey (Table 1). We viewed interpersonal stigma as a feature of the microlevel social environment that interacted recursively with the War on Drugs. Gateway2Health used respondent driven sampling methods to recruit adults living in five of the 12 counties who report recently (past 30 days) either using opioids to get high or injecting any drug to get high.

Descriptive statistics were calculated for all quantitative variables.

Results

Overview

Our analyses suggest that most pharmacists developed buprenorphine dispensing practices that rejected some or all patients with legitimate buprenorphine prescriptions. They also suggest that these practices embody features of the macrolevel, mesolevel, and microlevel risk environment (Figure 1). Mindful that post-structuralist analyses can overemphasize microlevel features, we have organized results by the three macro-, meso-, and microlevel risk environment features that were prominent in pharmacist discussions of dispensing: the perceived “DEA cap;” OA marketing and consequent overprescribing, and the war on drugs and drug-related interpersonal stigma. We describe each in detail, and the ways that it materialized as dispensing practices within this particular rural risk environment, as pharmacists interpreted, resisted, or embraced it. We open, though, with a description of this case’s setting, as experienced by pharmacists, to orient readers.

Setting

The analysis of pharmacist transcripts achieved saturation with a sample of 14 pharmacists, who operated 15 pharmacies in nine of the 12 counties; 2/3rds were men and all identified as non-Hispanic White. These pharmacists constituted 23% of all retail (i.e., non-hospital based) pharmacies located in the 12-county area. We were, however, only able to interview one pharmacist at a retail pharmacy chain: other chain-based pharmacists either reported they had no time for an interview, or were forbidden from participating in the interviews.

Most of the 14 pharmacists had deep roots in the communities they served. Nine had grown up in or near the counties where they practiced; several came from families who had lived in these counties “forever.” They spoke of the out-migration and economic hardships that their hometowns had experienced, rooted in the loss of coal jobs and farming, and expressed concern about boredom and lack of opportunity plaguing younger generations.

Administrative data echoed these concerns. Nine of the 12 counties were or had been coal-producing. With coal jobs declining, all 12 counties met the federal definition of a poverty area (i.e., an area with a poverty rate $\geq 20\%$), with poverty rates varying from 22.7%–45.1%.

In this midst of these significant concerns, pharmacists also celebrated multiple strengths of the communities they served. Pharmacists observed that these “rural,” “small” counties were

“tight-knit” communities where residents were “loyal” and “trustworthy” people with “strong work ethics.” Residents were “kind” and “took care” of one another, lending a “helping hand” in times of hardship. They felt that “the people here are our greatest strength.” They took pride in their communities: “this is our home and it is special to us.”

Pharmacists reported that they operated “hometown pharmacies” that were often tightly woven into the local social fabric. In these sparsely populated counties, residents developed close ties with pharmacists:

These people, I know their kids’ names. I know that they got a dog last week. I know what the dog’s name is, that they are going out of town to visit their grandkids.

In their roles as healthcare professionals and, often, longstanding community members, pharmacists were acutely aware of the local opioid crisis. With rare exception, pharmacists reported that they still dispensed a high volume of OA prescriptions:

it’s incredible, like, the amount of opioids that we [dispense] here, anything from... Oxycodone [to] methadone.

They reported that OUD was “rampant” and that their community was “humming” with opioids. When nine pharmacists were asked to estimate the percent of adult county residents who either used opioids to get high or injected any drug to get high, their median response was 40% (range: 14%, 70%). Unprompted, five reported having family members who struggled with some kind of substance use disorder.

They expressed sorrow and frustration over the impact of the opioid epidemic locally. Some focused on increasing crime, others on a generation raised in foster care, others on the suffering of people who used drugs, and still others on lost collective futures:

[drugs have] hindered what we could become by ...not allowing our community to reach its full potential...who knows what [we] could be if there was not a drug problem?

In the midst of this opioid epidemic, the number of buprenorphine prescriptions pharmacists received was “exploding.” Six pharmacies dispensed over 100 buprenorphine prescriptions each month; five dispensed 20–50 prescriptions each month. Notably, however, pharmacists had crafted dispensing practices that often curtailed the flow of this medication into the community: four refused to dispense buprenorphine, and 12 of the 15 pharmacies limited the number of buprenorphine prescriptions they filled. At issue in this analysis is why so many pharmacists –though deeply concerned about the opioid epidemic and the toll it took on their beloved communities and families – developed dispensing practices that failed to meet the exploding demand for buprenorphine among their patients.

The perceived “DEA cap” and other features of the buprenorphine regulatory environment

Overview

The buprenorphine regulatory environment – and in particular the perceived “DEA cap” – was a highly salient feature of the macrolevel healthcare service/criminal justice environment for pharmacists. Ten of the 14 pharmacists discussed this perceived cap on dispensing, reporting that the DEA (or wholesalers – pharmacists disagreed about the monitoring agency) directly monitored the percent of controlled substances that were opioids that each pharmacy dispensed. They reported that pharmacies that surpassed a particular threshold (i.e., the “cap”) would be investigated by the DEA. They explained that buprenorphine was included in these calculations, and so they moved closer to the cap with every buprenorphine prescription they dispensed. The policy review confirmed this monitoring, and revealed that surveillance and enforcement were particularly aggressive in Kentucky. Pharmacists actively grappled with the cap – interpreting it, adapting to it, challenging it – when crafting their buprenorphine dispensing practices.

Macrolevel “DEA caps” in the healthcare service/criminal justice environment

The policy review clarified the origin of the “cap:” while federal law does *not* directly impose “caps” or thresholds on the quantity of buprenorphine prescriptions that pharmacies can dispense, DEA regulations and the SUPPORT Act require that wholesalers design and implement a system to detect suspicious orders of opioids and other controlled substances, and impose a duty to promptly notify DEA officials of orders that are atypically large or otherwise questionable. (Department of Health and Human Services, ND; Murphy, Xu, Kochanek, & Arias, 2018) To comply with federal law, wholesalers have devised elaborate, proprietary algorithms and other internal systems to monitor dispensing. For example, McKesson Corporation describes its controlled substance monitoring program (CSMP) as follows:

Our CSMP uses sophisticated algorithms designed to monitor for suspicious orders, block the shipment of controlled substances to pharmacies when certain thresholds are reached and ultimately report those suspicious orders to the DEA.(McKesson Corporation, 2019).

Buprenorphine is included in these systems, and pharmacists experienced these algorithm-generated thresholds for buprenorphine as “caps.”

Pharmacies flagged by these wholesaler algorithms can face dire consequences. At a minimum, wholesalers may freeze the supply of the medication, leaving pharmacists’ customers to suffer. At worst, if the DEA detects a potential violation, it can initiate an investigation into the pharmacy that can result in denial, revocation, or suspension of a pharmacy’s registration, and criminal charges.(Office of Public Affairs in the U.S. Department of Justice, 2019).

Federal and state enforcement of these policies is especially aggressive in Kentucky. As discussed in detail below, Kentucky has a history of excessive OA overprescribing that is tightly linked to aggressive pharmaceutical marketing and rural occupations that produce high rates of injury and chronic pain (e.g., mining, farming). Accordingly, the DEA opened a diversion field office in Louisville, Kentucky in 2018. This office was the first diversion field office opened in the US in two decades, and increased the physical presence of agents in the state. (Larson, 2017) In a parallel initiative, Kentucky's OAG has prioritized prosecuting manufacturers, prescribers, and distributors for diverting Schedule II opioids and buprenorphine, and has called for more stringent regulations to prevent diversion of buprenorphine from clinics and pharmacies, comparing "rogue" buprenorphine clinics to the pill mills that flooded Kentucky's rural communities with OAs. (Hazard Herald Staff Report, 2018; National Public Radio, 2017).

Qualitative results: "DEA Caps" and "stumbling blocks"

While some pharmacists may have misunderstood the cap's origins (i.e., ascribing it directly to the DEA, instead of to wholesalers endeavoring to comply with DEA regulations), the ten pharmacists who discussed the cap engaged deeply with it when developing buprenorphine dispensing practices:

The DEA has a magic number ["the cap"]. No one knows what that number is... So everybody says, 'we're going to assume that the number is 20%... No one knows, but you want [the percentage of buprenorphine prescriptions you dispense] to be low.

Unaware of the true value of this "magic number" and seeking to avoid an investigation, pharmacists at five pharmacies established an internal cap on buprenorphine dispensing (e.g., two prescriptions per day) to reduce their risk of a DEA investigation. Patient demand, however, routinely exceeded these internal caps. In response, these pharmacists developed a practice of limiting buprenorphine dispensing to local residents or to long-term customers. One pharmacist explained that rationing allowed him to be loyal to known customers:

[Each new prescription] takes the medicine away from people that have been coming here for a year and a half... [I want to support] my people that live... where I work and where I prosper.

Rationing, however, created challenges that rippled through the local risk environment. As the mesolevel, it strained pharmacists' relationships with prescribers, who called repeatedly in search of a pharmacy that would dispense buprenorphine to new patients. It angered patients who were turned away, despite presenting legitimate prescriptions. Pharmacists also worried that the "DEA caps" and consequent rationing undermined drug-use cessation options for local residents:

You can have all the funding in the world to have all these programs to [prescribe] all of these medicines. If your pharmacies can't physically get it [from the wholesalers], it ain't doing no good.

In contrast, five pharmacists explicitly chose not to adopt rationing practices. These pharmacists were either confident that their pharmacy's opioid dispensing did not exceed the

“DEA cap,” or actively championed harm reduction at possible professional and personal risk:

We do not [limit buprenorphine dispensing]...And I don't think we should because...if I limit to 20 individuals a day...then I just don't think that that's fair to the 21st person. Because the 21st person could be the person that's actually about to get clean.

Summary

The DEA and OAG fiercely monitored buprenorphine dispensing in this rural state with a history of OA overprescribing. This monitoring was a feature of the macrolevel healthcare service/criminal justice environment, and pharmacists determined whether and how it materialized locally. After carefully analyzing the “cap,” some pharmacists developed rationing practices that allowed them to conserve buprenorphine for loyal patients without risking investigation or prosecution. The consequences of this rationing practice reverberated through the local risk environment, damaging relationships with other mesolevel agents (i.e., prescribing clinicians) and with patients, and perhaps undermining local harm reduction efforts, even as it preserved treatment access for known patients. Other pharmacists actively resisted the “cap,” championing their buprenorphine patients and ensuring access to a lifesaving medication, though with potentially catastrophic personal and professional consequences.

OA marketing and prescribing

Overview

Pharmacists also crafted dispensing practices in dialogue with a legacy of aggressive and fraudulent OA marketing by pharmaceutical companies, a macrolevel feature of the healthcare service/criminal justice environment that was acute in Appalachian Kentucky, and that catalyzed mesolevel physician OA overprescribing. We first describe results of an analysis of Kentucky OAG lawsuits against five pharmaceutical companies and OA prescribing in the area, and then explore whether and how pharmacists incorporated this legacy into their buprenorphine dispensing practices.

Macrolevel fraudulent OA marketing and mesolevel OA overprescribing in the healthcare service/criminal justice environment

Analyses of Kentucky OAG lawsuits against five pharmaceutical companies identified three principle strategies that these companies deployed in the state to increase OA sales: (1) promoting misleading messages about OA risks and purposes; (2) employing aggressive sales tactics; and (3) compensating physicians. The OAG concluded that these companies used these strategies – which they charge were “illegal,” “fraudulent,” and “deceptive” – to saturate the environment in which physicians practiced with misinformation and incentives designed to promote over-prescribing. As noted previously, all documents referenced here describe allegations, and so have not been proven.

(1) Promoting misleading messages about OA risks and purposes—Kentucky OAG documents maintain that Purdue, Teva, Endo, Janssen, and InSys “trivialized” OA risks in venues targeting Kentucky physicians via journal supplements, speakers’ bureaus, detailing, and one-on-one contact with salespeople. According to OAG documents, for example, Teva, Janssen, and Endo falsely informed Kentucky physicians that addiction risk from their OAs was “modest” and “manageable,” and that screening protocols could effectively identify patients at risk of OUD. In 2015, Purdue agreed to pay Kentucky \$24 million to settle OAG claims that it had misled Kentucky physicians about OxyContin’s withdrawal potential, promoting it as a drug that posed no withdrawal risk if dosed at <60 mgs, and that it trained salespeople to present misleading graphs of blood plasma concentrations that implied that Oxycontin® was less likely to create euphoria than other OAs. Purdue’s salesforce call logs for Kentucky illustrate the dissemination of these messages to Kentucky physicians:

“Quick[ly] reminded him that Oxy gives flat blood levels, so less buzz than Lortab.”

“[The physician] loves the idea of getting effective pain relief, but not euphoria to get rid of druggies”

According to these OAG lawsuits, two companies also fraudulently described the *purpose* of their fentanyl-based OAs to Kentucky physicians. Approved solely to treat cancer pain, Subsys®, Fentora®, and Actiq® were promoted as effective treatments for non-cancer chronic pain. Teva, for example, promoted Actiq® as a treatment for migraines, sickle cell pain crises, injuries, anticipated wound dressing changes, and radiation, though approved exclusively for break-through cancer pain.

(2) Aggressive Sales Tactics—According to OAG documents, these misleading messages were aggressively promoted through intensive physician engagement by a salesforce whose incomes and employment were closely tied to their success. The OAG found that InSys, Teva, and Purdue created bonus and termination structures for their salespeople that tightly linked their income and job security to OA sales. Base salaries were low, and so salespeople had to sell large volumes of OA to earn bonuses to support themselves; former salespeople have maintained that the only way to attain their sales quotas was to ensure that physicians prescribed OAs for off-label use. Salespeople generating few sales were penalized not just by missed bonuses, but also by job loss, as illustrated by this 2013 email, sent by the InSys Vice President of Sales to sales managers:

Fridays, we literally do half in sales as the other 4 days. Every rep that does not produce a script two consecutive Fridays will be placed on a [performance improvement plan]...Below is the list [of salespeople] that failed to produce this past Friday, if you are on the list you must produce 1 single script this Friday to avoid a [performance improvement plan.]

This compensation structure incentivized aggressive engagement with Kentucky physicians. Teva salespeople visited Kentucky physicians 3013 times between 2012–2017 to sell one OA – Fentura® – alone. Purdue salespeople parsed the state into regions of 100–140 physicians who either already prescribed OA or might prescribe OA, and visited each of

these physicians every 3–4 weeks on average to sell OxyContin®. InSys and Teva salespeople monitored prescribing patterns of physicians in their territories, and InSys salespeople were instructed to contact each physician who prescribed a low dose of Subsyst®®, request an explanation, and admonish them for improperly treating pain.

(3) Physician Compensation—In October 2013, the InSys National Director Sales wrote to District Sales Managers that, “[w]hat drives us all? COMPENSATION.” Pharmaceutical companies used this motivating strategy not only for their salespeople, but also for Kentucky physicians. According to OAG lawsuits, Endo, Teva, and InSys invited high-prescribing Kentucky physicians to serve as well-paid speakers on their Speakers’ Bureaus; an audit unearthed by the OAG concluded that these events had little educational value. Pharmaceutical companies also compensated physicians by paying clinic staff salaries or offering pharmaceutical company staff to work in physician offices free of charge. OAG documents labeled this compensation “bribes” and “kickbacks” that were awarded to doctors with high OA prescribing rates, and withheld when prescribing rates were deemed too low.

An analysis of CMS data testifies to the magnitude of the funds flowing from pharmaceutical companies to physicians in these 12 Appalachian Kentucky counties to promote OA prescribing. These data indicate that between 2013–2015 pharmaceutical companies paid \$421,468 – or \$2712.35 per 1000 residents – to physicians practicing in these counties to promote OA prescribing. During this same period, published data suggest that the national average was \$1.57 per 1000 residents, 0.06% of the value for the 12-county region.

Pharmaceutical companies invested in physician compensation because it produced higher OA sales. OAG documents revealed that an analysis had found that,

“Physicians who attended [Purdue’s]...dinner programs or the weekend meetings wrote more than double the number of new prescriptions for OxyContin compared to the control group, and this was sustained over the three-month post-meeting evaluation.”

In accordance with this analysis, this macrolevel environment of misleading messages, aggressive marketing, and physician compensation in Eastern Kentucky helped produce significant physician overprescribing of OAs at the mesolevel in these 12 counties. Between 2006 and 2012, OA prescribing rates rose 30% in these 12 Kentucky counties, from 1.2 to 1.6 prescriptions per capita; they then declined (Table 3). In contrast, per capita OA prescribing rates in the 12 most populous US counties never exceeded 0.5 opioid prescriptions per capita. Between 2006 to 2017, OA prescriptions per capita in the 12 rural counties were 2 to 3 times that of the 12 most populous counties.

Qualitative results: “More of a greed thing” vs. “a tool to help you get off”

Pharmacists developed buprenorphine dispensing practices in dialogue with this legacy of macrolevel OA marketing and mesolevel overprescribing. Pharmacists and their dispensing practices cleaved into two groups, depending on the extent to which this legacy had frayed trust within the mesolevel healthcare service/ criminal justice environment.

Low-Trust Group—For six pharmacists, the OA legacy had destroyed trust in local buprenorphine prescribers and in buprenorphine itself. These pharmacists recognized that many of their patients suffered from injuries and chronic pain because manual labor was common in this rural area. Pharmacists practicing in coal-mining counties noted that the specific nature of mining labor caused back pain:

I guess back injury is probably the biggest [reason patients initiate OAs] around here....I think a lot of it has to do with the coal mining industry. People are crawling on their backs, and hands, and knees all day long, and it wears down your back. And it actually destroys your back.

These pharmacists recognize the need for pain treatment locally, but distrusted physician responses to this need. In counties beset with fraudulent and aggressive OA marketing, at best these pharmacists felt that local physicians were poor stewards of OAs when presented with patients who were in chronic pain. They maintained that physicians prescribed OAs when other analgesics would have sufficed. They believed that physicians prescribed OAs at doses that were too high, and for too long. They worried that physicians were manipulated into prescribing OAs to fraudulent patients who sought OAs to support OUD, divert for personal profit, or both. Consistent with data indicating high pharmaceutical company compensation to physicians in these counties, at worst these pharmacists believed that physicians overprescribed OAs for personal profit: “you’ve got a handful of doctors getting rich.”

This legacy of OA overprescribing eroded these pharmacists’ trust in physicians, and in buprenorphine itself. After decades of fraudulent OA marketing, physician compensation, and physician overprescribing, these pharmacists disbelieved physician and pharmaceutical company claims that buprenorphine was a legitimate treatment for OUD. Instead, they viewed it as simply the next wave of opioids fueling the local epidemic:

It is supposed to be the drug to help them [recover]. They want Suboxone® worse than they do the hydrocodone...It’s not what it’s designed to be.

They voiced concerns about physicians who prescribed buprenorphine that paralleled concerns about OA prescribing. At best, they viewed physicians who prescribed buprenorphine as poor stewards of the drug. They believed that patients should be tapered from buprenorphine, and reported that few physicians tapered rapidly enough or at all. They believed that physicians should link patients to mental health counseling, and were frustrated that this happened rarely. At worst, they viewed buprenorphine prescribers as simply perpetuating the dependence that they themselves had created by overprescribing OA for economic gain:

It’s almost like more of a greed thing... Especially if the same doctor decides that you’re addicted to the hydrocodone or whatever, and decides to put you on Suboxone®, and when they’ve written [the OA prescription] for the last 10 years.

These “low trust” pharmacists developed dispensing practices that reflected these intertwined concerns about OA, buprenorphine, and its prescribers. Federal and state laws require that, before dispensing buprenorphine, Kentucky pharmacists (1) judge the basis of a prescribers’ decision to recommend buprenorphine for a patient; (2) affirm the validity of the

prescription; and (3) take precautionary steps to prevent diversion (see Figure 2 for additional information). For these pharmacists, either buprenorphine itself or its prescribers failed to meet these standards. Three refused to stock buprenorphine. Two refused to accept new buprenorphine patients:

Since we have seen the increase in the amounts [of buprenorphine] that's being prescribed...we do try to limit [dispensing] to those [patients] that we initially started filling for. We try not to pick up any new ones because it is such an abused [drug].

High-Trust Group—Eight pharmacists retained their trust in physicians and their prescriptions despite the OA legacy; these “high-trust” pharmacists crafted dispensing practices that limited buprenorphine dispensing only to avoid DEA sanctions. While they recognized physicians’ roles in contributing to the local OA epidemic, they explicitly refused to blame them:

I don't think the majority of [the doctors] knew...[that they were] contributing, that it was going to get as bad as it did. I believe that.

These pharmacists believed that buprenorphine was an acceptable OUD treatment, rather than the next wave of the opioid epidemic. As one pharmacist reported telling their patients, buprenorphine is

...a tool to help you get off [opioids...or you can] take it forever...This will make you a better wife, husband, employee, whatever. I've seen people turn their life around and function.

Though several were apprehensive about prescribers who failed to wean patients from buprenorphine rapidly, overall they viewed buprenorphine prescribers as trusted colleagues who were providing a legitimate medical treatment that would alleviate their patients’ suffering.

These high-trust pharmacists chose to dispense the buprenorphine prescriptions these physicians wrote. To help ensure DEA compliance, four developed practices to limit dispensing to patients who lived in the community or to known customers. Three further limited dispensing to known or local prescribers. These pharmacists were, however, ambivalent about these limits: they recognized that patients often had to travel miles from home to find a prescriber in this rural area, and might either want to fill their prescription at a pharmacist operating near the prescriber (and thus be a stranger to the pharmacist) or return home to do so (and thus present the pharmacist with prescription from an unknown prescriber). The remaining pharmacists discussed no limits based on patient or prescriber characteristics.

Summary

Pharmacists constructed buprenorphine dispensing practices in dialogue with the legacy of OA marketing and prescribing. These counties had experienced decades of fraudulent OA marketing, in part because their rural occupational structure generated chronic pain and injury. This feature of the macrolevel healthcare service/criminal justice environment

transformed the mesolevel healthcare service/ criminal justice environment by inciting high rates of OA overprescribing. For some pharmacists, OA marketing and overprescribing destroyed trust in prescribers and in the buprenorphine they prescribed. These pharmacists developed practices to refuse to dispense buprenorphine at all, or refuse new patients. Trust remained resilient for other pharmacists, and they only curbed prescribing to comply with DEA regulations.

Escalating War on Drugs

Overview—Pharmacists also generated dispensing practices that either reflected and reinforced, or opposed, the local mobilization of the War on Drugs and interpersonal stigma. We first analyze (1) this local mobilization, conceptualized as a feature of the mesolevel healthcare service/criminal justice environment, and (2) interpersonal drug-related stigma, conceptualized as a feature of the microlevel social environment that may recursively give rise to and amplify this mobilization. We then describe how pharmacists crafted dispensing policies that embodied or explicitly challenged these risk environment features.

Mesolevel War on Drugs and microlevel stigma—An analysis of county-level data on incarceration rates in the 12 rural Kentucky counties and 12 most populous US counties reveals diverging engagement in the war on drugs across these two sets of counties. Analyses indicate that the war on drugs remains embedded in the 12 rural counties (Figures 4 & 5). Jail-based incarceration rates per 100,000 adults (aged 15–64 years) surged by 588% between 1980, the year before Reagan declared the US war on drugs, and 2006, from 99/100,000 to 582/100,000. Thereafter jail-based incarceration rates stabilized at approximately 560/100,000. Rates of pre-trial detention followed a similar temporal trajectory, surging by 614% from 65/100,000 adults in 1980 to a high of 464/100,000 adults in 2006, and then fluctuating between 300/100,000 and 459/100,000 thereafter. Incarceration rates for residents of the 12 counties in state and federal prisons also increased dramatically: prison admissions increased by 1,259% from 53/100,000 in 1983 (the first year for which we have data) to a high of 720/100,000 in 2014, and the prison-based incarceration rate increased by 1,241% from 63/100,000 in 1983 to a high of 845/100,000 in 2012; both rates declined slightly thereafter.

A comparison of these trends with municipal data from the US's 12 most populous counties reveals a different pattern (Figures 4 & 5). Rates of jail-based incarceration, pre-trial detention, and prison admissions in these populous counties started increasing in the 1980s; plateaued in the 1990s–2008s; and then declined, sometimes quite sharply. Incarceration rates in federal and state prisons peaked later (2000).

Because of these divergent urban/rural trends, jail-based incarceration and detention rates have been *higher* in these 12 rural counties than in these urban centers since 2000/2002, and rates of prison admissions and incarceration have been higher since the late aughts. By 2015, residents of these 12 rural counties were 138% more likely to be incarcerated in a local jail, 216% more likely to be detained in a jail, 247% more likely to be admitted to prison, and 40% more likely to be incarcerated in a prison than residents of the 12 most populous US counties.

Survey data from the Gateway2Health cohort testify to high incarceration rates among people who use drugs (PWUD) specifically. Gateway2Health sampled 321 adults in five of the 12 counties who recently either used opioids to get high or injected any drug to get high; 56.3% were men, 71% reported injecting drugs in the past 30 days, and the mean age was 35.9 (SD=9.0). In this sample, 27.4% reported that they had spent 1 day in jail or prison in the past six months. For comparison, published 2015 CDC surveillance data drawn from 9676 people who inject drugs in 20 large US metropolitan statistical areas indicate that 36.5% spent 1 day in jail or prison in the past *year*, a reporting period twice that for Gateway2Health.(Centers for Disease Control and Prevention, 2018).

In this area with intense criminalization of drug use, Gateway2Health participants reported experiencing significant enacted and anticipated drug-related stigma within microlevel interpersonal relationships. Approximately 66% of the sample reported feeling that it was somewhat or very true that people were uncomfortable around them because of their drug use, and that people avoided them because of their drug use. Approximately 45% of the sample reported fearing that friends would reject them because of their drug use, and 2/3rds reported fearing that family might reject them.

Qualitative results: “thieves” and “commendable” people—Low-trust pharmacists crafted dispensing practices that aligned with the War on Drugs and stigma, while high-trust pharmacists forged these practices in explicit opposition to these features of the local risk environment. The six “low-trust” pharmacists rejected the medical model of OUD, and believed that OUD was a choice:

People play the victim a lot – say it’s a “disease.” “Not my fault.” “Evil drug has befallen me.”

Aligned with War on Drugs approaches, they viewed PWUD as “thieves” who endangered their tightknit communities, and as a “black eye” in their community. Their discussions of buprenorphine focused extensively on diversion, and on the profit that patients could make by selling their drugs: they will “...sell it. That’s how they make their money.”

Consistent with a stigmatizing risk environment, these pharmacists distanced themselves from PWUD, remarking, for example, that “I can’t wrap my mind around [using opioids to get high].” They worried that dispensing buprenorphine would attract PWUD to their store, often from other counties, where they would scare off other customers:

Suboxone® draws a certain crowd that I don’t really want to deal with on a daily basis. And I don’t think my regular customers would appreciate coming in here and seeing [them].

As discussed above, these pharmacists viewed buprenorphine as the next wave of the opioid epidemic. Rejecting buprenorphine prescriptions was thus a way to protect their hometowns, by refusing to fuel the opioid epidemic and support criminal enterprises. Seeking to protect their communities, they either refused to dispense buprenorphine at all or refused to treat new patients.

In contrast, the eight “high-trust” pharmacists often expressed positive views of buprenorphine patients. They viewed them as “commendable” and “brave” people who were committed to significant and difficult life change. While they noted the possibility of diversion and worried about the impact of PWUD on their other patients, they actively tried to maintain compassion:

I feel like there’s no bigger pain in the ass patient than a Suboxone® patient. With that said, every time I get fed up with them you’ll see someone that it worked for and it makes you just wonder like are these other people that I’m fed up with close to getting to that point...?

These views were embedded in medical models of OUD. As one pharmacist said, “it’s a disease and you don’t get to choose.” Rather than distancing themselves from PWUD, they often viewed them as respected members of their tightknit community who were suffering:

One gentleman ... had a major trauma, and his doctor had prescribed opioids which were very much warranted...after so long he grew addicted to where he had to keep taking them. And if he didn’t he would just be in incredible pain, so it’s not that he chose to be misusing drugs.

As noted, these pharmacists crafted dispensing practices that were designed to serve as many patients as they could without sparking an investigation. Dispensing buprenorphine appeared to be a manifestation of a community strength they took pride in: offering a helping hand to a neighbor in distress:

Our goal here is to serve....If I can help any of the addicts out here, that’s going to serve the whole community.

Summary

These 12 counties continued to deploy War on Drugs approaches, as measured by incarceration rates and survey data, even as these indicators revealed a de-escalation of this war in the 12 most populous US counties. Anti-PWUD stigma within the microlevel environment was also high. All pharmacists developed dispensing practices to protect their community, but the extent to which they espoused the War on Drugs and stigma led to two distinct sets of practices. Low-trust pharmacists who embraced the War on Drugs and stigmatizing beliefs protected their community by refusing to dispense buprenorphine to people perceived as criminals, or by limiting dispensing to them. High-trust pharmacists, in contrast, actively strove to reject stigmatizing views of their patients, and sought to protect their communities by providing an acceptable medical treatment to community members suffering from a legitimate health problem.

Negative Case

One negative case emerged from the analysis. One pharmacist’s attitudes paralleled those described for the “high-trust” pharmacists, but they did not stock buprenorphine. As explanation, they reported that “there is just no demand for it at all over here.” This pharmacist worked in a county with an ordinance prohibiting new buprenorphine clinics from opening. This ordinance may have reduced the likelihood that their patients would have

buprenorphine prescriptions; it may also have created a mesolevel political context that overrode their personal beliefs.

Discussion

In the midst of multiple federal and state initiatives to close the implementation chasm for MOUD, this case study found that most of the pharmacists we interviewed in 12 rural counties in an epicenter of the US opioid epidemic developed buprenorphine dispensing practices that turned away all or some patients with legitimate prescriptions. Pharmacists crafted their dispensing practices in dialogue with three prominent features of the macrolevel, mesolevel, and microlevel risk environment: (1) the perceived “DEA cap;” (2) a legacy of fraudulent OA marketing and consequent physician OA overprescribing; and (3) an intensive war on drugs and interpersonal stigma. For some pharmacists, these risk environment features reinforced stigma against PWUD and MOUD, commonly cited barriers to MOUD dispensing internationally. (Chaar et al., 2013; Matheson et al., 2016; Uosukainen et al., 2014) Consistent with a post-structuralist approach, however, several barriers appear to be unique to US rural areas (e.g., the perceived “DEA cap,” distrust in buprenorphine prescribers (Ventricelli et al., 2019)), perhaps because they are generated by pharmacist interpretations of risk environment features that are particular to this setting.

This analysis is embedded in two intertwined evolutions within REM that are especially salient to drug-related crises in rural areas: the precarious presence of the mesolevel in REM’s theoretical writings, and post-structuralist approaches. REM is not alone in under-engaging with the mesolevel: Richter and Dragano have observed the precariousness of the mesolevel in multilevel public health research in general, and have called for deeper engagement with the mesolevel in this work because institutions are significant actors in amplifying and buffering macrolevel features. (Richter & Dragano, 2018) Conversely, implementation scientists, who focus extensively on mesolevel organizations, are now awakening to their failure to engage with the macrolevel. (Bruns et al., 2019) Notably, independent of REM, Rhodes and Lancaster have proposed a shift in implementation science toward an “evidence-making” approach that recognizes “intervention[s] as matters of local knowledge-making practices” and that “focuses on the processes and practices through which ‘evidence’, ‘intervention’ and ‘context’ come to be.” (Rhodes & Lancaster, 2019, p 112488) We propose that REM in particular would benefit from routinely integrating the mesolevel using post-structuralist approaches. A post-structuralist approach can deliberately explore the roles of mesolevel institutions in bringing the “forever ‘outside’” macrolevel into settings where people use drugs. This approach creates space for varied embodiments of macrolevel features in these settings, with heterogeneities forged through interplays of features and agents operating within and across multiple levels. As applied here, a post-structuralist approach allowed us to recognize and analyze pharmacist agency to interpret, reject, revise, and embrace select features of the macrolevel, mesolevel, and microlevel risk environment as they crafted their pharmacies’ buprenorphine dispensing practices. These theoretical evolutions will be especially important for ending drug-related epidemics in rural areas, as we seek to scale up harm reduction programs in these settings and local actors transform them in dialogue with constellations of risk environment features that may uniquely manifest in rural areas.

The perceived “DEA cap” was highly salient to these pharmacists as they developed their buprenorphine dispensing practices. As features of the national healthcare/criminal justice environment, the DEA and SUPPORT regulations that gave rise to these “caps” should affect pharmacies everywhere. As noted, however, papers published to date describing pharmacy-level barriers to buprenorphine dispensing in the US are only emerging from rural areas. As discussed by pharmacists, the high OUD prevalence in rural areas, coupled with rising buprenorphine prescriptions, may result in acute concerns about exceeding the cap in rural areas. Additional features of the risk environment might also conspire to raise concerns about DEA reporting among these rural pharmacists. Some studies suggest that rural areas are home to fewer pharmacies per capita than urban areas.(Bissonnette, Goeres, & Lee, 2016; Klepser, Xu, Ullrich, & Mueller, 2011) In rural states hard-hit by the OUD epidemic (e.g., Kentucky, Tennessee, West Virginia), pharmacies may thus receive far more buprenorphine prescriptions “per facility” than their urban counterparts, and thus face greater risk of exceeding the “cap.” In addition to being more vulnerable to exceeding the cap, rural pharmacists may also treat more patients who are likely to trigger their state’s Board of Pharmacy “red flag.” The Kentucky Board of Pharmacy and other state Pharmacy Boards have identified specific “red flags” for dispensing, and one such flag is a travelling a long distance to fill a prescription.(American Academy of Family Physicians & et al, 2016) Long travel distances are a defining characteristic of rural physical environments, and so patients suffering OUD may have to travel long distances to reach the nearest buprenorphine prescriber.(Andrilla et al., 2019; Joudrey et al., 2019) Pharmacists who recognize this constraint and dispense, however, may face DEA investigation for failing to fulfill their duty, as articulated by their state Pharmacy Board. Features of the risk environment that are common in rural areas – high OUD burden, low pharmacy density, long travel distances – may thus conspire to make federal and state regulations figure more prominently for rural pharmacists as they craft buprenorphine dispensing practices than for their urban counterparts.

We also found that pharmacists in these 12 counties crafted dispensing practices in dialogue with the legacy of fraudulent and aggressive OA marketing strategies and consequent physician OA overprescribing. Rural areas have witnessed far higher levels of overprescribing than urban areas.(García et al., 2019) Published explanations for this disparity have focused on higher rates of chronic pain and injury in rural areas, driven by their local occupational structure; local prescribers’ lack of training in pain and addiction medicine; and pharmaceutical companies’ intentional exploitation of these rural characteristics.(Macy, 2018; Meier, 2018; Quinones, 2016) We contextualize these explanations in broader transitions in the macrolevel economic environment, and their manifestation in this particular rural risk environment. Beginning in the 1980s, US corporations shifted their emphasis to “shareholder value” and prioritized rapid returns on investment that might accrue in months rather than years.(Freudenberg, 2014) Generating these rapid returns required that corporations expand into new markets; these expansions were often facilitated by the repeal of regulations designed to protect the public. (Freudenberg, 2014) In a context of deregulation, these expansions often targeted vulnerable populations (e.g., marketing menthol cigarettes to Black and Latinx people)(Freudenberg, 2014). In the case of OAs, generating rapid returns required expanding into non-cancer

chronic pain, despite FDA prohibitions. Extensive evidence shows that pharmaceutical companies disproportionately implemented this expansion into non-cancer pain treatment in Appalachia, a highly vulnerable market where mining, farming, and other forms of manual labor common in rural areas had produced high prevalences of injury and chronic pain, and where few physicians treating these patients were trained in either pain or addiction.(Macy, 2018; Meier, 2018; Quinones, 2016).

Much of the local devastation caused by pharmaceutical companies in Appalachian Kentucky has been well-documented: the region is experiencing largescale epidemics of OUD, HCV, overdoses, neonatal opioid withdrawal syndrome, and other harms.(Brown, Goodin, & Talbert, 2018; Slavova et al., 2017; Zibbell et al., 2015) Here, we find that OA marketing also undermined efforts to treat and prevent the OA epidemics that it caused. Decades of marketing that misled about the purposes and risks of OAs left some pharmacists deeply skeptical of buprenorphine. Years of OA overprescribing, sometimes accompanied by physician compensation, eroded relationships among mesolevel institutions, as some pharmacists stopped trusting buprenorphine prescribers' motives. The "low-trust" pharmacists practicing in this historical and contemporary rural risk environment framed curtailing buprenorphine dispensing as a way to protect their beloved community from exploitation. Initiatives seeking to expand buprenorphine access should recognize the legitimate threat that OA marketing and prescribing posed, and respect pharmacists' protective resilience, exploring alternative narratives that would allow pharmacists to conceptualize buprenorphine itself as part of a resilient response.

We view the manifestation of this macrolevel economic transition in Appalachian Kentucky (i.e., pharmaceutical companies' expansion into rural markets to generate rapid returns for investors) as the next stage in a longer history in which external companies exploit Appalachian physical and social resources to generate vast wealth for themselves, while devastating local rural ecosystems and communities. Though often portrayed as isolated from the rest of the US, Appalachian Kentucky has always, in fact, been tightly linked to the national economy and has often fueled ascendant national sectors. In its earliest days as a colony and state, Kentucky mined and exported salt so food could be preserved as it traveled from farms to urban tables in emerging cities and feed soldiers during the Civil War; salt mining is exceptionally hazardous, and supporting these national endeavors generated high mortality rates.(Billings & Blee, 2000) Salt mining gave way to logging, and by 1900 Kentucky and neighboring states had transformed their forests into >3.5 million board feet of timber to feed burgeoning East Coast factories, damaging one of the world's most biologically diverse temperate ecosystems in the process.(Billings & Blee, 2000) After the widespread dissemination of combustion engines, Kentucky mined the coal that fueled US factories and that powered steamships and railroads, using methods that devastated local ecosystems and people.(Eller, 2008) As coal mining dwindled and rapid returns became ascendant in a transitioning national economy, pharmaceutical companies appear to have replaced mining, extracting billions of dollars from the state by fraudulently marketing OAs. One OAG document, for example, reported that the state of Kentucky paid Purdue \$318 million for Oxycontin alone between 2000–2007.(Commonwealth of Kentucky, 2007) We view these payments as the current iteration of a centuries-long intersection of the macrolevel economic environment with features of the local rural physical and social

environment, in which macrolevel economic growth is fueled by devastating Appalachian Kentucky's people and, historically, ecosystems. Many of the pharmacists we interviewed came from families with generations-long roots in the area. Future research should explore whether these pharmacists developed dispensing practices in conversation with this longer history of exploitation, rather than simply with current OA marketing and overprescribing, and how those conversations could be shifted to support buprenorphine dispensing as another link in a centuries-long chain of resilience.

Some pharmacists also reported curtailing dispensing because they were concerned that buprenorphine patients were criminals; stigma is a commonly cited barrier among pharmacists for engaging in harm reduction in the US and elsewhere (Chaar et al., 2013; Rivera et al., 2015; Sheridan et al., 2007; Uosukainen et al., 2014). These pharmacists were developing buprenorphine dispensing practices in a risk environment that powerfully criminalized drug use, both in absolute terms (the prison admission rate in 2015 exceeded 700/100,000 residents) and in relative terms (e.g., by 2015, residents of these 12 rural counties were 247% more likely to be admitted to prison than residents of the 12 most populous US counties). Extensive policing and incarceration of PWUD may impede buprenorphine dispensing by reinforcing stigmatizing attitudes. We found that "low-trust" pharmacists viewed people living with OUD as "thieves" who chose to use opioids; they explicitly rejected the medical model of OUD and expressed deep concerns about diversion, concerns shared by pharmacists practicing elsewhere (Bach & Hartung, 2019; Nielsen et al., 2007). This skepticism may have been reinforced by Kentucky's Board of Medical Licensure, which promulgated administrative regulations focused on patient monitoring to detect potential diversion.

These 12 rural counties are not unique: incarceration rates and other war on drugs strategies are emerging as potent features of the healthcare/criminal justice environment in rural areas across the US. (Kang-Brown & Subramanian, 2017) Though well-documented in cities, the implications of war on drugs strategies for harm reduction practices, programs, and health in rural areas are understudied. Expanding this line of research to encompass rural areas will require revising conceptual models: urban research has typically conceptualized the war on drugs as a key strategy to maintain racialized social systems in the wake of Jim Crow. (Alexander, 2020; Cooper & Fullilove, 2020) This cannot, of course, be its function in these 12 counties, where the vast majority (95%–98%) of residents identify as non-Hispanic White. To support future conceptual work, we propose a possible role for this feature of the risk environment in rural areas that parallels those proposed for cities. There are multiple similarities between these rural counties and the urban targets of the war on drugs, particularly when considered at the height of the urban war on drugs (the mid-1990s). Both populations suffer low rates of employment, and high poverty rates. In the 95 largest US metropolitan areas in the mid-1990s, the median employment rate among Black adults was 70%; 25.8% of Black-headed households were in poverty; and the median household income for these households was \$38,725 (in 2015 dollars, adjusted for inflation). (Cooper, West, et al., 2016) In 2017, the median household income in Appalachian Kentucky was \$19,823, 46.2% of the national average; and the poverty rate was 25.6%, 175.2% of the national average. (The Appalachian Regional Commission, ND) Both areas also have histories of potent uprisings seeking economic and social justice. Predominately Black and

Latinx urban residents mobilized repeatedly for their civil rights in the decades preceding the 1981 declaration of the War on Drugs.(Garrow, 2015) Appalachian Kentucky has likewise been the site of some of the bloodiest civil uprisings in US history: since the 1800s, Central Appalachian workers have repeatedly mobilized to protect their rights, including waging the Battle of Blair Mountain, which was the largest labor uprising in US history, and also fighting the year-long paint creek mine war, in which scores of strikers were shot and many more starved to death with their families.(Green, 2015).

We posit that war on drugs strategies have been deployed in both places for the same purpose: to prevent future uprisings by disrupting political power (e.g., persons with a felony conviction cannot vote) and undermining the social networks needed to support widespread mobilizations. From this perspective, the impacts of the war on drugs on harm reduction programs – including buprenorphine dispensing – and PWUD health in both urban and rural areas can be conceptualized as unintended consequences of broader national strategies to maintain inequality. Future research should explore these resonances across urban and rural risk environments, and consider implications for unified action to advance harm reduction by eliminating war on drugs strategies.

This analysis offers an illustration of the creation of buprenorphine stigma, and in particular illustrates Seear, Lancaster, and Ritter's proposition that stigma creation is a political and relational process in which stigma is emergent, multiple (e.g., uneven and contradictory), ontologically constitutive (e.g., enacted by subjects, objects, and the abject), and normative. (Seear, Lancaster, & Ritter, 2017) Here, buprenorphine stigma emerged unevenly across pharmacies as pharmacists engaged with the DEA cap, the war on drugs, and OA marketing and overprescribing. The DEA, wholesalers, and the Kentucky OAG conflated buprenorphine with OAs, and this conflation – the result of a political process – reinforced low-trust pharmacists' concern that buprenorphine was not a legitimate OUD treatment. The intensive deployment of the war on drugs locally –another political process – reinforced stigma against all PWUD, and lent legal weight and empirical support to “low-trust” pharmacists' perceptions of buprenorphine patients as “thieves” who might sell their medication for profit. Often, biomedical models are deployed to counter stigma against drug use and mental illness.(Hammer et al., 2013; Rusch, Kanter, & Brondino, 2009) Here, however, aggressive and fraudulent OA marketing and local physician complicity delegitimized these biomedical actors for “low-trust” pharmacists, severing trusting relationships between these pharmacists and prescribers. Collectively, these processes may have created norms that stigmatized buprenorphine as simply another OA that was prescribed to criminals by greedy or inept prescribers. Low-trust pharmacists then enacted stigma by crafting buprenorphine dispensing practices that rejected buprenorphine patients. High-trust pharmacists, in contrast, actively opposed these norms, forming a local bulwark against buprenorphine stigma as best they could: they explicitly embraced compassionate views of buprenorphine prescribers and patients; differentiated buprenorphine from OAs; and only yielded to the political processes that would spark a DEA investigation.

Results should be interpreted in light of study limitations and strengths. Qualitative interviews were transcribed verbatim, enhancing descriptive validity.(Maxwell, 2012) A practicing pharmacist in Kentucky with deep knowledge of policies and pharmacy practice

(PF) scrutinized findings, enhancing interpretive validity. Theoretical validity was somewhat undermined by our inability to interview more pharmacists operating in chain retail pharmacies (Maxwell, 2012); buprenorphine dispensing in such pharmacies might differ qualitatively from dispensing in independent pharmacies. We did, however, interview pharmacists operating 23% of all pharmacies operating in the 12-county area, and analyses reached saturation for the sample. An analysis of negative cases further enhanced theoretical validity, as did the integration of pharmacy-level qualitative data with multiple sources of existing data on the local healthcare/criminal justice environment. (Maxwell, 2012).

High levels of pharmacy-based engagement in MOUD dispensing has been achieved in other countries. In Scotland, for example, 88% of pharmacists reported dispensing MOUD in 2014. (Matheson et al., 2016) We reflect on our and others' findings to offer some multilevel pathways to support the development of dispensing practices that meet the need for buprenorphine in this rural area, and perhaps in other US rural areas:

1. **Buprenorphine and other MOUDs should be excluded from DEA and wholesaler monitoring protocols designed to reduce diversion of OAs.** At a minimum, wholesalers should be required to track buprenorphine separately from OAs. Motives for using diverted buprenorphine are rarely euphorogenic. "Generous constraints" on MOUD (e.g., less monitoring) create space for PWUD to generate an array of harm reduction practices tailored to their needs, (Harris & Rhodes, 2013) including using diverted MOUD to self-medicate OUD or withdrawal. (Cicero, Ellis, Surratt, & Kurtz, 2014; Lofwall & Walsh, 2014)
2. In addition to continuing to file and win lawsuits against pharmaceutical companies and as suggested by Tennessee physicians, (Ventricelli et al., 2019) relevant **professional organizations could convene local meetings of prescribing physicians and pharmacists to restore trust and build shared non-stigmatizing MOUD norms.** Meetings could encompass academic detailing by a trusted source to address MOUD misconceptions (e.g., the need for rapid tapering). The Opiate Medication Initiative for Rural Oregon Residents provides a useful template for such initiatives. (McCarty, Rieckmann, Green, Gallon, & Knudsen, 2004)
3. **Advocacy efforts to end the War on Drugs could be expanded to rural areas.** Extensive advocacy in US cities has helped to de-escalate highly punitive drug-related enforcement, prosecutorial, and correctional strategies. (Cullen, 2016; Kang-Brown & Subramanian, 2017; National Conference of State Legislatures, 2019) Efforts to expand advocacy could recognize resonances between the purpose, nature, and effects of this war across urban and rural areas, and build a unified response across these historically distinct regions.
4. In addition to the above recommended interventions – each of which should interrupt political and relational processes that create stigma - **local governmental and non-governmental organizations could implement multilevel interventions to reduce stigma toward PWUD and buprenorphine.** Interventions specifically targeting pharmacists could be

modeled after anti-stigma initiatives targeting physicians and other healthcare providers, which reduce stigma and promote behavior change.(Knaak, Modgill, & Patten, 2014) These interventions, however, will be most effective if accompanied by anti-stigma interventions targeting the entire community.(Rao et al., 2019) The Ohio Opioid Project provides a template for multilevel interventions seeking to reduce drug-related stigma in rural areas, and targets media, law enforcement and judges, faith organizations, and PWUD.(Miller & Go, 2019)

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Figure 1.
Overview of findings

Federal and State Policies Governing Pharmacist Dispensing of Buprenorphine

Federal Policies

Federal law imposes several requirements on pharmacies that are intended to prevent diversion of controlled substances. Per the Controlled Substances Act (CSA) and DEA regulations, pharmacists have a legal duty and corresponding responsibility to ensure the validity of prescriptions for controlled substances before filling them (Yeh, 2018) Specifically, they must ensure that they are “issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice.”(21 C.F.R. § 1306.03) For example, the DEA practice manual for pharmacists stipulates that,

The law does not require a pharmacist to dispense a prescription of doubtful, questionable, or suspicious origin. To the contrary, the pharmacist who deliberately ignores a questionable prescription when there is reason to believe it was not issued for a legitimate medical purpose may be prosecuted along with the issuing practitioner, for knowingly and intentionally distributing controlled substances.(Drug Enforcement Administration Diversion Control Division, 2010)

State Policies

Similarly, under Kentucky law, pharmacists breach their professional duties by “engaging in conduct which substantially departs from accepted standards of pharmacy practice... with or without established proof of actual injury; . . . or [f]ailing to exercise appropriate professional judgment in determining whether a prescription drug order is lawful.”(2.; 315.121(2))

Kentucky is one a few states that has issued regulations to explicitly govern buprenorphine prescribing by physicians and Advanced Practice Registered Nurses (APRNs).(9:270; 20:065) These rules guide pharmacists’ evaluations of the legitimacy of a buprenorphine prescription before dispensing. For example, these regulations stipulate that, with rare exception, doctors and APRNs cannot prescribe buprenorphine single entity products or buprenorphine with naloxone combination products for off-label use, and only for withdrawal or maintenance purposes. Additionally, these regulations require prescribers of buprenorphine to conduct activities designed to detect potential buprenorphine diversion, including regular urine drug screening, random pill counts and establishment of a plan for handling lost or stolen medication. These rules establish the professional standard for prescribing buprenorphine, and therefore guide what pharmacists must consider before dispensing to a patient.

In summary, US federal law requires that pharmacists scrutinize the legitimacy of all prescriptions before dispensing. In KY, pharmacists have a specific duty to scrutinize buprenorphine prescriptions. For low-trust pharmacists, KY physicians and buprenorphine itself failed to meet their standards of legitimacy.

Figure 2.

Federal and State Policies Governing Pharmacist Dispensing of Buprenorphine

Figure 3.

Per capita opioid prescription trends for 12 Kentucky counties and the 12 most populous U.S. counties, 2006 – 2017

Figure 4.
Prison admissions and incarceration trends for 12 Kentucky counties and the 12 most populous U.S. counties per 100,000 population (aged 15–64), 1983–2015

Figure 5.

Jail pre-trial detention and incarceration trends for 12 Kentucky counties and the 12 most populous U.S. counties per 100,000 population (aged 15–64), 1980–2015

Table 1

Data sources analyzed to assess features of the risk environment

Construct	Data Source(s)	Comments
Pharmaceutical company opioid analgesic marketing		
Pharmaceutical company marketing strategies for opioid analgesics	Kentucky Attorney General Lawsuits against pharmaceutical companies for opioid marketing. ¹	Note that all lawsuits referenced here describe allegations, and so have not been proven.
Pharmaceutical company opioid analgesic marketing expenditures, per 1000 residents	Hadland et al.'s county-level analysis of Centers for Medicare and Medicaid Services (CMS) data, aggregated across 2013–2015. ² Numerators captured pharmaceutical company payments to physicians for promoting an opioid analgesic, in US\$. Denominators captured the total population size, drawn from the US census.	Payments include the cost of meals and travel, as well as speaking fees, honoraria, consulting fees, and educational costs. Payments were linked to counties via the physician's practice location.
Physician opioid analgesic prescribing, per 100 residents	The numerator was drawn from annual CDC county-level data on opioid analgesic prescribing. ³ The denominator captured the total population size, drawn from the US census.*	IQVIA's Xponent database was the source for CDC data. For more information on IQVIA coverage, see . ⁴ Opioid analgesic prescriptions were included; medications typically used to treat opioid use disorder were excluded. In the CDC prescription database, "a prescription is an initial or refill prescription dispensed at a retail pharmacy in the sample and paid for by commercial insurance, Medicaid, Medicare, or cash or its equivalent." Mail order prescriptions were excluded. Prescriptions were linked to counties via the location of the dispensing pharmacy.
War on Drugs		
Jail and prison Incarceration rates	Annual, county-level numerators were drawn from the Vera Institute of Justice "Incarceration Trends Dataset." ⁵ Denominators captured the total population, drawn from the US Census.	To contextualize findings for our 12-county area, we drew on parallel data for the 12 most populous counties in the US. Vera data grouped two "populous" counties (New York and Kings counties) together into a single larger municipality (New York City). Expenditures were standardized using 2017 US\$, and include federal, state, and municipal contributions.
Self-reported incarceration rates among people who use drugs	Gateway2Health survey, administered in 2018–2019	Gateway2Health used respondent driven sampling to recruit adults (18 years) living in five of the 12 counties who recently (past 30 days) either used opioids to get high or injected any drug to get high. Items captured incarceration for >24 hours in the past 6 months, and experiences of interpersonal and enacted drug-related stigma.
Self-reported drug-related stigma among people who use drugs		

¹ COMMONWEALTH OF KENTUCKY, ex rel. ANDY BESHEAR, ATTORNEY GENERAL., (2018). *COMMONWEALTH OF KENTUCKY, ex rel., ANDY BESHEAR, ATTORNEY GENERAL, v TEVA PHARMACEUTICALS USA INC.*
Commonwealth of Kentucky, ex rel. ANDY BESHEAR, ATTORNEY GENERAL., (ND-a). *COMMONWEALTH OF KENTUCKY, ex rel., ANDY BESHEAR, ATTORNEY GENERAL, Plaintiff. v. ENDO HEALTH SOLUTIONS INC.; ENDO PHARMACEUTICALS INC.*
Commonwealth of Kentucky, ex rel. ANDY BESHEAR, ATTORNEY GENERAL., (ND-b). *COMMONWEALTH OF KENTUCKY, ex rel., ANDY BESHEAR, ATTORNEY GENERAL, Plaintiff. v. INSYS THERAPEUTICS, Inc.*; Frankfort, KY
Commonwealth of Kentucky, ex rel., ANDY BESHEAR, ATTORNEY GENERAL., (ND-c). *COMMONWEALTH OF KENTUCKY, ex rel., ANDY BESHEAR, ATTORNEY GENERAL, Plaintiff. v. JOHNSON & JOHNSON*; Louisville, KY
Commonwealth of Kentucky, ex rel. Gregory Stumbo, Attorney General, and Pike County for itself and for all other Kentucky Counties Similarly situated., (2007). *Commonwealth of Kentucky, ex rel., Gregory Stumbo, Attorney General, and Pike County for itself and for all other Kentucky Counties Similarly situated, v. Purdue Pharm LP, Purdue Pharma Inc, The Purdue Frederick Company Inc, Purdue Pharmaceuticals.*
Commonwealth of Kentucky, ex rel., v Purdue Pharma et al., (2015). *Commonwealth of Kentucky, ex rel., v Purdue Pharma et al video deposition for the plaintiff.*

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²Hadland, S. E., Rivera-Aguirre, A., Marshall, B. D., & Cerdá, M. (2019). Association of pharmaceutical industry marketing of opioid products with mortality from opioid-related overdoses. *JAMA network open*, *2*(1), e186007–e186007.

³Centers for Disease Control and Prevention. (2017, July 31 2017). U.S. County Prescribing Rates, 2017. Retrieved from <https://www.cdc.gov/drugoverdose/maps/rxcountry2017.html>

⁴Centers for Disease Control and Prevention. (2017, July 31 2017). U.S. County Prescribing Rates, 2017. Retrieved from <https://www.cdc.gov/drugoverdose/maps/rxcountry2017.html>

⁵Vera Institute of Justice, Incarceration Trends Data. <http://trends.vera.org/incarceration-rates?data=pretrial>