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Prescription Drug Monitoring Programs Operational Characteristics and Fatal Heroin Poisoning

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Abstract

Background: Prescription drug monitoring programs (PDMP), by reducing access to prescribed opioids (POs), may contribute to a policy environment in which some people with opioid dependence are at increased risk for transitioning from POs to heroin/other illegal opioids. This study examines how PDMP adoption and changes in the characteristics of PDMPs over time contribute to changes in fatal heroin poisoning in counties within states from 2002 to 2016.

Methods—Latent transition analysis to classify PDMPs into latent classes (Cooperative, Proactive, and Weak) for each state and year, across three intervals (1999-2004, 2005-2009, 2010-2016). We examined the association between probability of PDMP latent class membership and the rate of county-level heroin poisoning death.

Results: After adjustment for potential county-level confounders and co-occurring policy changes, adoption of a PDMP was significantly associated with increased heroin poisoning rates (22% increase by third year post-adoption). Findings varied by PDMP type. From 2010-2016, states with Cooperative PDMPs (those more likely to share data with other states, to require more frequent reporting, and include more drug schedules) had 19% higher heroin poisoning rates than states with Weak PDMPs (adjusted rate ratio [ARR] = 1.19; 95% CI = 1.14, 1.25). States with Proactive PDMPs (those more likely to report outlying prescribing and dispensing and provide

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broader access to law enforcement) had 6% lower heroin poisoning rates than states with No/Weak PDMPs (ARR = 0.94; 95% CI = 0.90, 0.98).

Conclusion: There is a consistent, positive association between state PDMP adoption and heroin poisoning mortality. However, this varies by PDMP type, with Proactive PDMPs associated with a small reduction in heroin poisoning deaths. This raises questions about the potential for PDMPs to support efforts to decrease heroin overdose risk, particularly by using proactive alerts to identify patients in need of treatment for opioid use disorder. Future research on mechanisms explaining the reduction in heroin poisonings after enactment of Proactive PDMPs is merited.

Keywords

Prescription drug monitoring programs; fatal heroin poisonings; latent classes; overdose

Introduction

Heroin poisonings in the United States have increased nearly 5-fold from 2010 to 2017, significantly contributing to the ongoing epidemic of opioid-related harm (NIDA, 2018). There are at least four potential explanations in the published literature for this increase: increased availability of heroin in regions with previously little access to the drug (Compton, Jones, & Baldwin, 2016; DEA, 2015; Jalal et al., 2018; NIDA, 2014), increases in heroin purity and decreases in price (Compton et al., 2016; ONDCP, 2014; Unick, Rosenblum, Mars, & Ciccarone, 2014), the emergence of heroin adulterated with illicitly manufactured fentanyl (Carroll, Marshall, Rich, & Green, 2017; Jalal et al., 2018; Mars, Ondocsin, & Ciccarone, 2018) and other analogs, and increased heroin use due to transitions from prescription opioid use, misuse, or dependence to heroin use (Banerjee et al., 2019; Jones, 2013; Kerridge et al., 2015; Kolodny et al., 2015; Mars et al., 2015; Martins, Sarvet, et al., 2017; Martins, Segura, et al., 2017).

Prescription drug monitoring programs (PDMPs) are state-level databases that collect information on controlled prescription medications dispensed in that state. The data PDMPs collect is made available only to approved health care providers, law enforcement officials, and sometimes other parties, depending on state law (Davis, Pierce, & Dasgupta, 2014). As of December 2017, all US states except Missouri had an operational PDMP (NAMSDL, 2018). Despite their stated goals, however, evidence on whether PDMPs reduce opioid-related harm, particularly harm related to prescription opioids (PO) (Fink et al., 2018), by reducing inappropriate and potentially dangerous opioid prescribing, is mixed. (Davis et al., 2014; Dowell, Zhang, Noonan, & Hockenberry, 2016; Haffajee, 2019; Pew Charitable Trusts, 2016; Smith et al., 2019). A recent systematic review (Fink et al., 2018) of 10 studies found weak evidence that PDMP implementation is associated with reductions in fatal opioid-related poisonings; however, three (Delcher et al., 2016; Kilby, 2015; Meinhofer, 2018) of six studies (Delcher et al., 2016; Dowell et al., 2016; Kilby, 2015; Meinhofer, 2018; Nam, Shea, Shi, & Moran, 2017; Radakrishnan, 2015) that measured that outcome found an increase in heroin poisonings after PDMP implementation.

While evidence is mixed on whether PDMPs are associated with overall changes in opioid prescribing, it is hypothesized that increased utilization of PDMPs and more restrictive

PDMP features may result in reductions in opioids prescribed to patients on high dose opioid therapy, and may be one driver within the overall policy environment that may lead some of these patients to seek heroin on the illicit market as an alternative to prescription opioids (Bao et al., 2016; Beletsky, 2018; Deyo et al., 2018; Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2014). A recent survey of 37 PDMP administrators, law enforcement officials and administrative agency employees in Florida, Kentucky, New Jersey and Ohio, showed that some believe that this substitution is currently occurring in some patients (Yuanhong Lai et al., 2019).

The few studies that have shown PDMP implementation to be associated with increasing rates of heroin poisoning have all treated PDMP as present or absent, and so did not take into account that PDMP characteristics vary greatly across states and over time, as each state enacts laws that define specific aspects of their program (Davis et al., 2014) and updates PDMP legislation as the opioid epidemic evolves (Cerda et al., In Press). In addition, one of these studies examined data from a single US state (Delcher et al., 2016), and another examined data only from a subset of 38 US states and D.C. (Kilby, 2015). Given evidence that specific PDMP operational features are associated with greater reductions in prescription opioid-related mortality rates (Fink et al., 2018), further research is needed to identify whether different combinations of PDMP features can explain the heterogeneous results in previous studies and, if so, which combinations of PDMP features have made the strongest contribution to changes in heroin poisoning. Finally, all prior studies that examine the relationship between PDMPs and fatal heroin poisoning have been conducted at the state level, and do not account for within-state heterogeneity in rates of change in heroin poisoning and in the distribution of key demographic covariates that may affect heroin poisoning, thus generating the potential for aggregation bias in published findings (Cerda et al., In Press; W. A. V. Clark & Avery, 1976).

To better understand which combinations of PDMP features are associated with changes in heroin poisoning, we took three steps. First, we used latent transition analysis (LTA) to reduce complex and frequently co-occurring PDMP features into simpler latent classes (i.e., combinations) of PDMP characteristics that are likely to be adopted together, and that may reflect distinct underlying “typologies” of PDMPs in three distinct PDMP program periods (1999-2004, 2005-2009, and 2010-2016) as defined in a prior paper (Smith et al., 2019). Second, we examined two types of associations: (1) the association between year of electronic PDMP implementation and the rate of heroin poisoning; and (2) the association between transitions across types of PDMP latent classes and changes in fatal heroin poisoning in counties within states from 2002 to 2016. This approach allowed us to identify the combinations of PDMP features that were associated with the greatest change in relative rates of heroin poisoning fatalities over time across the United States. Third, we adopted a geospatial approach to examine the impact of state-level PDMPs on county-level fatal heroin poisonings, thus accounting for within-state variation in the level and rate of growth of heroin poisonings, and for spatial autocorrelation in heroin poisonings across counties and states. Hence, our main aim in this study was to examine how transitions across types of PDMP classes over time contributed to changes in fatal heroin poisoning in counties within states from 2002 to 2016.

Methods

Outcomes

We used the National Vital Statistics System to extract data on heroin poisoning deaths ([dataset] NCHS, 2017). Using the International Classification of Disease, Tenth Revision (ICD-10) underlying cause-of-death codes, we identified drug-poisoning deaths, defined as unintentional poisoning (X40-44), suicide by drug self-poisoning (X60-64), homicide by drug poisoning (X85), and undetermined intent (Y10-14). Among these deaths, we restricted our analyses to deaths involving the ICD-10 multiple cause-of-death code for heroin poisoning (T40.1), these include deaths that had codes for other drug poisoning together with heroin. We computed annual county-level counts of heroin poisoning for 3,109 counties in 49 US states and Washington D.C. in 2002-2016. Alaska was not included due to frequent changes in county boundaries during the study period (U.S. Census Bureau, 2019a, 2019b). We classified poisonings by county of death, rather than county of residence, since county of death likely more closely represents the place where the poisoning occurred (overlap between county of residence and county of death across years was of 81.5%-85.2%).

Exposures

We used latent transition analysis (LTA) to identify typologies of PDMPs, or "classes," described in detail elsewhere (Smith et al., 2019). Briefly, we obtained dates of electronic PDMP access from the National Alliance for Model State Drug Laws (NAMSDL) and state PDMP administrators, and we compiled PDMP characteristics from the Prescription Drug Abuse Policy System (PDAPS) database of legal provisions ([dataset] PDAPS, 2017). Next, we considered PDMP characteristics that have been identified by prescription opioid policy experts as potentially important determinants of prescribing practices and heroin poisoning events (see supplemental Figure 1) (Davis et al., 2014; Pew Charitable Trusts, 2016). These included: a) state authorizes prescribers to access PDMP data; b) state authorizes in-state law enforcement to access PDMP data; c) state permits or requires PDMP to proactively identify suspicious or statistically outlying prescribing, dispensing, or purchasing activity; d) timeframe in which dispensers are required to report data to the PDMP; e) number of drug schedules state requires to be reported to the PDMP; f) state requires prescribers to check the PDMP before prescribing controlled substances; and g) law permits the PDMP to share data with other state PDMPs (Smith et al., 2019).

We used LTA (Duncan et al., 1997; Lanza, Dziak, Huang, Wagner, & Collins, 2015; Muthén, 2004; Muthen & Muthen, 2000; "PROC LCA & PROC LTA (Version 1.3.2) ", 2015) to identify groups of states with similar combinations of PDMP characteristics for each year of the study and identified latent classes for three separate intervals: 1999-2004, 2005-2009, and 2010-2016. The methods used to create these classes and the results from this analysis have been described elsewhere (Smith et al., 2019); results are also presented in the online Supplement. The three intervals represent different historical periods in the opioid poisoning epidemic and the evolution of PDMPs including: (1) 1999-2004, when PDMPs first started to transmit data electronically; (2) 2005-2009, when federal funding for PDMPs from the Bureau of Justice Assistance and SAMHSA, among others, increased; and (3) 2010-2016, when PDMP capacity expanded (T. Clark, Eadie, Kreiner, & Strickler, 2012; Gugelmann,

Perrone, & Nelson, 2012; Hedegaard, Warner, & Minino, 2017; Rudd, Aleshire, Zibbell, & Gladden, 2016).

In the final LTA models, three distinct classes of PDMPs were identified for each time period. Since the pattern of PDMP characteristics within each class was most comparable in the first two intervals, we used the same labels for classes in 1999-2004 and 2005-2009: No/Weak PDMP, Reactive PDMP, and Proactive PDMP. The key distinguishing features of the three latent classes were: (1) the No/Weak PDMP class represented states with no operational or limited PDMP; (2) the Reactive PDMP class represented states with no requirements to proactively report outlying patterns to law enforcement, licensing bodies and prescribers/dispensers, limited data access for law enforcement, and less frequent reporting requirements for dispensers; and (3), the Proactive PDMP class represented states that tend to permit and/or require proactive reporting of outlying patterns to law enforcement, licensing bodies and prescribers/dispensers, to provide access to PDMP data to law enforcement without requiring a warrant, subpoena, or active investigation, and to require dispensers to report data to the PDMP on a more frequent basis. In the last interval (2010-2016), two additional variables not available in earlier years were included, so we used different class names to reflect the evolving nature of the PDMPs: Weak PDMP, Cooperative PDMP, and Proactive PDMP. In this interval, the Weak PDMP class represented states with fairly basic PDMPs; the Proactive PDMP class was similar to the Proactive PDMP class in the first 2 intervals, and the Cooperative PDMP class had a lower probability than states in the Proactive PDMP class of permitting/requiring reporting of outlying patterns to PDMP users, or providing broader access of PDMP data to law enforcement, but had a higher probability of allowing PDMP data to be shared with other states, requiring dispensers to report data to the PDMP on a more frequent basis, and reporting more federal drug schedules than states in the Proactive class (Cerda et al., In Press; Smith et al., 2019).

Covariates

Based on prior studies (Bohnert et al., 2011; Cerda et al., 2017; Paulozzi, Kilbourne, & Desai, 2011), we accounted for the following county-level demographic characteristics, obtained from annual Geolytics data ([dataset] Geolytics Estimates Premium, 2014): population density (thousands of people/square mile); age composition (% of the population aged 0-19, 20-44, 45-64, and >65 years); racial/ethnic composition (% non-Hispanic White, non-Hispanic Black, Hispanic); % male; and socioeconomic conditions (% of families in poverty, median household income, % unemployed). We also accounted for the overall mortality rate per 1,000 residents in the county. Finally, we accounted for co-occurring policy changes associated with opioid poisoning in prior studies that may confound the association between PDMP characteristics and heroin poisoning, including: medical marijuana legalization (Bachhuber, Saloner, Cunningham, & Barry, 2014; Shi, 2017), overdose Good Samaritan laws, and naloxone access laws (McClellan et al., 2018; Rees, Sabia, Argys, Latshaw, & Dave, 2017). We obtained annual, state-level information on these laws through PDAPS ([dataset] PDAPS, 2017; Smith et al., 2019). The research study protocol was reviewed and approved by Columbia University's Institutional Review Board.

Analyses

We modeled the county-by-year mortality counts using hierarchical Bayesian Poisson models, with county population included as the offset (Bernardinelli et al., 1995; Besag, York, & Mollie, 1991; Carlin & Louis, 2000). Other covariates, including demographic characteristics and the overall mortality rate, were modeled as concurrent predictors of heroin poisoning deaths.

The models captured baseline differences between states in heroin poisoning rates using state dummy variables, while county-specific unit random effects allow for varying levels within each state. A linear fixed-effect time trend predicted constant proportional growth due to the log link function within Poisson models. In combination with county random trend effects, this accounts for heterogenous accelerated growth between counties over time (i.e., growth mixtures that could otherwise bias estimates of covariate effects). A conditional autoregressive spatial random effect allowed for greater similarity between adjacent counties than between distant ones (spatial autocorrelation), a lack of independence that could bias uncorrected models (Waller & Gotway, 2004). The model also incorporated a non-spatial county random effect which effectively controlled for over-dispersion (Lord, Washington, & Ivan, 2005). These Bayesian Poisson models were performed using the R-INLA package (Integrated Nested Laplace Approximation) (Blangiardo & Cameletti, 2015; Rue, Martino, & Chopin, 2009). The analytic approach used was similar to a difference-in-difference approach, as: it used each state as its own control (through the specification of state fixed effects); it assumed (by fitting a county-level random intercept) that each county was different at baseline; and it specified that counties and states experienced linear growth (by fitting a linear time trend common to all states). However, the approach also improved upon difference-in-difference models by specifying a separate growth parameter (i.e., random slope) for each county, thus allowing us to obtain unbiased estimates in the context of heterogeneous policy effects across counties within states, and avoiding biases due to over- and under-differencing.

First, we examined the association between the proportion of each year with electronic PDMP implementation and the rate of heroin poisoning death. Using linear distributed lags over three years, we assessed both the concurrent impact within the year of PDMP implementation and three subsequent years (Greene, 2012). Then, we examined the association between probability of PDMP latent class membership in each year and interval and the rate of heroin poisoning death. All models accounted for demographic characteristics, overall mortality rates, and distributed-lag specifications for co-occurring marijuana, Good Samaritan and naloxone laws.

Sensitivity Analyses

We conducted two sensitivity analyses to address sources of bias that may arise from relying on ICD coding of death certificate data, notably that specific drugs involved in drug poisoning are often not identified on death certificates, resulting in differential underestimation of drug-specific poisoning rates between states (Ruhm, 2017). We replicated our analyses excluding states that were found to have a >5% absolute difference in reported versus corrected heroin poisoning rates in a prior study that imputed county-level

opioid poisoning rates when no drug was specified (i.e., Alabama, Indiana, Louisiana, and Pennsylvania) (Ruhm, 2017). Finally, we replicated our analyses using the county-level overall drug poisoning rate (thus not specific to any drugs) as the outcome, as this rate would not depend on state-level changes in coding of specific drugs.

Results

Figure 1 presents the overall impact of state adoption of an electronic PDMP on the log relative rate of heroin poisoning fatalities in the years since the electronic PDMP became operational. We observed a consistent, positive, and significant association between state adoption of an electronic PDMP that provides electronic access to data and heroin poisoning fatalities in all years, an effect which increased over time. By the third year of adoption of an electronic PDMP, there was a 22% increase in heroin poisoning fatalities (Adjusted Rate Ratio [ARR]=1.22; 95% Credible Interval [CI]=1.16,1.29), compared to no PDMP adoption.

Table 1 presents the association between each PDMP latent class and the relative rate of county-level heroin poisoning at each of the three intervals of study. In the first interval (1999-2004), states that had adopted Reactive PDMPs had 12% lower heroin poisoning fatality as compared to states with No/Weak PDMPs (ARR = 0.88; 95% CI = 0.82, 0.94). However, there were no differences in heroin poisoning fatality between states that adopted Proactive PDMPs as compared to states with No/Weak PDMPs, as well as between states that adopted Proactive PDMPs as compared to states that adopted Reactive PDMPs. In the second interval (2005-2009), states with Reactive PDMPs had 5% higher heroin poisoning fatality rates than states with No/Weak PDMPs (ARR = 1.05; 95% CI = 1.01, 1.09). There were no differences in rates of heroin poisonings between states with Proactive PDMPs and states with No/Weak PDMPs or between states with Proactive PDMPs and states with Reactive PDMPs. Finally, in the last interval (2010-2016), states with Cooperative PDMPs had 19% higher heroin poisoning rates than states with No/Weak PDMPs (ARR = 1.19; 95% CI = 1.14, 1.25), while states with Proactive PDMPs had 6% lower heroin poisoning rates than states with No/Weak PDMPs (ARR = 0.94; 95% CI = 0.90, 0.98). States with Proactive PDMPs also had 21% lower heroin poisoning rates than states with Cooperative PDMPs (ARR = 0.79; 95% CI = 0.74, 0.83).

Sensitivity analyses

Findings remained largely unchanged in the two sensitivity analyses: excluding those states with high levels of underreporting of specific drugs (Table 1), and focusing on the overall drug poisoning rate as the outcome (Table 1). In both cases, results yielded small differences in earlier years as compared to those of the main analysis.

Discussion

Our findings indicate that there is a consistent, positive, significant association between state adoption of electronic PDMPs and heroin poisoning mortality; however, the overall effect of PDMP implementation on heroin-related poisoning mortality depended on both the type of PDMP being implemented and the years over which the effects were assessed. In particular, in recent years, Proactive PDMPs, which had a higher probability than the other classes of

permitting/require proactive reporting of outlying patterns to authorized PDMP users, as well as of providing broader access to PDMP data to law enforcement, have been associated with reductions in heroin poisoning mortality. On the other hand, Cooperative PDMPs, which had a higher probability of allowing PDMP data to be shared with other states, requiring dispensers to report data to the PDMP on a more frequent basis, and reporting more federal drug schedules than states in the Proactive class, were significantly associated with increases in heroin poisoning fatality.

There were mixed findings regarding Reactive/Cooperative PDMPs as compared to No/Weak PDMPs. From 2005 to 2016, Reactive/Cooperative PDMPs might have had unintended consequences, similar to what has been reported by some prior studies focusing on a binary PDMP classification (Delcher et al., 2016; Kilby, 2015; Meinhofer, 2018). In this period, Reactive and Cooperative PDMPs may have contributed to the transition of a subgroup of prescription opioid users moving to the illicit heroin market.

In the third time period (2010-2016), Proactive PDMPs showed as much as a 21% decrease in heroin poisoning fatalities as compared to Cooperative PDMPs. Findings associated with Proactive PDMP programs from the 2010-2016 period differ somewhat from those reported by prior studies, in which there were increases in fatal heroin poisonings or no effects after PDMP implementation (Smith et al., 2019). None of these prior studies examined specific characteristics of PDMP programs in the level of detail that we examined in this study, and most of them assumed PDMP to be absent or operational with no variation across time and across states, an assumption proven false by prior studies (Fink et al., 2018). Most importantly, proactive PDMPs might potentially reflect PDMPs that reduce non-evidence based prescribing practices. That is, PDMPs that provide feedback about potentially problematic dispensing and prescribing practices may help change inappropriate prescribing and help better identify patients in need of treatment for opioid use disorder secondary to prescribed opioid use, thus decreasing the potential probability of transition from prescription opioid into heroin use (Carlson, Nahhas, Martins, & Daniulaityte, 2016; Cerda, Santaella, Marshall, Kim, & Martins, 2015; Jalal et al., 2018; Martins, Sarvet, et al., 2017). In addition, our findings corroborate results from a previous study that show that operational PDMPs with robust features including sending unsolicited reports and requiring more frequent reporting from dispensers, can have a protective effect on those at risk of developing OUD (Pauly, Slavova, Delcher, Freeman, & Talbert, 2018).

To the best of our knowledge, this study is the first to identify specific classes of PDMP characteristics that are most strongly associated with changes in rates of fatal heroin poisonings. These results demonstrate that, while PDMPs overall are associated with an increase in fatal heroin poisonings, in more recent years PDMPs that were characterized as Proactive have shown a decrease in heroin poisonings. A better understanding of how specific characteristics of these programs (i.e., to require dispensers to report data to the PDMP on a more frequent basis) may contribute to a reduction in heroin poisonings is needed. In addition, it should be noted that certain features of Proactive PDMPs (in particular greater sharing of prescription information with law enforcement) may implicate privacy concerns and have the potential to perpetuate biases towards and reduce access to care for underserved and stigmatized populations (Beletsky, 2018). Thus, those authorized to

access Proactive PDMP data should be trained to protect individual privacy and confidentiality and ensure that PDMP data is used only to improve care for the patient.

Our study's findings should be considered in light of the following limitations. First, we relied on ICD coding of death certificate data, which may not reliably identify the drugs involved in fatal drug poisonings and may lead to differential underestimation of fatal heroin poisoning rates across states (Ruhm, 2017). However, our findings were robust to sensitivity analyses conducted to address this concern. Second, our study was not able to examine the mechanisms through which specific PDMP features influence the risk of heroin poisoning. Future research should identify whether specific PDMP typologies inadvertently influence inappropriate opioid prescribing behavior (e.g., abrupt discontinuation of opioid therapy without referral to follow-up care), which subsequently may cause a subset of patients to seek opioids through the illicit market. Future in-depth studies of single states could potentially provide more granular data and combine data from multiple sources to assist in elucidating causal pathways/mechanisms between PDMPs typologies and heroin poisonings. Our results may also be due to confounding, since states that adopted stricter PDMP models may also have been more likely to implement other policies or state-level initiatives aimed at reducing heroin poisoning rates that were not considered in the LTA. It should be noted that PDMPs are only one of a group of potential ecological determinants (i.e., other system efforts and measures of prescription opioid control; public health and treatment interventions for opioid disorders, changes in illicit market supply) that can contribute to changes in heroin use and heroin poisoning mortality. However, our model did adjust for several important state level policies (medical marijuana legalization, Good Samaritan Laws and naloxone access laws) and included state fixed effects, which addressed all time-fixed sources of confounding. Fourth, this study focused on the impact of PDMPs on heroin fatal poisoning only. Future studies should consider the potential unintended effects of PDMPs on other opioid-related outcomes (i.e., illicit fentanyl exposure) and on non-fatal heroin poisoning.

In conclusion, our study suggests that that, at least in recent years, Proactive PDMPs are associated with the greatest reductions in heroin poisoning fatalities. Unfortunately, both Reactive and Cooperative PDMPs were associated with increases in fatal heroin poisonings in different time periods. Future studies need to closely monitor the mid- to long-term effects different subtypes of PDMPs have on both fatal and non-fatal heroin poisonings. States with No/Weak and Cooperative PDMPs should consider implementing features of Proactive PDMPs. Future research is needed to identify how PDMP interface may be modified to support providers in not only identifying patients and providers with potentially problematic prescription histories but also linking patients who may benefit from specialized pain management or substance use disorder treatment to the most appropriate services and care for their conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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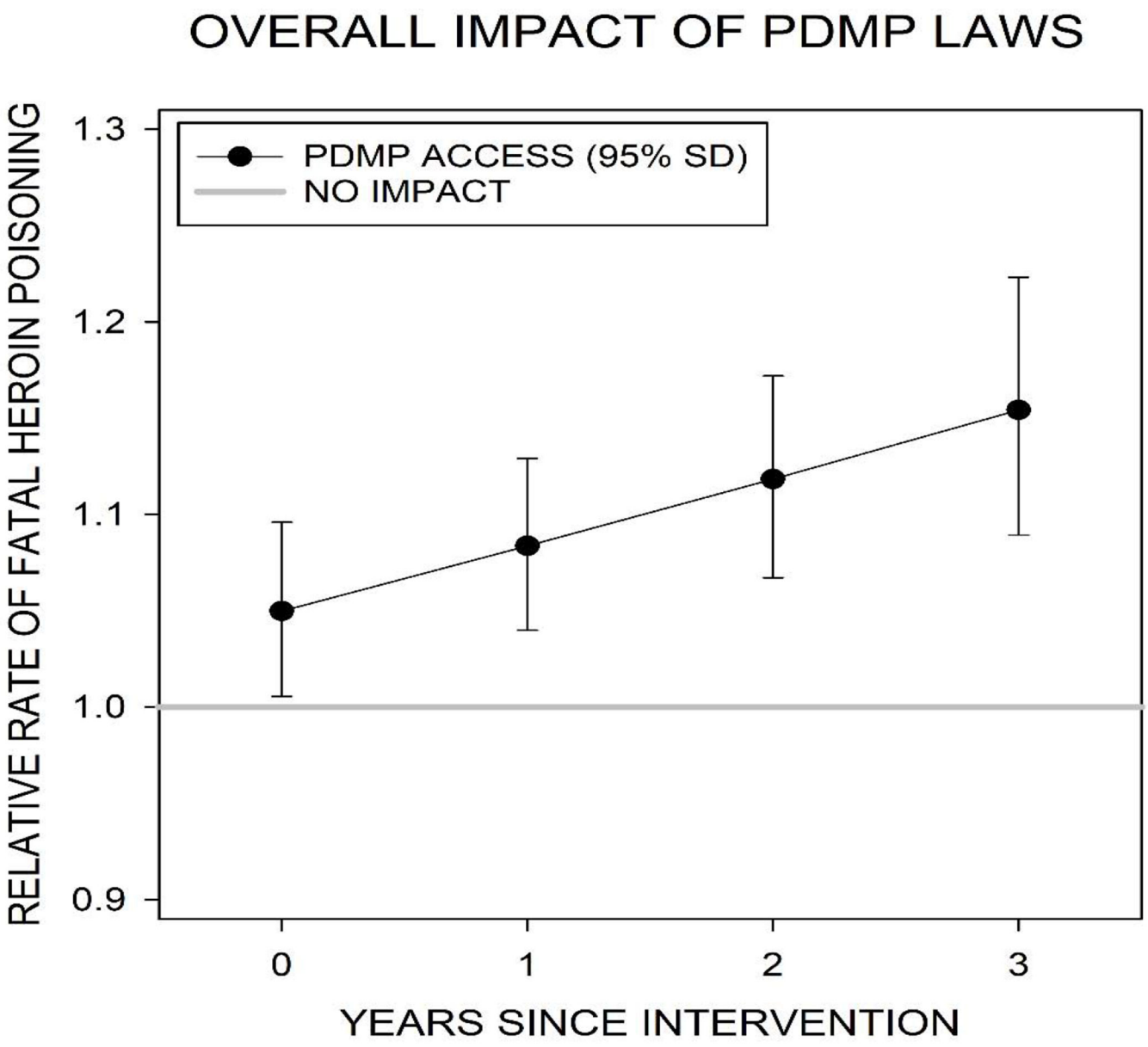

Figure 1:

Linear distributed-lag model showing the overall impact of state adoption of an electronic PDMP on the relative rate of fatal heroin poisoning

Note: Results based on models that adjust for annual county-level age, race/ethnic, sex, and socioeconomic composition, population density, and the overall mortality rate; annual state-level medical marijuana laws, Good Samaritan laws, and naloxone poisoning prevention laws; calendar year; and state-level fixed effects.

Table 1.

Estimated relationship between PDMP latent class membership probability, and the county-level rate of heroin poisoning fatalities, 2002-2016, United States[1]

PDMP latent classes	Full sample (49 states and D.C.)		After dropping 4 states with highest levels of underreporting for specific drugs		All drug poisonings as an outcome	
	Median RR	95% CI	Median RR	95% CI	Median RR	95% CI
Interval 1: 1999-2004						
Reactive PDMP relative to No/Weak PDMP	**0.88**	**0.82,0.94**	**0.77**	**0.72, 0.83**	**0.98**	**0.96, 0.99**
Proactive PDMP relative to No/Weak PDMP	1.00	0.83,1.20	0.93	0.77,1.11	0.96	0.93, 1.00
Proactive PDMP relative to Reactive PDMP	1.14	0.95,1.37	1.20	1.00,1.44	0.99	0.95, 1.03
Interval 2: 2005-2009						
Reactive PDMP relative to No/Weak PDMP	**1.05**	**1.01,1.09**	1.01	0.97, 1.05	**1.09**	**1.07, 1.09**
Proactive PDMP relative to No/Weak PDMP	1.05	0.98,1.11	0.96	0.90,1.02	1.01	0.99, 1.03
Proactive PDMP relative to Reactive PDMP	1.00	0.94.1.06	0.95	0.89,1.01	0.94	0.92, 0.95
Interval 3: 2010-2016						
Cooperative PDMP relative to Weak PDMP	**1.19**	**1.14,1.25**	**1.17**	**1.11,1.24**	1.01	0.99, 1.03
Proactive PDMP relative to Weak PDMP	**0.94**	**0.90,0.98**	**0.95**	**0.91,0.99**	**0.90**	**0.89, 0.92**
Proactive PDMP relative to Cooperative PDMP	**0.79**	**0.74,0.83**	**0.81**	**0.76,0.86**	**0.90**	**0.88, 0.91**

[1]Results based on models that adjust for annual county-level age, race/ethnic, sex, and socioeconomic composition, population density, and the overall mortality rate; annual state-level medical marijuana laws, Good Samaritan laws, and naloxone poisoning prevention laws; calendar year; and state-level fixed effects.

Note: estimates significant at $p \leq 0.05$ are bolded.