Systematic Literature Review of Prescription Drug Monitoring Programs

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Abstract
Prescription opioid abuse has become a serious national problem. To respond to the opioid epidemic, states have implemented prescription drug monitoring programs (PDMPs) to monitor and reduce opioid abuse. We conducted a systematic literature review to better understand the PDMP impact on reducing opioid abuse, improving prescriber practices, and how EHR integration has impacted PDMP usability. Lessons learned can help guide federal and state-based efforts to better respond to the opioid crisis.

Background:

Opioid abuse has become an increasing issue in the US. Since 1999, overdose deaths and prescription drug sales have quadrupled.[1] In 2016, there were over 63,000 deaths associated with drug overdoses in the US.[2] The age-adjusted drug overdose rate has increased from 6.1 per 100,000 in 1999 to 19.8 per 100,000 in 2016.[2] National and state guidelines have been implemented to help providers make more informed decisions when prescribing these medications.

Prescription drug monitoring programs (PDMPs) are being implemented throughout the country as a decision support for prescribers, pharmacists and regulators. PDMPs are electronic databases that collect and analyze patient prescription data. Providers, such as prescribers and pharmacists, are required to check the PDMP before they prescribe controlled substances such as amphetamines, benzodiazepines, and opioids. Providers may be alerted by a PDMP message if a patient is at risk of substance abuse. Most algorithms quantify use based on the morphine milligram equivalent (MME), which is a value assigned to opioids to represent their relative potencies.

Controlled substances are categorized by Schedules I through V. Schedule I drugs are substances with the highest abuse potential, hence, never prescribed by a provider. An example of a Schedule I opioid is heroin. Schedule II, III, IV, and V drugs are commonly prescribed by providers. Of these, Schedule II substances have the highest potential for physical dependence. Schedule II drugs include the branded opioids, Vicodin and Percocet. Schedule III, IV, and V drugs are considered to have very low physical dependence potential. Each state has a requirement for providers to check the PDMP before prescribing and/or dispensing certain scheduled drugs, but these requirements vary from state to state.

The PDMP goal is inform prescribers about concurrent prescriptions and expose drug misuse at the time of prescribing. With Missouri's PDMP adoption in July 2017, all 50 states in the United States have a PDMP in place. For PDMPs to be effective tools, prescribers and pharmacists must integrate the PDMP into their respective workflow. Improved integration of PDMPs into electronic health records (EHR) could have a significant impact on usability.

Objectives:

The main study objective was to conduct a systematic literature on PDMPs. Specific research questions were defined as PICO questions[3]:

Q1: How have PDMPs impacted opioid-related clinical outcomes and other related metrics?

Q2: How has the integration of PDMPs into EHRs impacted utilization and usability?

Methods:

Systematic review

Using the identified research questions, we initiated our literature review using PubMed database to identify search terms and inclusion and exclusion criteria. Based on these results, we modified our review methodology according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), which consists of guidelines designed to aid authors in improving the quality of review reports.[4]

Search Process

Following the PRISMA method, we searched PubMed for English-language studies performed in US between 01/01/2010 and 02/28/2018, using the "most recent" searching approach.[5] The PubMed "most recent" search is the recommended searching approach when conducting a literature review. Through an iterative process, papers were summarized and organized in tables based on their contributions to the chosen research questions. Searches were independently performed by AD and AG. Outcomes were compared for consistency.

Article selection

The PRISMA approach guided the organization of the papers based on more one than perspective or topic. This is a suitable approach for new topics, such as PDMP, for which relevant research questions are not yet clearly defined. For Q1, sources were included if they report PDMP effects in terms of opioid-related clinical outcomes and other relevant metrics. Sources were excluded if they were not published in the US or if they were published before 2010. The goal was to find data which evaluated the effects that PDMPs have had in the US on the opioid epidemic. For Q2, papers were included if they discussed usability or utilization metrics related to PDMP integration with EHRs or other databases. Papers were excluded if they were published outside the US or before 2010.

The first author (AP) performed the initial selection based on article's title and abstracts. Outcomes were independently checked by AG and AM, based on articles' title and abstracts. Inconsistency were resolved by consensus, after complete paper review.

Data management and collection process

Data was managed and collected by first author using tabulated data.

Results:

Our search, outlined in Table 1, returned 408 papers. We included in the full review, 27 publications [6-32], summarized in Tables 2 and 3. We excluded duplicated papers, and papers that did not satisfy the inclusion criteria or satisfied the exclusion criteria. Of the included studies, five represented a time-series analysis and nine used either an interview, intervention, or survey. Other study types that were utilized included a scoping systematic review, a mixed-method approach, a retrospective cohort study, a cross-sectional study, and a longitudinal observational study.

Table 1: Queries Q1 and Q2 performed in PubMed, results returned, and papers retained

Question	Search Terms	Returned Results	Results Retained
Q1	("Outcomes" OR "Effects" OR "Metrics" OR "Impact") AND ("Prescription drug monitoring program" OR "PDMP" OR "PMP" OR "CSPMP") NOT ("platelet-derived microparticles") Filtered 2010-2018	372	25
Q2	(("electronic health records" OR EHR OR "health records" OR HR OR "electronic medical records" OR EMR OR "medical records" OR "patient records") AND (Prescription drug monitoring program" OR "PDMP" OR "PMP" OR "CSPMP") NOT ("platelet-derived microparticles")) Filtered 2010-2018	36	1

Table 2: Summary of retrieved publications for Q1. Main outcomes analyzed in each paper are italicized.

Author (year)	Study Purpose	Principal Findings	State	Study Type
Al Achkar et al. (2018)[6]	Compare *volume of prescribed opioids* before and after implementation of opioid prescribing emergency rules. Stratify changes in opioid prescribing by patient and provider subgroups.	MME decreased after implementing the new emergency rules. Rules also associated with decline in number of prescribers and in drug day supply.	IN	Interrupted time series analysis
Deyo et al. (2018)[7]	Determine if prescriber use of	Decrease in opioids dispensed over 3-year study, commencing	OR	Retrospective cohort study

	PDMP associated with fewer high-risk *opioid prescriptions or overdose events*.	with first quarter of PDMP operation.		
Pauly et al. (2018)[8]	Examine associations between specific administrative features of PDMPs and changes in the risk of *prescription opioid-related poisoning* (RxORP) over time.	States without PDMPs experienced an average annual increase in the rate of opioid poisonings, 9.51%, vs. states with PDMPs at 3.17%.	KY	Longitudinal, observational study
Pardo (2017)[9]	(1) Estimate the relationship of PMP strength with *opioid pain relievers (OPR) overdose deaths* across states and over time; (2) Measure what threshold in PMP strength is associated with the greatest reduction in *OPR overdose*; and (3) Assess the relationship of medical marijuana dispensaries with *OPR overdose deaths*.	States with more robust PDMPs have fewer prescription opioid overdose deaths than states with weaker PMPs. States with medical marijuana dispensaries also report fewer opioid overdose deaths than states without these.	50 States	Analysis using Fixed Effects
Finley et al. (2017)[10]	(1) Describe available evidence regarding impact of PDMPs on *opioid epidemic* in the US; and (2) propose a conceptual model to inform future PDMP implementation and evaluation efforts.	Evidence for the impact of PDMPs as an opioid risk mitigation tool is mixed. There are significant gaps in empirical research on this subject.	TX	Scoping systematic review
Moyo et al. (2017)[11]	Compare *opioid use* before and after implementation of PDMPs.	PDMP implementation was associated with reduced opioid volume and no changes in mean MME or opioid prescriptions 12 months after implementation compared with non-PDMP states.	FL, LA, NE, NJ, VT, GA, WI, MD, NH, AR	Analysis of opioid prescription claims in US
Phillips and Gazmararian (2017)[12]	Determine whether specific state legislation (including cannabis-related) influences *opioid overdose mortality* rates compared to	PDMPs were associated with an increase of 11.4 % in mean age-adjusted opioid-related mortality. Medical cannabis laws were associated with an increase of 21.7% in mean age-adjusted opioid-related mortality.	50 States	Multivariate repeated measures analysis

	states without such legislation.			
Rutkow et al. (2017)[13]	Learn about PDMP staff, law enforcement officials, and administrative agency employees' *attitudes and experiences with PDMPs*.	Interviewees identified key PDMP goals: improve patient treatment decisions; influence prescribing practices. Interviewees identified three promising future areas: data sharing and analysis; integration of PDMP data with electronic medical records; and training for current and potential PDMP users.	MD	Semi-structured interviews
Yarbrough (2017)[14]	Measure the impact of PDMPs on *prescribing of opioid and nonopioid painkillers*.	PDMPs were associated with a 5.2% decrease in days supply prescribed per physician for oxycodone, with smaller reductions for hydrocodone and opioids overall and a small increase in prescribing for Schedule IV opioids.	GA	Study using difference-in-differences models
Nam et al. (2017)[15]	Examine the impact of PDMPs on *drug overdose deaths*.	PDMP implementation not associated with reductions in overall drug overdose or prescription opioid overdose mortality rates relative to expected rates absent a PDMP.	AL, AZ, CO, CT, IA, LA, ME, MT, MN, NC, ND, NM, OH, SC, TN, VA, VT, WA, WY, AK, AR, DE, FL, GA, KS, MD, MO, NE, NH, NJ, OR, SD, WI, MS, DC	Multivariate regression models and preprogram tests
Delcher et al. (2017)[16]	Examine trends in *registration rates and use* of Florida's PDMP by physicians and pharmacists.	PDMP registration among physicians and pharmacists is limited and use among registrants even more limited.	FL	Time-series forecasting
Branham (2017)[17]	Evaluate the impact of PDMPs on *heroin use* across several different states through use of treatment admissions records obtained from the Treatment Episode Data Set	Positive relationship between heroin use and prescription opioid admissions noted post PDMP implementation.	KY	Interrupted time-series analyses
Young et al. (2017)[18]	To evaluate the impact on *opioid prescription* of unsolicited reports sent by PDMP to prescribers of persons with Multiple Provider Episodes.	Unsolicited PDMP reporting to prescribers can help reduce risk measures in patients' prescription histories and may improve health outcomes for patients receiving opioids from multiple providers.	MA	Intervention

Blum et al. (2016)[19]	Assess *providers' experiences* on mandatory PDMP use.	Many providers believe New York's PDMP (iSTOP) is cumbersome and ineffective Many oppose mandatory use.	NY	Survey
Chang et al. (2016)[20]	Evaluate how PDMPs and pill-mill laws affect *opioid use* in high-risk prescribers in Florida.	High-risk prescribers are disproportionately responsive to state policies. However, opioid-prescribing remains highly concentrated among high-risk providers.	FL	Intervention
Sajid et al. (2016)[21]	Examine PDMP tracking as a novel measure of *opioid addiction treatment outcomes.*	Supports PDMP utility for measuring opioid addiction treatment outcomes, and routine use of PDMPs in clinical and research settings.	IN	Repeated measure parametrics
Manasco et al. (2016)[22]	To characterize aspects of each state's PDMP that impact *usability* and *effectiveness*.	Considerable heterogeneity between state PDMPs on basis of: reporting time, data sharing, provider identification and high-risk patient or provider reporting.	49 states, Missouri and the District of Columbia were excluded	Web-Based Survey
Rutkow et al. (2015)[23]	Quantify the effect of the PDMP and pill mill laws on *overall and high-risk opioid prescribing and use.*	Twelve months after statute implementation, observed a 1.4% decrease in opioid prescriptions, 2.5% decrease in opioid volume, and 5.6% decrease in MME per transaction.	FL	Comparative interrupted time-series analyses
Delcher et al. (2015)[24]	Evaluate the effects of the PDMP on *oxycodone-caused mortality*.	Oxycodone-caused mortality abruptly declined 25% one month after Florida PDMP implementation.	FL	Time-series
Wixson et al. (2015)[25]	Identify *pharmacists' utilization* of Kentucky All Schedule Prescription Electronic Reporting Program (KASPER), Kentucky's PDMP.	Utilization of Kentucky PDMP, KASPER, differed by pharmacists' practice environments. Practice environments associated knowledge is necessary to remove barriers to access and increase PDMP use.	KY	Survey
Ringwalt et al. (2015)[26]	Identify if increase in providers querying PDMPs and number of days queried would be related to *decrease in opioid prescriptions*.	No association between the two variables of interest. However, a slight positive relationship between the growth in PDMP utilization and the number of prescriptions filled for opioids.	NC	Data analysis
Rasubala (2015)[27]	Evaluate the impact of mandatory PDMP on *frequency and quantity of opioid prescriptions* by dentists.	Total number of prescribed opioid pills in a 3-month period decreased from 5,096 to 1,120, a 78% reduction in absolute quantity.	NY	Data analysis
Deyo et al. (2014)[28]	Describe outreach efforts in Oregon,	Less than 25% of providers have PDMP accounts over 2	OR	Survey

	quantify uptake of *PDMP use*, identify *barriers*, and identify *system improvements*.	years of operation. Half were unaware they could register for PDMPs. Two thirds of current users did not use PDMPs due to time constraints.		
Fleming et al. (2014)[29]	Explore the theory of planned behavior's utility in predicting pharmacists' *intention to utilize an online accessible PDMP*	Pharmacists' utilization of PDMPs may lead to a decrease in morbidity and mortality associated with prescription drug abuse. Pharmacists with positive attitudes were almost twice as likely to have high intention to use PDMPs	TX	Cross-sectional questionnaire
Green et al. (2013)[30]	Assess differences in PDMP use between two states with different PDMP accessibility. To examine associations between *PDMP use and doctor shopping*.	PDMP users more likely to detect drug abuse and doctor shopping. PDMP users less likely to discuss their concerns of suspicious medication use behaviors with their patients.	CT, RI	Descriptive nonexperimental study
Fleming (2013)[31]	Describe *PDMP use* by providers with and without online access and by controlling agency	Prescriber request rates were higher than pharmacists and overall for online access. In law enforcement-governed PMPs, health care provider utilization was lower compared with PMPs under health or pharmacy boards.	TX	Cross-sectional study

Table 3: Summary of retrieved publications for Q2

Author (year)	**Study Purpose**	**Principal Findings**	**State**	**Study Type**
Poon et al. (2016)[32]	Evaluate the *usability of the PDMP* and its *integration with EHRs*	For emergency medicine providers, usability barriers are high and deter frequent use. Using PDMPs, on average, took 3 more minutes and 30 more mouse clicks than using other commonly performed computer tasks such as using EHRs. PDMPs should be integrated into EHRs for more efficient use.	MA	Semi-structured interviews and analysis

Table 4: Metrics identified to evaluate PDMP (Q1)

Metric	**Number of Papers**
Changes in Opioid Prescriptions	12 [6,7,10,11,13,14,18,20, 21, 23,26,27]
PDMP Utilization and Usability	9 [13,16,19,22,25,28-31]
Changes in Opioid-Related Overdoses	8 [7-10,12 13,15,17]

How have PDMPs impacted opioid-related clinical outcomes and other related metrics?

Measuring the success of PDMPs is essential to guide improvements in both policy and implementation. We found that there were decreases in opioid prescriptions, total MME, poisoning from opioids and other controlled substances, overdose deaths, and providers prescribing methods were changed, such as consistently checking PDMP and prescribe less controlled substances (Table 4).

Several studies showed that PDMPs have led to decreases in opioid prescriptions. Studies in the state of Florida demonstrated that after the implementation of the PDMP, the Oxycodone-caused mortality abruptly declined 25%[24], opioid prescriptions declined 1.4%, opioid volume decreased 2.5%, and MME per transaction decreased 5.6%.[23] Pauly et al. showed that states without PDMPs had an average annual increase in the rate of the risk of prescription opioid-related poisoning of 9.51%.[8] States with a PDMP, however, had an average annual increase of 3.17%[8], showing that states with PDMPs had a smaller increase when compared to non PDMP states. Rasubala et al. concluded that after implementing a mandatory PDMP use policy in a dental clinic, there was a 78% reduction in the total numbers of prescribed opioid pills over a 3-month period.[27] Branham noted that patients unable to obtain opioid prescription due to stringent prescribing practices are more likely to begin heroin use.[17] Branham conducted a time-series analysis and concluded that PDMPs and heroin do have a positive relationship. The goal of PDMPs is to curb prescription drug abuse, not to increase heroin use among patients. Opioid prescribing policies need to be improved such that patients do not encounter detrimental situations when they are not prescribed their desired dosages or are cut off from prescription drugs.

In five studies, PDMP was related to a decline in opioid-related overdoses and deaths.[8,9,12,17,24] States with "stronger" PDMPs demonstrated the largest decrease in opioid related deaths when compared with states with "weaker" PDMPs.[9] In this study by Pardo, PDMP strength criteria included 11 factors, each assigned a point value, the higher the total point value, the stronger the PDMP. In contrast, a study by Nam et al. concluded that PDMPs were not associated with a reduction in drug overdose mortality rates: PDMPs operational for over five years have been associated with increased mortality rates in legal narcotics and other illicit drugs.[15] The authors concluded that different approaches must be considered to effectively affect opioid overdose. Finley et al. concluded that the impact of PDMPs still remains mixed.[10] The study used thematic analysis to identify domains which are frequently evaluated when discussing PDMP implementation: opioid prescribing, opioid diversion and supply, opioid misuse, and opioid related morbidity and mortality. After examining these four domains, it was concluded that there were significant gaps in empirical research in each domain. Finally, Fleming et al. suggested that if prescribers use PDMPs more often there may be a decrease in morbidity and mortality associated with prescription drug abuse.[29] As prescribers use PDMP more often the chance of identifying a potential at risk patient increases.

PDMPs can be effective if providers use them.[18] Several studies demonstrated a reduction in opioid prescriptions with use of PDMDs.[6,7,11,14,18,23,26,32] Prescribers were also more likely to detect prescription drug abusers and doctor shoppers if accessing the PDMP database regularly.[30] Some states require providers to check the PDMP before they prescribe opioids; however where it is not required, providers are not fully utilizing PDMPs.

What are the barriers to PDMP use? Prescribers are not using PDMPs because they are cumbersome, perceived as ineffective and are resistant to mandatory use.[19] In Kentucky, PDMP use by pharmacists differs based on practice environment, practice type, and location. Pharmacists who practiced in chain pharmacies had a KASPER (Kentucky's PDMP) utilization rate of 75% while independently practicing pharmacists had a utilization rate of 94%.[25] Fleming et al. concluded that prescribers use PDMPs more often than pharmacists, and online accessibility has led to higher utilization as well.[31] Regarding provider utilization rates, it is important to understand the barriers providers face when trying to use PDMPs. If these barriers are identified and resolved, PDMP utilization rates may rise.

Online accessibility may affect PDMP utilization, but there is a need for further research to discover and quantify other factors that may affect PDMP utilization. In 2013, Fleming et al. also found that PDMPs annual operational costs were around $12,515 ± $14,911 per 100,000 population.[31] If annual PDMP costs are lowered, hospital systems and states can afford to implement newer PDMP systems and invest in other PDMP improvements, such as EHR integration.

Ringwalt et al. concluded that PDMPs had no effect on the prescribing practices of the providers they had tracked.[26] In a study done by Delcher et al., PDMP registration among physicians was limited and even among the providers who were registered, PDMP use was limited.[16] This may be due to providers not being aware of the availability and registration process for PDMPs, as noted by Deyo et al. In this study, almost 50% of the providers surveyed did not know they could register to use the PDMPs.[28]

Providers with a positive attitude were nearly twice as likely to have a high intention rate to utilize PDMP.[29] If PDMP are better integrated into clinical workflow, providers will potentially stop considering PDMP a hassle and would adopt using them. New solutions need to be proposed to increase the efficiency of providers when they are using PDMPs alongside EHRs.

Providers and other employees who use PDMPs regularly were interviewed to see what they would like in a PDMP. Interviewees identified three promising areas for future PDMP efforts: data sharing and analysis, integration of PDMP data with EHRs, and training for current and potential PDMP users.[13] If these goals are achieved, there could be in a significant increase in the number of PDMP users which in turn could lead to a decrease in opioid prescriptions.

How has integration of PDMPs into EHRs impacted PDMP utilization and usability?

Relevant stakeholders have indicated the need for better integration of PDMPs into EHRs.[13,19] However, only one paper was retrieved that explicitly discussed PDMP- EHR integration and its impact on utilization and usability. The retrieved paper combined outcomes from interviews and usability metrics. Provider interviews indicated that lack of standards for PDMP integration into EHRs results in poor usability and decreased use.[32] A Massachusetts hospital system reported limited success with a PMDP link embedded in the EHR but providers had to log into the PDMP for each access, deterring PDMP use.

Discussion:

The systematic literature review highlighted concentrated activity in a few states. We retrieved six papers from Florida[11,15,16,20,23,24], three each from Kentucky[8,17,25], Oregon[7,15,28], Texas[10,29,31], Massachusetts[18,22,32], and Georgia[11,14,15]. These six states alone published 19 of the 27 retained papers, as seen in Tables 2 and 3. We are encouraged by the increasing number of papers about PDMP implementation published recently. Nearly half of the 27 retained papers were published between 2018 and 2017, including three papers from early 2018 and ten from 2017.

As in our Q1, a previous literature review focused on evidence evaluating the impact of PDMPs in the US. Finley et al. searched for papers between 2000 and 2016. They retained 11 of 296 retrieved articles, including several that we retained.[23,24,27] Our study included nine papers published after Finely et al. review.[6-9,11-13,16,17] When comparing discovered metrics, both studies found that prescribing practices, opioid related overdoses and mortality, and changes in opioid prescriptions were relevant, measurable outcomes. With Q2, an additional dimension to inform PDMP impact assessment is suggested, specifically, PDMP utilization and usability. Our literature review indicates that most PDMPs have had a positive impact, based on the most commonly reported outcome measures as outlined in Table 4. We agree with the conclusion by Finley et al. that further research is needed to systematically assess the effectiveness of PDMPs and to explore unintended consequences. The current PDMP literature is scant and study designs are not uniform, so it is hard to conduct statistical analysis of the cumulative evidence.

According to our analysis, the most pressing current issue for PDMPs is low utilization among providers. PDMPs are not being used to their fullest potential due to adoption and usability barriers. PDMPs are not well-integrated with prescribers' clinical workflows and EHRs. More work is needed develop effective PDMP solutions that overcome these barriers and to understand how PDMP utilization rates impact the opioid epidemic. We found no publications that discussed the impact of prescribers' trust on the quality of the data collected by PDMPs or its impact on usability and prescribe practices. We need to better understand how providers can most effectively use PDMP data as part of routine care while integrating state and federal guidelines and requirements in statute.

There are limitations to this study that can be addressed in future work. This study only retrieved papers from the PubMed database. The literature review should be extended to other databases, such as Web of Science and Google Scholar. Only papers from the US were included in the study, so there may be answers to our research questions in papers published outside of the US. As well, we did not assess the risk of bias of individual studies.

The most significant limitation, however, is that our results are based solely on scientific papers. In this rapidly evolving landscape, we might enrich our study by systematic review of federal and state websites and online resources. Interviewing stakeholders, including state government representatives and policy makers[22] could help us to better understand the benefits as well as shortcomings of PDMPs. Contacting health care IT experts and software vendors could provide insight into solutions to PDMP challenges. Access to national resources, such as the Strategic Health Information Exchange Collaborative (SHIEC)[33] may help us understand efforts around data standardization and interoperability to increase integration of PDMPs into EHRs and HIEs and to support data exchange between state PDMPs.

We must keep in mind that PDMPs are but one approach to combatting the opioid epidemic. Tackling the root cause, addiction, is the most important focus.

Conclusion:

Our results suggest that PDMPs have had a mixed, but overall, positive impact on opioid use and related morbidity and mortality. However, the varying metrics and implementation landscape underscore the need for a meta-analysis of PDMP impact. We also observed that usability and EHR integration issues are significant barriers to

effective PDMP use. We conclude that a better understanding of the technology and related human factors are needed to improve the usability, utility and use of PDMPs.

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