

Advances in prescription drug monitoring program research: a literature synthesis (June 2018 to December 2019)

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Purpose of review

Nearly every U.S. state operates a prescription drug monitoring program (PDMP) to monitor dispensing of controlled substances. These programs are often considered key policy levers in the ongoing polydrug epidemic. Recent years have seen rapid growth of peer-reviewed literature examining PDMP consultation and the impacts of these programs on diverse patient populations and health outcomes. This literature synthesis presents a review of studies published from June 2018 to December 2019 and provides relevant updates from the perspective of three researchers in this field.

Recent findings

The analyzed studies were primarily distributed across three overarching research focus areas: outcome evaluations (n=29 studies), user surveys (n=23), and surveillance (n=22). Identified themes included growing awareness of the unintended consequences of PDMPs on access to opioids, effects on benzodiazepines and stimulant prescribing, challenges with workflow integration across multiple specialties, and new opportunities for applied data science.

Summary

There is a critical gap in existing PDMP literature assessing how these programs have impacted psychiatrists, their prescribing behaviors, and their patients. Although PDMPs have improved population-level monitoring of controlled substances from medical sources, their role in responding to a drug epidemic shifting to illicitly manufactured drugs is under scrutiny.

Keywords

controlled substances, evidence synthesis, opioid policy, prescription drug monitoring programs

INTRODUCTION

Prescription drug monitoring programs (PDMPs) are state-operated data systems that monitor patients and their controlled substance records dispensed primarily in outpatient pharmacies [1]. This describes the common data model but data collected in each state PDMP database can vary widely: from drug arrest records in Kentucky to documentation of prescription forgery in California [2]. As PDMP research advances, these 'ecosystems' [3] are viewed as integral to monitoring medical sources of opioids but are also met with skepticism; recently described as 'promising practices in need of refinement' [4]. This phrase echoes a major theme in PDMP research: the balance between intended and unintended prescribing consequences especially when healthcare providers are legally obligated to consult PDMPs ('mandatory use') [5]. Our work extends that of two previously published systematic reviews of PDMPs – one examining overdose outcomes (literature up to December 2017) and another (1993 to 2014) primarily assessing opioid prescribing and multiple provider episodes (MPEs) [6,7]. In this article, we provide a literature synthesis of recent developments in PDMP research that covers a non-

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KEY POINTS

- Rigorously operated PDMPs produce robust effects but impact on certain types of prescribing remains variable.
- Utilizing PDMPs in clinical practice presents some workflow barriers pointing to the importance of PDMP integration with electronic health records.
- PDMP use among psychiatrists and psychiatric practice is understudied.
- PDMP data for primary and secondary data research is growing.
- PDMP data linkage to other datasets creates opportunities to develop and apply novel data analytics and research methods.

overlapping, recent time period with a broader set of themes.

METHODS

We searched for the term 'prescription drug monitoring program' in the core Web of Science collection: Science Citation Index Expanded, Social Sciences Citation Index, Arts and Humanities Citation Index, and Emerging Sources Citation Index. Restricting to the period June 1, 2018 to December 31, 2019 (18 months) yielded 136 entries and 96 articles were included. Studies were primarily excluded if they only referred to PDMPs but did not contain meaningful discussion, examined drug monitoring of noncontrolled substances, were conducted in a non-US setting, abstracts, or not peer reviewed. We developed themes based on our professional judgment. The strength of evidence was not rated but we provided indications of study quality, sample size, and other limitations as appropriate. We highlighted findings that may interest readers in the field of psychiatry [8].

RESULTS

Health outcomes

Novel studies of health outcomes that quantify evolving PDMP 'rigor' through time have emerged but demonstrate contrasting effects on fatal and nonfatal overdoses where drugs involved were either prescription (semisynthetic/natural) or synthetic opioids [9–11]. Briefly, rigorous PDMPs reduced prescription opioid deaths/hospitalizations but increased deaths/hospitalizations associated with synthetic opioids. Similarly, 'comprehensive' PDMPs reduced Medicaid-funded inpatient stays,

emergency departments (ED) visits, and opioid prescription fills. This was one of the only studies to estimate cost aversion (\$155 million) [12*]. PDMPs showed more effectiveness in populated and urbanized areas with high access to medical opioids after mandatory use laws [13]. Studies from one group found that PDMPs had no effect at the *state-level* on benzodiazepine deaths (even when opioids were involved), benzodiazepines dispensed, dosage, or spending [14,15].

Prescribing outcomes

PDMP interstate data sharing was not associated with opioid prescriptions written to noncancer chronic pain patients. Studies of interstate data sharing are rare but this was a single year, cross-sectional study from the National Ambulatory Medical Care Survey [16]. The impact of physician warning letters (not primary aim) was new to the PDMP literature [17]. In Ohio, mandatory PDMP laws were associated with significant reductions in opioids dispensed and MPEs and benzodiazepines dispensed (in contrast to [15]). Another study reported similar impacts on opioids dispensed and MPEs in Kentucky but not West Virginia [18]. Integrating PDMP data with the health information exchange at one community healthcare center appeared to increase opioid prescribing; potentially attributable to increased provider awareness of need among ED patients with chronic painful conditions [19]. Opioid prescribing measures in a commercially insured population declined (greater extent for women and enrollees >50 years old) 1–2 years after Iowa's voluntary PDMP implementation [20]. Kentucky's PDMP showed more consistent effects (compared with Tennessee, New York, and New Mexico) using high-risk measures among commercially insured opioid recipients [21]. New York's mandatory PDMP use law decreased problematic opioid use measures typically associated with 'doctor shopping' in New York City [22]. The law had statewide effects in New York as measured by significant reductions in the number of quarters patients had at least three prescribers [21"]. There were two rare examples of randomized clinical trial designs assessing the effect of 'proactive notification' (a rigorous feature). In Nevada, prescribers getting reports on suspected 'doctor shopping' patients had minimal effect on prescribers who were already discontinuing opioid prescribing, in contrast to positive effects on prescribing behaviors when prescribers received reports in Massachusetts [23,24]. PDMP implementation and features had minimal impact in opioid prescribing to older adults in Medicare but were associated with reductions in prescribing to disabled nonelderly adults [25].

Prescription drug monitoring program use among healthcare providers

Several small studies indicated that PDMPs had limited influence in the vast majority of prescribing decisions. In an elective surgical population from one New Hampshire institution, mandatory PDMP use had no effect on opioid prescribing and PDMP consultation required 15 minutes per patient [26]. For ED providers at one Pennsylvania institution, opioid prescribing decisions remained unchanged after providers checked the PDMP, but PDMPs could also alleviate abuse/diversion concerns [27]. Psychiatrists studied from multiple outpatient mental health facilities in Ohio still prescribed controlled substances (primarily benzodiazepines and stimulants) after PDMP consultation [28]. 'Red flags' influenced prescribing behaviors but authors questioned the appropriateness of multiple provider alerts given comorbid conditions (chronic pain, anxiety) [28]. In dentistry, one study questioned the necessity of PDMP consultation for opioid-naive individuals

Authorized delegates (a third-party approved to access the PDMP) are less costly options for PDMP consultation but primarily when time and effort offsets are for physician specialties with higher pay and rates of controlled substance prescribing (e.g., psychiatrists) [30]. Mandatory PDMP registration in California increased physician and pharmacist PDMP engagement but a high registration-touse ratio (2:1) signaled that registration did not translate to use [31]. Although use is mandated in California, noncompliance was substantial, consistent with a study reporting approximately 10% noncompliance with legislation mandating PDMP use for ED physicians in Washington State. Notably, a majority of Washington State Medicaid prescribers were not PDMP-registered [32].

Prescribing surveillance

PDMP research predominantly focuses on opioids [33,34*,35*,36-53,54*] but research assessing the impact on coprescribing of opioid and benzodiazepines is increasing [33,34*,35*,39,42,46,51]. A study in an outpatient psychiatry setting in Pennsylvania used PDMP data to examine con-comitant opioid-benzodiazepine use 12 months previsit. It found that 49.4% of opioid recipients also received a concurrent benzodiazepine, and this group was more likely to have MPEs [35*]. The authors promoted the usefulness of PDMP consultation among psychiatrists but their results, consistent with [28], highlight challenges of managing severe comorbidities. Few studies have investigated stimulants and gabapentin prescribing [34*,54*]. Faryar *et al.* [54*]

analyzed gabapentin exposures from poison control center calls (Kentucky) from 2012 to 2015 coincident with PDMP mandatory use legislation. Gabapentin-only and multiagent exposures were primarily suspected suicides (versus unintentional overdoses from misuse/abuse). At least eight state PDMPs monitor gabapentin [55].

Prevention of controlled substance diversion

Two North Carolina Medicaid-PDMP linkage studies investigated trajectories of prescription opioid fills before/during/after pharmacy lock-in program (LIP) enrollment [51,53]. LIPs had limited impact on five different profiles of average daily opioid dosages trajectories [53]. Another examined cash-pay for opioids and benzodiazepines before/after LIP enrollment [51]. Two-thirds reduced Medicaid-covered opioid fills with no increase in cash-pay fills after LIP, concluding that LIPs seem to reduce prescription opioid use for most enrolled patients. Mixed findings suggest that LIPs are blunt tools for heterogeneous high-risk patient populations with limited capacity to deter illicit behaviors among patients intent on misusing medications that could simultaneously reduce access to care. A study of patients with hip or knee osteoarthritis in Arkansas compared self-reported 'narcotic' use with PDMP reported prescription fills [47]. The study found 22% self-reported use but 34% had PDMP records, and only 54% with a prescription in the past three months reported it. Self-report underestimated use and the authors recommended that orthopedic surgeons check their state's PDMP. Notably, the Orthopedic Trauma Association's Musculoskeletal Pain Task Force organization endorsed PDMP use in 2019 [56]. Medication discrepancies of this sort were also reported in a population of liver transplant patients [57].

Data linkage, system design, and predictive modeling

State overdose fatality reviews examine decedents' PDMP records to find opportunities for prevention but have limited utility in identifying nonprescription drugs. To address this, a novel approach was described whereby postmortem toxicology-to-PDMP data linkage helped attribute overdoses to prescription and/or diverted opioids, heroin, and illicitly manufactured fentanyl [50]. From 2013 to 2015, 61.4% and 45.3% of opioid overdose decedents in Massachusetts were positive for heroin and illicitly manufactured fentanyl, respectively, and active prescriptions on the date of death were rarely detected by postmortem toxicology. One study

examined the accuracy of a PDMP-to-mortality record linkage in Tennessee. Patient name spelling standardization with deterministic linkage led to robust matching (>83%) but with high potential for false positives [58]. Three studies used PDMP consultation as a tool to document all opioid use for spine surgery patients and one for Medicaid recipients receiving an opioid from the ED [59–62]. Three studies used PDMP data as the 'gold standard' as compared with opioid misuse screening or clinical assessments [2,63,64].

A novel measure called 'doctor hopping' was positively associated with high-risk opioid use; distinct and complementary to 'doctor shopping.' Doctor hopping was defined as patients bypassing nearby prescribers in favor of distant providers [36]. The authors recommend PDMP systems incorporate spatial analyses of patient-to-prescriber travel patterns. Others championed the development of predictive spatial and statistical analytic techniques stating that 'Maps move the dial through their power as communication devices' [42]. In another study, a novel prescribing continuity index (calculated from dispensing records alone) as measured by validated continuity of care indices, was tested and associated with opioid-related harms [46]. One study created a visually enhanced PDMP report and tested it against the standard line-list format. Outlier and hard-to-interpret features were easily detected but not faster than the standard, and prescribing behavior rarely changed even though satisfaction with the new format was high [65].

One study linked overdose fatalities (classified as prescription or illicit opioid involved) to PDMP data in Maryland and built acceptable predictive models using typical PDMP data fields. Buprenorphine and muscle relaxant prescriptions were significant predictors of overdose fatality but MPEs were not [66]. One national-level study examined five different 'aberrant behavior' algorithms (primarily MPE variants) for predicting opioid-related adverse events in Medicaid and commercial populations. Positive predictive value was low for all algorithms with limited agreement between algorithms [67]. Several studies used PDMP implementation as covariates in statistical models and reported results. One study found no association of PDMPs with Schedule II/III opioid prescriptions in Medicaid (models included states with legal medical cannabis). The study period covered the 'weaker' period of PDMP evolution (1993 to 2014) and a large increase in Schedule II/III prescribing occurred coincident with Medicaid expansion [68]. PDMPs, regardless of rigor, were not associated with trends in the percentage of Medicare patients with osteoarthritis on long-term opioids [69].

Surveys

Multiple surveys/interviews of diverse medical and nonmedical stakeholders, primary care providers (PCPs), ED physicians, surgeons, obstetricians/gynecologists, dentists, cardiologists, oncologists, pharmacists, patients, and state policymakers were recently published [70,71,72*,73–79,80*]. Often, these studies limited in scope and generalizability [70,71,73,75–78,81,82] with a notable gap for psychiatrists. With limited exceptions, these studies have consistently found that clinicians generally perceive PDMPs as useful tools and recommend consultation for routine clinical practice [72,73–76,78,83,79]. Two studies provided a nuanced picture of how PDMPs are utilized and perceived by various stakeholders [72,80]. Among pharmacists and PCPs, one study found that PDMPs were considered valuable tools for making prescribing and dispensing decisions [72]. Among PDMP administrators and other stakeholders, another found that PDMPs were perceived as useful for raising awareness about excessive controlled substance prescribing and also enabling proactive monitoring of controlled substance prescribing [80]. However, that study also found that stakeholders were concerned about unintended barriers for patients in need and whether PDMPs contribute to heroin-related morbidity and mortality [80]. Patients also perceived PDMPs as both necessary and useful tools to address the opioid epidemic [78].

Registration and utilization among providers

Despite generally positive perceptions, PDMP registration/use varies by actual or perceived patient risk and specialty. Providers seem to register/use PDMPs more when they perceive greater risk of potential drug diversion/misuse. Among clinicians, those with knowledge of a patient overdose were more likely to be registered with the state PDMP [71]. PCPs and pharmacists were more likely to consult PDMPs when patients had concerning 'red flags' [72*,84]. Two other pharmacy studies and a review of pain management in oncology are notable for either providing salient definitions of 'red flags' [85,86] or none at all [87].

PDMP use also varies by provider specialty. Cardiologists were more likely than oncologists to query the state PDMP [77], perhaps because oncologists are less concerned about controlled substance misuse in populations with chronic cancer-related pain although concern of nonmedical use among cancer patients is increasing [86]. Research is needed to evaluate the impacts of PDMPs on pain treatment and opioid-related harms in specific populations such as those with cancer. The latter population, for example, is likely to be flagged as "doctor"

shoppers", given high healthcare encounters, using the pharmacy/prescriber counting algorithms commonly used by PDMPs [88]. Another study comparing ED physicians and surgeons found greater PDMP use among ED physicians [75]. This finding is intuitive given that emergency departments physicians may encounter more potential 'doctor shopping' than in a postoperative setting. Not surprisingly, providers in states that mandate PDMP registration/use are more likely to register/use the PDMP [72*,79,89].

PDMP data design and integration remains a barrier. Studies routinely find that PDMP consultation is hampered by lack of integration with clinical workflow (one offered an algorithm for integrating into practice [90]), and poor user friendliness [72,75,79,91–93]. A single-institution in Michigan study showed very low rates of documented PDMP use (<3%) in a musculoskeletal pain population [94]. Most PDMPs are decoupled from electronic health records or provider portals so, even on the scale of minutes, providers perceive the process as burdensome [70]. One study found that PDMP use presented almost universal workflow challenges for both PCPs and pharmacists, backed by similar findings for state stakeholders [72,92]. Delegated access is a potential solution but several studies suggest limited delegation [72,79,92]. As expected, PDMP reports that are enhanced, yet simple and intuitive, are preferred [92,93].

Pharmacists

Research encourages expanded roles for clinical pharmacists to provide and interpret PDMP data, but PDMP consultation still varies [95]. A recent scoping review found that pharmacists' perceptions of PDMP utility positively influenced the likelihood that they would register/use them [96]. PDMP consultation also varies by pharmacy setting [72,81]. Some chain pharmacies have enacted PDMP consultation policies, whereas independent pharmacies showed more variability [72*]. Some pharmacists may hesitate to confront patients about their PDMP reports even if pharmacists believe the discussion would be beneficial [97], whereas others may use PDMP queries as impetus to contact the prescribing physician rather than intervene directly with patients [81]. Pharmacists, who interact with patients more frequently than PCPs or specialty providers, may have increased opportunities to educate patients on opioid risks, distribute naloxone, and recommend addiction treatment [98]. PDMPs also enhance a pharmacists' ability to more safely dispense opioids [99].

CONCLUSION

This literature synthesis has identified several themes related to the evolution of PDMPs as data systems and research tools in the context of an opioid epidemic shifting to illicit opioids [100]. Recent studies have assessed a multitude of health and other outcomes including high-risk opioid prescribing, "doctor shopping", and opioid-related morbidity and mortality. These studies reveal heterogeneous impact partly because of varied study populations and generally low rates of use among some providers – sometimes despite mandates requiring providers to register with and use the systems. PDMPs are generally perceived as necessary and beneficial tools; however, they will need to overcome perceived workflow and integration barriers before they are widely utilized by more stakeholders in the medical field. PDMP data have also been used in several recent studies to develop novel methods for identifying potential medication misuse beyond opioids (e.g., benzodiazepines, stimulants) or have been linked to other data sources to provide new insights into medication dose trajectories. Additional research is needed to better understand scenarios where PDMPs improve patient care or differentially impact certain populations such as those with chronic pain or cancer.

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Conflicts of interest

There are no conflicts of interest.

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- of special interest
- of outstanding interest
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This study assessed the impact of comprehensive PDMP mandates on quarterly opioid prescription rates, opioid-related inpatient discharge rates, and ED visit rates among U.S. Medicaid beneficiaries from 2011 to 2016. The authors identified PDMPs with comprehensive mandates using three criteria (similar to Haffajee et al. [5]), which were mandating all healthcare professionals to access PDMPs, mandating professionals to query PDMPs before prescribing, and providing objective criteria for the professionals to assist their decisions using PDMPs. Comparator states were those that did not meet these criteria in PDMPs during the study period. The analysis used a difference-in-differences design. Comprehensive PDMP mandate implementation reduced opioid prescription rates by 8.9%. Implementation showed a 7.4% decline in the Schedule II opioids prescription rate. It also decreased hospital utilization, a 4.3% reduction in opioid-related impatient discharge rate and 17.8% reduction in the ED discharge rate. Accordingly, savings on opioid-related hospital utilization was estimated at \$155 million for Medicaid expenditures. The authors suggest that implementing comprehensive PDMP mandates could improve health outcomes.

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This study evaluated the effectiveness of robust PDMP features on quarterly mean MED, the number of opioid fills, and high-risk opioid prescribing per enrollee among commercially insured adults age 18-64 from 2010 to 2014. The authors defined robust PDMPs as adding new features such as allowing prescribers access PDMP and detailed rules for prescribers reviewing PDMP prior to prescribing controlled substances. As a result, four states - Kentucky, New Mexico, Tennessee, and New York - were identified as robust PDMP adopters compared with other PDMPs during the study period. Each treatment state has a comparator state that had not implemented a robust PDMP. Interrupted time series and difference-in-differences designs were used to analyze a potential causal relationship. All four states exhibited significant reduction in MED (range of 6-77 mg per enrollee) compared with each control state by the end of 2014. Also, the number of opioid fills (range of 0.04-0.39 fills per enrollee) reduced significantly after the policy change. Notably, only Kentucky showed significant decreases in the percentage of people receiving opioids with more than 100 mg MED by 0.2% per enrollee, and on mean opioid fills from multiple prescribers and dispensers by 0.02% and 0.01% per enrollee, respectively, compared with its comparison state, Missouri. The authors concluded that PDMPs with robust features could significantly improve prescription opioid use among privately insured adults.

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Prior evaluations of PDMP impact often overlook variations in program features across states and time. To estimate PDMP rigor, the authors developed yearspecific composite scores to track each state's PDMP features relating to a defined set of best practices, that is, promising practices likely to facilitate maximum PDMP effectiveness. They then evaluated the association between the composite measure of PDMP strength and opioid prescribing in a 2007-2012 Medicare sample of individuals diagnosed with noncancer pain-related conditions. The results indicated that compared with non-PDMP states, strong PDMP states had reduced prescription fills, average daily opioid doses, and days supplied but an increased prevalence of opioid doses (≥120 MED) among disabled nonelderly adults. PDMP implementation and features had little to no impact in older adults. Findings in states with weak PDMPs were substantively similar to those of strong PDMP states which suggests diminishing returns with adoption of additional best practices and that a limited set of PDMP features actually add value in impacting opioid prescribing practices.

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This study employed qualitative interviews with PCPs and pharmacists to assess how and why providers and pharmacists access and utilize PDMPs. Interviews were conducted in a wide variety of practice settings in four different states. Nearly all pharmacists interviewed were registered with their state's PDMP and most reported using the PDMP daily; however, frequency of utilization varied by practice setting. Pharmacists employed by large chain pharmacies generally reported more frequent use because of corporate policies. Almost all pharmacists reported that PDMPs are valuable tools that improved decision making, but they also identified several barriers to effective implementation, including: workflow issues; lack of integration with existing dispensing systems, and suboptimal use by prescribers. PCPs reported a variety of reasons for using PDMPs. Most commonly, PCPs reported that they used the PDMP when treating new patients, when they identified 'red flags,' or when states had specific mandates requiring them to use it in certain situations. PCPs reported that aberrancies identified in PDMP data would often lead them to have a conversation with patients, and in some cases, terminate the patient-relationship. Although PCPs generally viewed PDMPs as useful tools, they also reported that these systems could be improved through integration with existing electronic medical records and improvements to user interface.

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This study used qualitative interviews with PDMP staff, law enforcement officials, and administrative agency employees to assess potential negative and positive unintended consequences associated with PDMP implementation. Interviewees were located in four different states – Kentucky, Ohio, Florida, and New Jersey. Respondents identified three major negative unintended consequences associated with PDMP implementation, including access barriers for those with legitimate medical needs, increasing heroin use (and related morbidity and mortality) as a substitute for opioid analgesics, and increased need for adequate data security measures. Respondents also identified three prominent, positive, consequences of PDMP implementation, including community formation and improved awareness of the opioid epidemic, improved population-level opioid monitoring, and increased knowledge of controlled substance prescribing practices.

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