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SUMMARY WITH CRITICAL APPRAISAL

Prescription Monitoring Programs for Optimizing Medication Use and Preventing Harm: A Review of Safety and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Abbreviations

ASIPP	American Society of Interventional Pain Physicians
CDC	Centers for Disease Control and Prevention
CRD	Centre for Reviews and Dissemination
DoD	Department of Defense
MME	Milligram Morphine Equivalent
PDMP	Prescription Drug Monitoring Program
PMP	Prescription Monitoring Program
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
VA	Department of Veterans Affairs

Context and Policy Issues

The misuse of prescription monitored drugs is a major health issue of national and international concern. Monitored drugs include any controlled substance under the federal *Controlled Drugs and Substances Act* (e.g., narcotic analgesics and nonnarcotic controlled drugs, such as methylphenidate, benzodiazepines, and barbiturates) and other opioid medications not listed in the *Controlled Drugs and Substances Act* (i.e., tramadol containing products and tapentadol).[1] The misuse of prescription monitored drugs can lead to addiction, poisoning, and death of its consumers.[2]

In Canada, the rates of hospitalization due to opioid poisoning have increased by 27% over the past five years.[2] On average, 17 hospitalizations per day occurred in 2017 due to an opioid-related poisoning and nearly 4,000 Canadians died from an apparent opioid-related overdose.[2] Importantly, the misuse of prescription monitored drugs is an issue across many different areas of Canada — from small towns to large urban cities.[2] The United States has also been significantly affected; for example, an estimated USD $78.5 billion is spent annually on the two million individuals who have an addiction associated with prescription opioids.[3] Interventions to improve the safety of populations receiving prescription monitored drugs are urgently needed to address but also to prevent monitored drug misuse.

Prescription (Drug) Monitoring Programs (PMPs/PDMPs) proactively collect and analyze information about prescription and dispensing of certain monitored drugs.[4] In Canada, some of the main objectives of PMPs are "to enhance patient care and assist in the safe use of controlled prescription drugs by monitoring outpatient prescription dispensing information, to help reduce the harms resulting from the use of controlled prescription drugs, and to assist in reducing the diversion of controlled prescription drugs."[5] (p. 3). A 2015 report stated that at least eight provinces or territories within Canada are using a PMP in some capacity.[5] Despite this, there is a lack of synthesized evidence about the safety of PMPs for optimizing medication use and preventing harm. Health care decision makers require knowledge on key safety outcomes, such as unintended patient consequences, street diversion and dispensing errors, to ensure that PMPs are achieving their desired outcomes as opposed to creating unintended harm. Information describing safety outcomes will improve our understanding of the health impacts of PMPs, which may aid the provinces and territories within Canada in deciding whether to commence, continue, and/or expand PMPs, or focus resources on other mitigation efforts.

The aim of this report is to summarize the clinical evidence regarding the safety of PMPs and evidence-based guidelines informing the use of PMPs for optimizing medication use and preventing harm.

Research Questions

1. What is the clinical evidence regarding the safety of prescription monitoring programs for optimizing medication use and preventing harm?
2. What are the evidence-based guidelines regarding the use of prescription monitoring programs for optimizing medication use and preventing harm?

Key Findings

No clinical evidence describing the safety of prescription monitoring programs for optimizing medication use and preventing harm were identified.

Three evidence-based guidelines and one systematic review of guidelines were identified providing recommendations on the use of prescription monitoring programs for optimizing medication use and preventing harm. All guidelines relevant to this report recommend the use of prescription monitoring programs; the rationale for using prescription monitoring programs varies between guidelines e.g., screening, (adherence) monitoring, risk mitigation, education. There are fewer details, however, about when and how frequently prescribers should review prescription monitoring programs. Evidence to inform the included guidelines was found to range from low-quality (clinical experiences) to high-quality (randomized controlled trials).

The absence of clinical evidence identified in the literature does not allow for conclusions to be drawn about how prescription monitoring programs may affect the safety of patients who are prescribed monitored drugs. Since the recommendations included in the guidelines were derived from a variable quality of evidence, caution should be exercised in their interpretation. Moreover, it is unclear how generalizable the recommendations of the included publications are to the Canadian population or to the Canadian healthcare system as they were all conducted and/or produced in the United States.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including Ovid MEDLINE, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and March 21, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients receiving monitored drugs
Intervention	Electronic submission prescription monitoring programs (e.g., immediate, end-of-day, or weekly submission of prescription data to the database, or access to the database by clinicians for purposes of verifying patient prescription data)
Comparator	Q1: No prescription monitoring program; Standard of care; Other monitoring programs (such as: multiple copy paper prescriptions, hotlines, telefacsimile alerts, etc.)
Outcomes	Q1: Safety (such as: unintended patient consequences, unintended redirection of patient to illicit sources, inadequate therapeutic management [e.g., therapy discontinued without taper, delayed or missed doses, etc], street diversion, dispensing errors, etc.) Q2: Guidelines on appropriate use.
Study Designs	Q1: Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, nonrandomized studies Q2: Evidence-based guidelines

Exclusion Criteria

Citations were excluded if they (i) did not meet the selection criteria outlined in Table 1, (ii) were published prior to 2014, (iii) were already captured in an included systematic review. Guidelines with unclear methodology were also excluded. Since this report focused on safety outcomes, studies that reported exclusively on prescription rate outcomes e.g., quantity opioids and benzodiazepines dispensed, morphine equivalent dose (MME), total opioid volume were excluded.

Critical Appraisal of Individual Studies

The included systematic review was critically appraised by one reviewer using AMSTAR II,[6] and guidelines were assessed with the AGREE II[7] instrument. Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 435 citations were identified in the literature search. Following screening of titles and abstracts, 370 citations were excluded and 65 potentially relevant reports from the electronic search were retrieved for full-text review. Three potentially relevant publications were retrieved through the grey literature search. Of these 68 potentially relevant articles, 64 were excluded for various reasons, and four met the eligibility criteria for inclusion in this report. These comprised one systematic review and three evidence-based guidelines. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[8] flowchart of the study selection.

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Study Design

One systematic review[9] and three guidelines were included in this review.[10-12]

The included systematic review was published in 2018, and included four guidelines published between January 2010 and August 2017 (three of which are relevant to this report).[9]

Each evidence-based guideline is commissioned by a different group: American Society of Interventional Pain Physicians (ASIPP),[12] Department of Veterans Affairs/Department of Defense (VA/DoD),[11] and the Centers for Disease Control and Prevention (CDC).[10] The 2017 ASIPP guideline focuses on synthesizing the available evidence describing the comparative effectiveness and safety, adverse effects of chronic opioid therapy in the treatment of chronic non-cancer pain, and provides a rationale and systematic approach to their prescription.[12] The working group assesses and makes recommendations based on benefits and harms, using a qualitative approach to grading of evidence modified from Manchikanti and colleagues[13] and the National Guideline Clearinghouse Extent Adherence to Trustworthy Standards (NEATS) instrument. The included recommendations relevant to this report are based on varying qualities of evidence (range: moderate to strong; see Table for definitions).[12] The 2017 VA/DoD guideline focuses on improving patients' health and well-being by providing evidence-based guidance to providers who are taking care of patients on or being considered for long-term opioid therapy.[11] This guideline uses GRADE to assess evidence quality. The included recommendations relevant to this report are based on strong evidence, classified in the guideline as 'new-replaced'. The new-replaced category suggests the recommendation is from previous the clinical practice guideline, carried over to the updated guideline, but is modified following review of the evidence.[11] The 2016 CDC guideline focuses on providing recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.[10] This guideline uses the CDC Advisory Committee on Immunization Practices GRADE to assess evidence quality. The included recommendations relevant to this report are based on level four evidence, defined as clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations (range of evidence: 1-4 i.e., lowest quality category of evidence).[10] All three included guidelines are externally peer-reviewed.[10-12]

Country of Origin

The four included publications all originated from the United States.[9-12]

Patient Population

The systematic review of guidelines was interested in adults requiring opioids to manage their acute non-cancer pain.[9] The three guidelines aim to inform health practitioners e.g., general/primary care clinicians, specialists.[10-12]

Interventions and Comparators

Pertinent to this report, the systematic review of guidelines included PDMPs as the intervention; comparators are not generally relevant for guidelines.[9]

Relevant to this report, all included guidelines reviewed PDMPs e.g., risk mitigation strategies for individuals who are on long-term opioid therapy, monitoring for adherence and side effects.[10-12]

Outcomes

The systematic review was interested in identifying best practices in screening/ monitoring/education prior to prescribing an opioid and/or during treatment.[9]

Relevant outcomes from the guidelines include drug abuse (prescription or illicit),[12] high opioid doses and dangerous combinations,[10] doctor shopping,[12] emergency room visits,[12] drug overdoses,[12] and deaths (i.e., fatal overdoses).[11,12]

A detailed summary of the characteristics of included publications are provided in Appendix 2.

Summary of Critical Appraisal

Systematic Review

The systematic review[9] generally met the criteria of the AMSTAR II checklist.[6] The review published a predefined protocol, described their research question and inclusion criteria in adequate detail, and searched for literature using multiple methods e.g., academic databases, clinical trial registries.[9] For transparency, the authors provided select keywords used for the literature search.[9] These strengths increase the reproducibility of the findings. In the systematic review protocol, the investigators reported that guideline selection and data extraction would be performed by four reviewers independently; however, the report of findings did not mention how guideline selection and data abstraction were performed.[9] A list of excluded studies/guidelines was not provided.[9] The review did assess the quality of each included guideline [9] using a validated instrument i.e., AGREE-II. The investigators acknowledged their funding sources and reported how their funding sources were involved in the conduct of the review, when applicable.[9]

Guidelines

The included guidelines[10-12] meet most criteria of the AGREE II[7] tool. Strengths of the guidelines include the fact that the overall objectives and populations to whom the guidelines apply are specifically described; guideline development groups include individuals from relevant professional groups; the target users of the guidelines are defined; systematic methods are used to search for evidence; the criteria for selecting the evidence, the strengths and limitations of the body of evidence, and the methods for formulating the recommendations are clearly described; there is an explicit link between the recommendations and the supporting evidence; the guidelines are externally reviewed by experts prior to its publication; a procedure for updating the guidelines is provided; the different options for management of the condition or health issue are clearly presented; and key recommendations are easily identifiable.[10-12] These features may increase the reliability of the recommendations as they demonstrate sound methodology and make these guidelines less prone to biases.

There were a few features of individual guidelines that are unclear. For instance, one guideline's recommendations were found to be ambiguous.[11] Specifically, it would be useful for the target user i.e., health practitioner to know how frequently the PDMP should be reviewed. For the same guideline, it is unclear about the potential resource implications of applying the recommendations and if the views of the funding body have influenced the

content.[11] For another guideline, it is unclear whether the guideline provides advice or tools on how the recommendations can be put into practice, the potential resource implications of applying the recommendations, and does not present monitoring or auditing criteria.[12] In addition, the funding source for one guideline is involved in the entire guideline process (development to approval for submission), and it is unclear whether the competing interests of guideline development group members have been adequately addressed.[10]

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Guidelines

Three guidelines included in the systematic review recommend checking PDMPs as part of best practices in screening/ monitoring/ education to occur prior to prescribing an opioid and/or during treatment. One guideline included in the review stated that the PDMP should be reviewed before prescribing opioids. All evidence regarding these recommendations was based on expert consensus.[9]

One of the evidence-based guidelines recommends using PDMPs to provide data on patterns of prescription use to potentially reduce prescription drug abuse and doctor shopping; the guideline suggests PDMPs may reduce emergency room visits, drug overdoses, and deaths.[12] Adherence monitoring of PDMPs is described as essential to the identification of those patients who are not compliant or are abusing prescription or illicit drugs. The guideline provides a flow chart for monitoring patients based on their risk and suggests checking the PDMP four times per year for low risk patients, and four to six times per year for medium and high risk patients. These recommendations were developed using evidence of variable quality, ranging from a moderate to strong quality of evidence (see Table for criteria).[12] Another guideline recommends checking state PDMPs as a standard opioid risk mitigation strategy upon the initiation of long-term opioid therapy.[11] This recommendation was developed using a strong quality of evidence.[11] The third guideline recommends that clinicians check the patient's history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving opioid dosages or dangerous combinations that put the individual at high risk for overdose.[10] This guideline also suggests that "clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every three months"[10] (p.13). Recommendations from this guideline were derived using a lower quality of evidence i.e., clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.[10]

Appendix 4 presents a table of the main study findings and authors' conclusions.

Limitations

The primary limitations to the body of evidence regarding the safety and use of PMPs are the lack of clinical evidence describing safety outcomes, the lack of studies investigating all prescription monitored drugs, and the paucity of evidence derived from the Canadian population/PMPs.

Though one systematic review was included in the report, it specifically examined guidelines. Therefore, no clinical evidence on the safety of PMPs was found. Moreover, the

recommendations provided in the guidelines are based on variable levels of evidence, from clinical experiences to randomized controlled trials.

The included publications focused on opioid prescriptions. Future research in Canada may benefit from widening the inclusion criteria to investigate all prescription monitored drugs listed under the *Controlled Drugs and Substances Act* (e.g., opioids, methylphenidate, benzodiazepines, and barbiturates).

All of the included publications were conducted and/or produced in the United States. Therefore, it is unclear how generalizable the recommendations of these included publications are to the Canadian setting, since Canadian laws and health care systems vary from that of the United States.

These limitations warrant the use of caution when interpreting the findings of this report.

Conclusions and Implications for Decision or Policy Making

No relevant clinical studies regarding the safety of PMPs for optimizing medication use and/or preventing harm were identified. Therefore, no conclusions addressing the safety of PMPs can be provided. To reduce uncertainty concerning the safety of PMPs, evidence of high methodological quality describing key safety outcomes is needed, including unintended patient consequences, unintended redirection of patient to illicit sources, inadequate therapeutic management, street diversion, and dispensing errors.

Three evidence-based guidelines and one systematic review of guidelines regarding the use of PMPs for optimizing medication use and preventing harm were identified in the search. Recommendations are derived from studies with a variable quality of evidence, ranging from clinical experiences to randomized controlled trials. Across all included guidelines, it is recommended that health practitioners review the PMPs, but the frequency of reviewing PMPs is less clear.

Caution is advised in interpreting the information presented in this report due to the absence of clinical evidence, studies investigating all prescription monitored drugs, as well as the paucity of evidence derived from the Canadian population and Canadian PMPs. Comparative studies evaluating the impact of PMPs on safety outcomes in Canada would enhance the utility of the evidence and better inform a determination concerning the safety of PMPs in the care pathway for patients receiving prescription monitored drugs.

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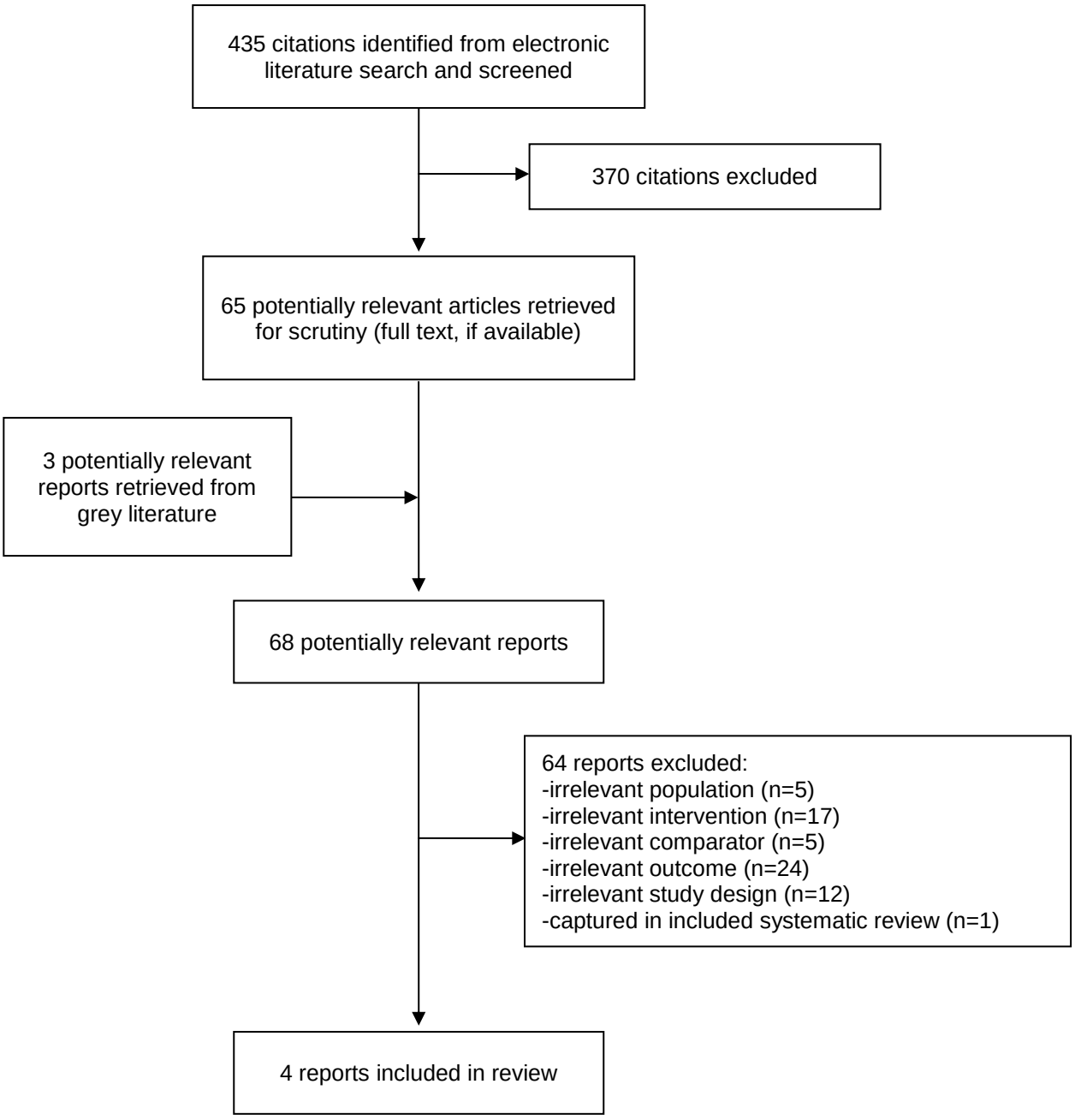
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Review

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Eligibility Criteria, Population	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Herzig, 2018,[9] US	3 guidelines relevant to this report (of a total of 4 guidelines included in the systematic review)	Guidelines on prescribing of opioids published from January 2010 to August 2017 that address acute, non–cancer pain management among adults. Patient group: Adults requiring opioids to manage their acute, non–cancer pain	Intervention: PDMPs Comparator: Not applicable for guidelines	Best practices in screening/monitoring/ education to occur prior to prescribing an opioid and/or during treatment Follow-up: Not applicable

PDMP = prescription drug monitoring program

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
ASIPP Guidelines, 2017[12]*						
Health practitioners	Initial steps of opioid therapy, monitoring for adherence and side effects, including PDMPs	Drug abuse (prescription or illicit), doctor shopping, emergency room visits, drug overdoses, deaths (i.e., fatal overdoses)	Developed objectives and key questions Followed IOM standards and NEATS instrument Utilized a Guideline Development Group (panel of experts from various specialties and groups) Sought patient and public perspectives to form guidelines Reviewed and synthesized literature	Qualitative approach to grading of evidence (Modified from: Manchikanti et al.[13]) and National Guideline Clearinghouse Extent Adherence to Trustworthy Standards (NEATS) instrument	Working group assessed and made recommendations based on benefits and harms, and the strength of the recommendations	Externally peer-reviewed
VA/DoD, 2017[11]*						
General clinicians and specialists	Risk mitigation strategies for individuals who are on long-term opioid therapy, including PDMPs	Assessing opioid risk mitigation strategies	Formulated and prioritized evidence questions Conducted systematic review to update CPG (search dates: March 2009 to	GRADE	Convened a face-to-face meeting with the CPG Champions and Work Group CPG drafted by the Champions and Work Group sent out for internal and external peer review and comment.	Externally peer-reviewed

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
			December 2016) Conducted focus groups with patients and caregivers		All feedback reviewed, discussed, and considered by the Work Group Modifications made throughout the CPG development process Final version approved by the VA/DoD Evidence-Based Practice Work Group	
CDC, 2016[10]*						
Primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care	PDMPs	Assessing risk and addressing harms of opioid use, including high opioid doses, dangerous combinations Frequency of PDMP review	Updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs Clinical experience and observations	ACIP GRADE	CDC obtained input from external experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee in the development process CDC drafted a set of recommendations CDC sought external peer review by Core expert group, partners from federal agencies, and a Stakeholder Review Group CDC published draft guideline online for public comment Guideline reviewed by Opioid Guideline Workgroup and submitted	Externally peer-reviewed

Table 3: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
					observations to BSC After an iterative process, BSC voted CDC adopt the guideline recommendations once revisions were made based on their feedback	

* Features described in the table are relevant to this summary with critical appraisal report; therefore, the guidelines may have included additional interventions and outcomes that were not applicable for this report.

ACIP = CDC Advisory Committee on Immunization Practices; AHRQ = Agency for Healthcare Research and Quality; ASIPP = American Society of Interventional Pain Physicians; BSC = National Center for Injury Prevention and Control Board of Scientific Counselors; CDC= Centers for Disease Control and Prevention; CPG = clinical practice guidelines; DoD = Department of Defense; GRADE = Grading of Recommendations Assessment, Development and Evaluation; IOM = Institute of Medicine standards; NEATS = National Guideline Clearinghouse Extent Adherence to Trustworthy Standards; PDMP = Prescription Monitoring Drug Program; VA = Department of Veterans Affairs

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Review using AMSTAR 2[6]

Strengths	Limitations
Herzig, 2018[9]	
• Study authors published a systematic review protocol in the PROSPERO database • Research questions clear and inclusion criteria for the review included the components of PICO • Multiple databases, websites of relevant specialty societies, organizations, and international search engines searched • Select keywords provided for the literature search • Reasons for excluding studies provided in flow chart • Included guidelines described in adequate detail • AGREE II instrument used to evaluate the quality of each included guideline • Review authors acknowledged their funding and reported: "*The Society of Hospital Medicine provided administrative and material support for the project, but had no role in the design or execution of the scientific evaluation*." (p.4)	• Protocol published in the PROSPERO database indicated the guideline selection and data extraction were to be performed by four reviewers independently, but the publication did not mention how guideline selection and data extraction were performed • List of excluded guidelines not provided • Sources of funding not reported for the included guidelines

AGREE II = Appraisal of Guidelines for Research and Evaluation II; PICO = Patient/Population, Intervention, Comparator, Outcome; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ROBINS-I = Risk Of Bias In Nonrandomized Studies - of Interventions

Table 5: Strengths and Limitations of Guidelines using AGREE II[7]

Item	Guideline		
	ASIPP, 2017[12]	VA/DoD, 2017[11]	CDC, 2016[10]
Domain 1: Scope and Purpose			
1. The overall objective(s) of the guideline is (are) specifically described.	✓	✓	✓
2. The health question(s) covered by the guideline is (are) specifically described.	✓	✓	✓
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	✓	✓	✓
Domain 2: Stakeholder Involvement			
4. The guideline development group includes individuals from all relevant professional groups.	✓	✓	✓
5. The views and preferences of the target population (patients, public, etc.) have been sought.	✓	✓	✓
6. The target users of the guideline are clearly defined.	✓	✓	✓
Domain 3: Rigour of Development			
7. Systematic methods were used to search for evidence.	✓	✓	✓
8. The criteria for selecting the evidence are clearly described.	✓	✓	✓
9. The strengths and limitations of the body of evidence are clearly described.	✓	✓	✓
10. The methods for formulating the recommendations are clearly described.	✓	✓	✓
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	✓	✓	✓
12. There is an explicit link between the recommendations and the supporting evidence.	✓	✓	✓
13. The guideline has been externally reviewed by experts prior to its publication.	✓	✓	✓
14. A procedure for updating the guideline is provided.	✓	✓	✓
Domain 4: Clarity of Presentation			
15. The recommendations are specific and unambiguous.	✓	X	✓
16. The different options for management of the condition or health issue are clearly presented.	✓	✓	✓
17. Key recommendations are easily identifiable.	✓	✓	✓
Domain 5: Applicability			
18. The guideline describes facilitators and barriers to its application.	✓	✓	✓
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	unclear	✓	✓
20. The potential resource implications of applying the recommendations	unclear	unclear	✓

Item	Guideline		
	ASIPP, 2017[12]	VA/DoD, 2017[11]	CDC, 2016[10]
have been considered.			
21. The guideline presents monitoring and/or auditing criteria.	X	✓	✓
Domain 6: Editorial Independence			
22. The views of the funding body have not influenced the content of the guideline.	✓	unclear	X
23. Competing interests of guideline development group members have been recorded and addressed.	✓	✓	unclear

ASIPP = American Society of Interventional Pain Physicians; CDC= Centers for Disease Control and Prevention; DoD = Department of Defense; VA = Department of Veterans Affairs

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings for Included Systematic Review

Main Study Findings	Authors' Conclusion
Herzig, 2018[9]	
"Best practices in screening/monitoring/education to occur prior to prescribing an opioid and/or during treatment: Three guidelines recommended checking PDMPs, all based on expert consensus (16–18). Only the WSAMDG guideline offered guidance as to the optimal timing to check the PDMP in this setting, specifically recommending to check before prescribing opioids (17)." (p.5)	*"Most guidelines recommended restricting opioid use to severe pain or pain that has not responded to non-opioid therapy, checking PDMPs, using the lowest effective dose, and using short-acting opioids and/or avoiding use of long-acting/extended-release opioids for acute pain."* (p.7)

PDMPs = prescription drug monitoring programs; ROB = risk of bias; WSAMDG = Washington State Agency Medical Directors' Group

Table 7: Summary of Recommendations for Included Guidelines

Recommendations	Strength of Evidence and Recommendations
ASIPP, 2017[12]	
"PDMPs must be implemented as they provide data on patterns of prescription usage, potentially reducing prescription drug abuse or doctor shopping. PDMPs may reduce emergency room visits, drug overdoses, or deaths." (p.S49) *"In order to reduce prescription drug abuse and doctor shopping, adherence monitoring by UDT and PDMPs provide evidence that is essential to the identification of those patients who are non-compliant or abusing prescription drugs or illicit drugs."* (p. S57 and S62) Monitoring based on risk stratification*** indicates: • Low risk patients: check PDMP 4 times per year • Medium risk patients: check PDMP 4-6 times per year • High risk patients: check PDMP 4-6 times per year	Evidence: Level I-II Strength of recommendation: Moderate* to strong**
VA/DoD, 2017[11]	
"We recommend implementing risk mitigation strategies upon initiation of long-term opioid therapy, starting with an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. The strategies and their frequency should be commensurate with risk factors and include: • *Ongoing, random urine drug testing (including appropriate confirmatory testing)* • *Checking state prescription drug monitoring programs* • *Monitoring for overdose potential and suicidality* • *Providing overdose education* • *Prescribing of naloxone rescue and accompanying education"* (p. 8, 46, 129) *"Clinicians should use standard opioid risk mitigation strategies such as checking the PDMPs."* (p.36)	Strength of evidence: Strong recommendation in favour of PDMPs Evidence reviewed: Yes Category: new-replaced (i.e., recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence)

Table 7: Summary of Recommendations for Included Guidelines

Recommendations	Strength of Evidence and Recommendations
CDC, 2016[10]	
"Clinicians should review the patient's history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months." (p. 13)	Recommendation category: A (i.e., Applies to all persons; most patients should receive the recommended course of action) Evidence type: 4 (i.e., Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.)

* Moderate = Evidence obtained from at least one relevant high quality randomized controlled trial or multiple relevant moderate or low quality randomized controlled trials or Evidence obtained from at least 2 high quality relevant observational studies or large case series for assessment of preventive measures, adverse consequences, and effectiveness of other measures[12]

** Strong = Evidence obtained from multiple relevant high quality randomized controlled trials for effectiveness or Evidence obtained from multiple relevant high quality observational studies or large case series for assessment of preventive measures, adverse consequences, effectiveness of other measures[12]

*** Please refer to page S51 and S52 of report for definitions of low, medium, and high risk.
ASIPP = American Society of Interventional Pain Physicians; CDC= Centers for Disease Control and Prevention; CPG = clinical practice guideline; DoD = Department of Defense; PDMP = Prescription Drug Monitoring Program; UDT = urine drug testing; VA/DoD = VA = Department of Veterans Affairs

Appendix 5: Additional References of Potential Interest

Previous CADTH reports/presentations on related topics

Opioid prescribing and pain management: Prescription monitoring program overview and the management of acute low back pain. Ottawa (ON): CADTH Tool; 2019 Mar. https://www.cadth.ca/sites/default/files/pdf/Opioid_Prescribing_module.pdf Accessed 2019 Apr 18

Prescribing and dispensing policies to address harms associated with prescription drug buse. Ottawa (ON): CADTH Environmental Scan; 2015 Oct. https://www.cadth.ca/sites/default/files/pdf/ES0291_Prescription_Drug_Abuse_e.pdf Accessed 2019 Apr 18

Narcotics, benzodiazepines, stimulants, and gabapentin: Policies, initiatives, and practices across Canada, 2014. Ottawa (ON): CADTH Environmental Scan; 2014 Oct. https://www.cadth.ca/narcotics-benzodiazepines-stimulants-and-gabapentin-policies-initiatives-and-practices-across-canada Accessed Apr 18

Reports and policy statements

Public policy statement on prescription drug monitoring programs (PDMPs). Rockville (MD): American Society of Addiction Medicine; 2018. https://www.asam.org/docs/default-source/public-policy-statements/2018-statement-on-pdmpsf406229472bc604ca5b7ff000030b21a.pdf?sfvrsn=63ba42c2_0 Accessed 2019 Apr 18

Alexander GC, Frattaroli S, Gielen AC, eds. The Prescription opioid epidemic: An evidence-based approach. Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland: 2015. https://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/research/prescriptionopioids/JHSPH_OPIOID_EPIDEMIC_REPORT.pdf Accessed 2019 April 18

Ineligible, nonrandomized study of potential interest

Deyo RA, Hallvik SE, Hildebran C, et al. Association between initial opioid prescribing patterns and subsequent long-term use among opioid-naive patients: A statewide retrospective cohort study. J Gen Intern Med. 2017 01;32(1):21-27.

Reviews that do not fulfill eligibility criteria and/or nonsystematic reviews

Ponnapalli A, Grando A, Murcko A, Wertheim P. Systematic literature review of prescription drug monitoring programs. In: AMIA Annual Symposium Proceedings 2018; Vol. 2018, p. 1478. American Medical Informatics Association.

Fink DS, Schleimer JP, Sarvet A, et al. Association between prescription drug monitoring programs and nonfatal and fatal drug overdoses: A Systematic review. Ann Intern Med. 2018 Jun 05;168(11):783-790.

Finley EP, Garcia A, Rosen K, McGeary D, Pugh MJ, Potter JS. Evaluating the impact of prescription drug monitoring program implementation: a scoping review. BMC Health Serv Res. 2017 Jun 20;17(1):420.

Fischer B. Prescription opioid use, harms and interventions in Canada: a review update of new developments and findings since 2010. Pain physician. 2015 Jul;18:E605-14.

Haegerich TM, Paulozzi LJ, Manns BJ, Jones CM. What we know, and don't know, about the impact of state policy and systems-level interventions on prescription drug overdose. Drug and alcohol dependence. 2014 Dec 1;145:34-47.

Furlan AD, MacDougall P, Pellerin D, et al. Overview of four prescription monitoring/review programs in Canada. Pain Research & Management. 2014 Mar-Apr;19(2):102-106.