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THE STATE of ALASKA
GOVERNOR BILL WALKER

Department of Commerce, Community, and Economic Development

DIVISION OF CORPORATIONS, BUSINESS AND PROFESSIONAL LICENSING

ALASKA PRESCRIPTION DRUG MONITORING PROGRAM
Alaska Board of Pharmacy
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Anchorage, Alaska 99501 3567
Main: 907.269.8404
Fax: 907.269.6003
akpdmp@alaska.gov

TO: 29th Alaska State Legislature

FROM: Alaska Board of Pharmacy

CC: Kevin Meyer, Senate President

Mike Chenault, House Speaker

DATE: February 11, 2016

RE: 2016 Alaska Prescription Drug Monitoring Program Report

The controlled substance prescription database was created by Senate Bill 196 and established within the Board of Pharmacy (Board). Statute states:

Alaska Statute 17.30.200. Controlled substance prescription database. (a) The controlled substance prescription database is established in the Board of Pharmacy. The purpose of the database is to contain data as described in this section regarding every prescription for a schedule IA, IIA, IIIA, IVA, or VA controlled substance under state law or a schedule I, II, III, IV, or V controlled substance under federal law dispensed in the state to a person other than those administered to a patient at a health care facility. The Department of Commerce, Community, and Economic Development shall assist the board and provide necessary staff and equipment to implement this section.

The database operates under the name of "Alaska Prescription Drug Monitoring Program" (AKPDMP) and is a statewide electronic database that gathers information from in-state and out-of-state pharmacies (or dispensers) on dispensed prescriptions for controlled substances. AKPDMP's purpose is to improve patient care by providing prescribers and pharmacists with a controlled substance dispensing history for their patients. An additional goal is to reduce drug diversion and inappropriate use of controlled substances by assisting in the investigation of specific cases.

AS 17.30.200 (6)(g) requires that the Board notify the Legislature if federal funding fails to pay for all or part of the costs of the database. The federal funding for the AKPDMP ended on August 31, 2013, and the board submitted notification in accordance with statute.

During FY2015, the Division of Corporations, Business and Professional Licensing (Division), Board of Pharmacy (Board), and the Department of Health and Social Services (DHSS) collaborated to compete for a federal grant. They were successful, and the grant is currently funding the AKPDMP. This is accomplished via a Reimbursable Services Agreement (RSA) from the Department of Health and Social Services who was the recipient of the grant. The grant funds the program from FY2016 to FY2021; however, after that time, new funding will need to be obtained.

In a separate collaboration, the Board and Division have partnered with DHSS to pursue an additional federal grant to continue funding for the program, augmenting the deliverables to include staffing and a more robust role in the state's opioid control initiatives.

The Board requests that the Legislature be aware of the ongoing need for sustainable funding that is in line with the legislative intent of Senator Lyda Green.

It is the intent of the Legislature that the Alaska Prescription Drug Monitoring Program be funded with federal grants and state appropriations. It is not the intent of the Legislature that the professional users of the database absorb the costs of managing this public program through their license fees or other fee structure.[1]

The AKPDMP began using a new vendor to provide prescription monitoring services for Alaska. The new vendor was able to provide the same services for $8,500 less annually than the State previously paid for the service, recognizing a $42.5K cost savings over the five year life of the contract. The Division chose to use the PMP AWARxE prescription monitoring program software, maintained by Appriss. More information about Appriss and PMP AWARxE can be accessed by visiting http://www.appriss.com/pmpaware.html.

APPRISS began collecting data from dispensers on January 21, 2016, and began allowing practitioners and pharmacists to obtain AKPDMP reports on patients under their care on January 25, 2016.

To maximize the AKPDMP for future availability and the effective use of data among the widest range of appropriate end users, several recommended changes have been identified by the board:

- Enact legislation to maintain sufficient funding over time
- Delegate access[2]
- Transmit unsolicited reports and alerts to *appropriate* users
- Improve data timeliness and access; increase reporting to weekly
- Provide enhanced education, enrollment, and use of AKPDMP to all users or data requestors.
- Streamline certification and enrollment processing
- Optimize reporting to fit user needs
- Publicize use and impact of AKPDMP via websites, presentations, and reports
- Incorporating AKPDMP data within health information exchanges, electronic health records and pharmacy dispensing systems.

Thank you for your consideration of these ideas as you evaluate how to increase the effectiveness of the program and improve public safety. The following pages provide data on the number of registered users of the AKPDMP, reports, reasons for requested reports, and patients receiving prescriptions.

If you have any questions regarding this data or the suggested areas for improvement, please contact the Program Manager Brian Howes at 907-269-8404 / akpdmp@alaska.gov.

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[1] http://www.legis.state.ak.us/basis/get_fin_page.asp?session=25&bill=SB196&grn=1785&chs=S

[2] Allowing prescribers to delegate access to AKPDMP records by office staff (sometimes called "sub-accounts"), may help increase utilization of AKPDMP data to detect patients at risk and improve prescribing

Registered Users

Registered Users	2014	2015	Change
Prescribers	923	1,122	22% ↑
Dispensers	343	442	29% ↑
Total	**1,266**	**1,564**	**24% ↑**

Licensed Pharmacies

Pharmacies	2014	2015	Change
Drug Room	33	36	9% ↑
Out of State Pharmacies	500	583	17% ↑
Pharmacy	132	138	5% ↑
Remote Pharmacy	1	1	0% ↔
Pharmacy Certification(s)[3]	120	143	19% ↑

Solicited Reports

Providing AKPDMP data, over a given date range, to an authorized user based upon their request for the information is called a solicited report. The reports can be produced through an automated online system; bodies that directly receive these reports are registered prescribers and dispensers. Upon certification of an open investigation and the submittal of a *search warrant, subpoena, or court order,* this information may be released to law enforcement and/or regulatory boards. Finally, a patient may also request a report of his or her own prescription information, upon payment of a $10 fee.

Number of Solicited Reports	2014	2015	Change
Pharmacists	38,615	43,831	14% ↑
Prescribers	45,145	69,282	53% ↑
Law Enforcement/Regulatory	10	8	-20% ↓
Total	**82,760**	**112,671**	**36% ↑**

Reason for Request *(Law Enforcement/Regulatory)*	2014	2015	Change
Forged Prescription	4	1	-75% ↓
Stolen Prescription	2	0	-100% ↓
Doctor Shopper	1	3	200% ↑
Drug Diversion	2	0	-100% ↓
Addiction	0	0	0% ↔
Other	1	4	300% ↑
Total	**10**	**8**	**-20% ↓**

Unsolicited Reports

The purpose of an unsolicited report is to provide prescribers and pharmacists with additional information that they may choose to use in their clinical decision-making. Unsolicited reports typically uses a threshold as a reference for sending such a report, e.g. number of prescribers from whom a patient has obtained a controlled substance prescription, and the number of pharmacies that have dispensed the prescriptions, in a specified period of time, to a patient.

[3] Pharmacies certifying (yearly) that they do not dispense controlled substances and so they do not report to the AKPDMP; it contains an agreement that they will begin reporting if their business practice changes.

The Board has established its threshold (or reference) as *a patient who obtained a controlled substance from five (5) prescribers and five (5) pharmacies in a three (3) month period.* [4]

The Board is aware that the Department of Law has expressed some concerns regarding the Board's ability to send out this unsolicited report and does support a change in the statutory authority to allow it. Proactive reporting of AKPDMP data to prescribers and pharmacists can serve to inform them of possible questionable activity and patients at risk, increase their awareness and utilization of the AKPDMP, and contribute to lower rates of questionable activity as measured by the subsequent number of individuals meeting a threshold and prescriptions obtained by suspected "doctor shoppers".[5]

Number of patients receiving prescription(s)	**2014**	**2015**	**Change**
CII	134,524	202,141	50% ↑
CII, III	154,831	238,581	54% ↑
CII, III and IV	243,546	429,185	76% ↑
Total	**534,915**	**869,907**	**63% ↑**
Number of patients exceeding 5/5 threshold			
CII	313	61	-81% ↓
CII, III	365	71	-81% ↓
CII, III and IV	525	103	-80% ↓
Total	**1203**	**235**	**-80% ↓**
Number of patients exceeding 10/10 threshold			
CII	4	1	-75% ↓
CII, III	4	1	-75% ↓
CII, III and IV	5	1	-80% ↓
Total	**13**	**3**	**-77% ↓**

Morphine Equivalent Dosage (MED) or Minimum Morphine Equivalent (MME)

Individuals using opioid analgesics for extended periods of time are at increased risk of dependency, overdose, and death. Patients using opioids in excess of 100mg of a total daily Morphine Equivalent Dosage (MED) are at significant risk of overdose; however, even utilization at lower doses presents risk to the patient.(*Page 1, Alaska Medicaid Prior Authorization Criteria*)[6] "An MED is a numerical standard against which most opioids can be compared, yielding an apples-to-apples comparison of each medication's potency. Although it's easy to presume that 10 mg of medication A are equal to 10 mg of medication B, differences in how opioid medications work in the body prohibits this sort of comparison, thus the need for calculating the MED of each. It is not about a medications efficacy or how well it works, but about its relative potency." (*Page 1, Shining a Light on MEDs / www.helioscomp.com*)[7]

Distribution of painkillers greater than 100-mg (MED), per day	**2014**	**2015**	**Change**
Adult	117	89	-24% ↓
Youth[8]	2	1	-50% ↓

[4] 5/5 or 10/10
[5] Doctor shopping is defined as seeing multiple treatment providers, either during a single illness episode or to procure prescription medications illicitly
[6] http://dhss.alaska.gov/dhcs/Documents/pharmacy/pdfs/Extended-Release-Opioids-PA_201504_APPROVED.pdf
[7] http://helioscomp.com/docs/default-source/White-Paper/cln14-15209_msd-white_paper_final.pdf?sfvrsn=8
[8] Youth - patients that are under 18 years of age as of the date the prescription was filled.

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Department of Commerce, Community, and Economic Development

DIVISION OF CORPORATIONS, BUSINESS AND PROFESSIONAL LICENSING

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March 22, 2016

The Honorable Pete Kelly
Alaska State Senate
Alaska State Capitol, Room 518
Juneau, AK 99801

Dear Senator Kelly,

In response to several anticipated questions regarding the Prescription Drug Monitoring Program (PDMP) you requested that the Division of Corporations, Business, and Professional Licensing provide answers on the function and specifics of the program. Please find those questions and answers below.

How secure is the PDMP and the information in it? What laws protect the information in the database from being shared?

Appriss facilitates the development, implementation, and oversight of all activities to be compliant with the Criminal Justice Security Policy (CJIS), Payment Card Industry (PCI) and HIPAA Security Regulations, and any other security and compliance frameworks. The database is compatible with DCCED's Information Security and Privacy Policy.

Statutorily:

- ***AS 17.30.200*** (d) the database and the information contained within the database are confidential, are not public records, and are not subject to public disclosure.
- Penalties for improper use or access

- ***AS 17.30.200*** (l) A person with authority to access the database under (d) of this section who knowingly:
- accesses information in the database beyond the scope of the person's authority commits a class A misdemeanor;
- accesses information in the database and recklessly discloses that information to a person not entitled to access or to receive the information commits a class C felony;
- allows another person who is not authorized to access the database to access the database commits a class C felony;
- without authority to access the database under (d) of this section who knowingly accesses the database or knowingly receives information that the person is not authorized to receive under (d) of this section from another person commits a class C felony.

How can we protect access and from it being expanded down the road? Does the Board of Pharmacy provide recommendations, or just the Controlled Substances Advisory Council?

Providing easier access without proper authentication, to "ease the burden" of registration will not secure the data. Proper authentication (or identification) of a user is essential to protect the patient's data. All permissions assigned by that user e.g. delegate accounts, must be enforced through of access penalties stated earlier for both the user and delegate. Licensee's will also be referred to their respective Board for discipline, if a violation is determined.

A Board of Pharmacy member, CJ Kim, RPh was assigned by the Board to the Controlled Substance Advisory Committee and was a contributor to the White Paper submitted to the Governor.

Regulations:

- 12 AAC 52.860. Conditions for access to and use of database. (a) A dispenser registered under 12 AAC 52.855(a) to receive information from the controlled substance prescription database may not
- share user account information, login names, or passwords with any person, regardless of whether that person is also an authorized user of the controlled substance prescription database;
- permit any authorized person to use the practitioner's or pharmacist's user account, account name, or password in order to access the controlled substance prescription database regarding any person or for any purpose.
- (b) Information obtained from the controlled substance prescription database shall be kept confidential in accordance with the confidentiality requirements of P.L. 104-191 (Health Insurance Portability and Accountability Act of 1996 (HIPAA)), 42 C.F.R. Part 2, and 45 C.F.R. Parts 160, 162, and 164.

Is it possible to get a screenshot of a blank entry page for members?

Inputs are normally processed through a dispensers software, that generates a file with the data required and then uploaded to the vendor. A Paper Universal Claim Form (UCF) (shown on the following page) shows the inputs required for submitting dispensed controlled substances. This form also shows how a veterinarian would provide data to the database, to identify the record as an animal prescription.

An online version is available for those that dispense infrequently – the dispenser logs on, fill out the UCF and the data is submitted electronically.

Thank you, please let me know if you have any further questions.

Sincerely,

Janey Hovenden
Director

First Name - Animal's name or species
Last Name - Owner's Last Name
DOB - Approximate
Gender - Animal gender
Address - Owner's address

ALASKA PRESCRIPTION DRUG MONITORING PROGRAM
UNIVERSAL CLAIM FORM

The State of Alaska now requires that ALL Prescriptions for Schedule II-V Controlled Substance and designated drugs of concern be reported to a data repository managed by the Alaska Board of Pharmacy

Fax: (888) 288-0337	**Fax or Mail to**	**391 Industry Dr**
Phone: (800) 225-6998	**Health Information Designs**	**Auburn, AL 36832**

PATIENT INFORMATION

First Name _____ MI ____ Last Name _____
Identification Number _____

Identification Number Identifier: (Optional) ☐ *Military ID* ☐ *State Issued ID* ☐ *Unique System ID* ☐ *Passport ID* ☐ *Driver's License ID* ☐ *SSN* ☐ *Tribal ID* ☐ *Other*

DOB ____/____/_____ Gender ☐ M ☐ F ☐ Unknown

Address _____ City _____ State ____ ZIP _____

DISPENSER INFORMATION

Dispenser Name _____ DEA _____
Phone # (_____)_____-_____ Fax # (_____)_____-_____
Address _____ City _____ State ____ Zip _____

PRESCRIPTION INFORMATION

Prescription # _____ Reporting Status ☐ New Record ☐ Revise ☐ Void
NDC ☐☐☐☐☐ - ☐☐☐☐ - ☐☐ Drug Name Strength) _____
Quantity Dispensed _____ Days Supply _____ Refill # _____
Date Written ____/____/_____ Date Filled ____/____/_____ Refills Authorized _____
Prescriber Name _____ DEA _____ NPI _____
Prescriber Phone # (_____)_____-_____ Prescriber Fax # (_____)_____-_____
Classification Code for Payment Type ☐ Private Pay ☐ Medicaid ☐ Medicare ☐ Commercial Insurance ☐ Military Installations/VA ☐ Workers' Compensation ☐ Indian Nations ☐ Other

Prescription # _____ Reporting Status ☐ New Record ☐ Revise ☐ Void
NDC ☐☐☐☐☐ - ☐☐☐☐ - ☐☐ Drug Name (Strength) _____
Quantity Dispensed _____ Days Supply _____ Refill # _____
Date Written ____/____/_____ Date Filled ____/____/_____ Refills Authorized _____
Prescriber Name _____ DEA _____ NPI _____
Prescriber Phone # (_____)_____-_____ Prescriber Fax # (_____)_____-_____
Classification Code for Payment Type ☐ Private Pay ☐ Medicaid ☐ Medicare ☐ Commercial Insurance ☐ Military Installations/VA ☐ Workers' Compensation ☐ Indian Nations ☐ Other

Prescription # _____ Reporting Status ☐ New Record ☐ Revise ☐ Void
NDC ☐☐☐☐☐ - ☐☐☐☐ - ☐☐ Drug Name (Strength) _____
Quantity Dispensed _____ Days Supply _____ Refill # _____
Date Written ____/____/_____ Date Filled ____/____/_____ Refills Authorized _____
Prescriber Name _____ DEA _____ NPI _____
Prescriber Phone # (_____)_____-_____ Prescriber Fax # (_____)_____-_____
Classification Code for Payment Type ☐ Private Pay ☐ Medicaid ☐ Medicare ☐ Commercial Insurance ☐ Military Installations/VA ☐ Workers' Compensation ☐ Indian Nations ☐ Other

PDMP CENTER OF EXCELLENCE Brandeis University The Heller School FOR SOCIAL POLICY AND MANAGEMENT

Prescription Drug Monitoring Program Center of Excellence at Brandeis

Briefing on PDMP Effectiveness

Updated September 2014

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BJA Bureau of Justice Assistance U.S. Department of Justice

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Briefing on PDMP Effectiveness

SUMMARY

Evidence continues to accumulate that prescription drug monitoring programs (PDMPs) are effective in improving clinical decision-making, reducing doctor shopping and diversion of controlled substances, and assisting in other efforts to curb the prescription drug abuse epidemic. This briefing was first released in March, 2012 with 35 references; this is the third revision, with over 60 references.

The Prescription Drug Abuse Epidemic

Addiction, overdoses and deaths involving non-medical prescription drug use, especially narcotic pain relievers, have risen dramatically over the last decade. In 2010, drug-related poisonings were the leading cause of death due to unintentional injuries in the United States. The number of overdose deaths involving prescription opioids has more than tripled since 1999; in 2010 these deaths were greater than those involving heroin and cocaine combined.[1] A recent study estimated that in 2006 the total cost in the United States of nonmedical use of prescription opioids was $53.4 billion.[2] More information regarding the epidemic is available on the PDMP Center of Excellence website.[3]

The Essential Role of Prescription Drug Monitoring Programs

PDMPs collect data from pharmacies on dispensed controlled substance prescriptions and make it available to authorized users, often by means of a secure, electronically accessible database. As of July 2014, 49 states and one territory had passed legislation authorizing a PDMP, and 48 states had an operating PDMP. Research and accumulated experience strongly suggest that PDMPs serve essential functions in combating the prescription drug abuse epidemic.[4, 5,6,7, 8] They can help identify major sources of prescription drug diversion such as prescription fraud, forgeries, doctor shopping[9] and improper prescribing and dispensing. PDMPs are also important resources for practitioners and third party payers, giving them information on patients' use of controlled substances that is crucial for providing good medical care and ensuring patient safety. A prospective cost-benefit analysis prior to the launch of the Wisconsin PDMP suggested that the economic benefits produced by the program would far exceed the costs of operation, producing savings for the state in health care costs, lost productivity, and reduced drug diversion investigation times in excess of 10 million dollars annually.[10] There are recent indications that prescription drug overdose deaths are declining in some jurisdictions, for instance Florida and Kentucky, likely due in part to the promulgation and increased use of PDMPs.[11] More information on PDMPs is available on the PDMP Training and Technical Assistance website.[12]

Listed below are a selection of research studies, evaluations, surveys, reports and data[1] suggesting that PDMPs are effective in improving medical care; reducing doctor shopping, inappropriate prescribing, drug diversion and prescription fraud; and assisting in drug investigations. Such outcomes can contribute to lowering rates of addiction, overdose and death associated with misuse of prescription drugs, thus reducing the health care and public safety costs attributable to such misuse. As PDMPs continue to mature and adopt evidence-based best practices, their effectiveness is likely to increase. Future revisions of this briefing will incorporate additional findings on PDMP effectiveness as they come to light.

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[1] The studies and reports mentioned in this briefing should not be considered exhaustive of all information bearing on PDMP effectiveness.

Improving clinical decision-making and patient care

- A study of medical providers in Ohio emergency departments found that 41% of those given PDMP data altered their prescribing for patients receiving multiple simultaneous narcotics prescriptions. Of these providers, 61% prescribed no narcotics or fewer narcotics than originally planned, while 39% prescribed more. [13] Another study found that consulting the PDMP increased physicians' confidence that the controlled substances they prescribed were medically warranted.[14] This indicates that PDMP data can help inform sound clinical decision-making to ensure prescriptions are medically necessary, reducing illicit use of controlled substances.
- Two studies have found that viewing data from a PDMP can help inform and confirm physician judgments concerning a patient's prescription drug seeking behavior, helping to improve prescribing.[15]
- A survey of prescribers in Rhode Island and Connecticut found that those who made use of PDMP data were more likely than non-users to take clinically appropriate action in response to suspected cases of prescription drug abuse or diversion by patients, such as conducting drug screens or referring them to substance abuse treatment.[16]
- The Center for Health Policy at the Fairbanks School of Public Health conducted a survey of medical professionals on awareness and impact of Indiana's PDMP. Of respondents who had changed their prescribing practices in the past year, over 90% reported prescribing fewer controlled substances, and over 50% of these respondents cited viewing PDMP data as the main reason for this change.[17]
- The Oklahoma PDMP conducts an ongoing survey of prescribers; preliminary findings suggest PDMP utilization has an impact on clinical decision-making. Results show that 63% of respondents report that PDMP data has helped them identify patients who were abusing prescription medications, and 64% said data helped identify patients who were doctor shopping. The survey also found that based on a PDMP report, 21% of prescribers referred patient(s) to treatment, 21% to a mental health professional, 64% to a pain management specialist, and 25% to law enforcement; 71% reported changing the type of controlled substance or refusing to prescribe a controlled substance as a result of viewing PDMP data.[18]
- A survey of prescribers and pharmacists in Oregon found that majorities of respondents thought that use of the PDMP would be very useful in monitoring prescriptions and reducing doctor shopping. Many reported taking clinically relevant action after viewing PDMP data, including talking to the patient to confirm or disconfirm suspicions of doctor shopping, altering prescribing in response to new information, and referring patients to substance abuse treatment or pain management.[19]
- In California, 74% of physician responders to a survey indicated they had changed their prescribing practices to a patient as a result of using PDMP Patient Activity Reports [PARs], and 91% rated the "effectiveness of the PAR in maintaining the care and health of your patient" as good to excellent.[20]
- A 2010 survey of users of Kentucky's PDMP, Kentucky All Schedule Prescription Electronic Reporting (KASPER), found that PDMP reports aided clinical practice, with 70% of respondents judging them "very" or "somewhat" important in helping them decide what drug to prescribe a patient. The survey also found that nearly 90% of prescribers and pharmacists responding to the survey "refused to prescribe or dispense a controlled substance based on the information contained in a KASPER report." [21]

- An impact evaluation of the Maine PDMP found that 97% of prescribers and pharmacies responding to a survey found the PDMP to be useful in monitoring prescriptions and controlling doctor shopping.[22]
- A recent survey of Massachusetts prescribers receiving unsolicited PDMP reports on possible doctor shoppers among their patients found that only 8.4% of respondents knew about all or nearly all the other prescribers for patients reported on. This indicates that proactive reporting of PDMP data alerts prescribers about possible doctor shopping, which in turn can inform their prescribing practices.[23]

Identifying and reducing doctor shopping

- A study of New York State's PDMP (referred to as a triplicate prescription program in the 1980s) found that in the year following the inception of the program in 1988, prescribing of benzodiazepines to individuals suspected of drug diversion fell by 95% as measured by insurance claims data.[24]
- Data from the Virginia PDMP show that in the period following a rapid increase in PDMP data utilization in 2009, the number of individuals meeting criteria for doctor shopping dropped by 44% in 2010.[25] From 2012 to 2013, as requests for information from the PMP increased 50%, this number dropped again, by 73%.[26]
- Following initiation of the Arkansas PDMP in March 2013, the numbers of individuals meeting a threshold for doctor shopping (seven or more prescribers and seven or more pharmacies within 90 days) fell from 114 (March-May 2013) to 31 (December 2013-February 2014).[27]
- After inception of the Florida PDMP in September 2011, doctor shopping (five or more prescribers and five or more pharmacies within 90 days) declined 51% from FY 2012 (October 1, 2011 to September 30, 2012) to FY 2013. This decline is partially attributable to use of the PDMP, which logged over 3.7 million queries to its database by prescribers and pharmacists in FY 2013.[28]
- In 2011, Ohio passed legislation instructing medical boards to promulgate rules requiring prescribers to check the PDMP in advance of prescribing certain controlled substances. Subsequently, doctor shopping (five or more prescribers and five or more pharmacies in a three month period) dropped by over half, from a rate of over 25 per 100,000 residents in the first quarter of 010 to just over 10 per 100,000 in the last quarter of 2013.[29]
- In New York and Tennessee, doctor shopping rates declined after utilization of their PDMPs rose rapidly in response to legislative mandates for prescribers to check the PDMP before first prescribing certain controlled substances (e.g., opioids, all schedule 2 drugs) and at regular intervals thereafter. After the mandate went into effect in Tennessee (April 2013), the number of individuals meeting a threshold for doctor shopping (being prescribed to by five or more prescribers and filling prescriptions at five or more pharmacies in a three month period) declined from 2,194 (August-October, 2012) to 1,395 (May-July 2013), down 36%. In New York, where the mandate went into effect in June 2013, the number of individuals meeting this threshold decreased by 74.8% from the fourth quarter of 2012 to the fourth quarter of 2013.[30]
- An analysis by Wyoming's PDMP indicates that as prescribers and pharmacists received unsolicited PDMP reports concerning likely doctor shoppers, and as they requested more reports on patients, the number of individuals meeting a threshold for doctor shopping declined, from 316 in 2009 to

169 in 2013. This suggests that PDMP reports prompt prescribers and pharmacists to reduce the availability of controlled substances to patients engaged in doctor shopping, thus reducing addiction, abuse and costs related to prescriptions. [31]

- An analysis of data from the Nevada PDMP indicates that for those probable doctor shoppers for whom unsolicited reports were sent, the mean number of dosage units of controlled substances dispensed to them declined on average 41% in the year following the reports. After the inception of unsolicited reporting in 1997, the mean number of prescribers who prescribed to those identified as probable doctor shoppers dropped from 22 in 1997 to 14 in 2002, a decline of 36%, and the mean number of pharmacies that dispensed to probable doctor shoppers dropped from 16 to 12, a decline of 25%.[32]
- Washington State's PDMP provides data to its Medicaid and workers' compensation programs. Access to PDMP data, which tracks all dispensed prescriptions including those paid for by cash, has allowed both programs to more quickly and reliably identify patients who may be doctor shopping or obtaining medically unnecessary prescriptions. For example, in a match of Medicaid enrollees to PDMP data, more than 2,000 persons were identified who obtained a controlled substance prescription paid by Medicaid and a second prescription paid in cash on the same day.[33]
- After four years of increases in the diversion of high dosage buprenorphine via doctor shopping in the Bouche de Rhone area of France, a measure of doctor shopping declined 22% in the period following the initiation of prescription monitoring for buprenorphine, with no marked effect on treatment access.[34]

Impact on controlled substance availability and prescribing

- An independent evaluation of Kentucky's PDMP noted that in 2006, distribution of oxycodone, as measured by grams per 100,000 population from the Automation of Reports and Consolidated Orders System (ARCOS) system, was highest in Florida compared to other states on interstate Route I-75, while distribution of hydrocodone was highest in Tennessee. Since 2004, oxycodone distribution in Kentucky, a state with a well-established prescription monitoring program, rose at a much lower rate than in either Florida or Tennessee, neither of which had active PDMPs during this period.[35]
- A national evaluation comparing states with and without PDMPs found that proactive PDMPs were associated with slower growth in the per capita availability of prescription pain relievers and stimulants.[36]
- A study comparing PDMP states with non-PDMP states found that PDMP states had decreases in the amount of opioid shipments.[37]
- The presence of PDMPs collecting prescription information on Schedule II controlled substances was associated with lower outpatient opioid prescribing as measured by insurance claims data when compared with states not collecting such information.[38]
- After inception of its PDMP, Florida saw a 24% decline in prescriptions for oxycodone, and an 8% decline for methadone, two drugs most implicated in prescription overdose and death.[39]
- Subsequent to adoption of mandates for prescribers to use their PDMPs, Kentucky, Tennessee and New York saw declines in the prescribing of opioids. In Kentucky, doses dispensed declined for

hydrocodone (-10.3%), oxycodone (-11.6%), and oxymorphone (-35%); in Tennessee the number of opioid prescriptions fell over 7% and the total mme (morphine milligram equivalents) dispensed declined nearly 6%; in New York total opioid prescriptions decreased by over 9%.[40]

- Numbers of prescriptions and doses for pain relievers have dropped in Virginia from 2012 to 2013 as utilization of the PMP has increased.[26]
- Within six months of the inception of a British Columbia prescription monitoring system, medically unwarranted prescriptions for opioids fell by 33% and for benzodiazepines by 49%.[41]

Association with improved health outcomes

- According to a report by the state Office of Drug Control Policy, in 2012 Kentucky had 1,004 opioid overdose deaths, down from 1,023 in 2011, the first decline in a decade. State health officials attribute this decline to laws mandating prescriber use of the PDMP and better regulation of pain clinics.[42]
- Following the implementation of the Florida PDMP in 2011 and adoption of other measures to address prescription drug abuse and diversion, drug-related deaths in Florida have declined. Deaths attributable to oxycodone overdose fell by 41% from 2011 to 2012 and deaths caused by any prescription drug fell by 18%.[43]
- Oklahoma recorded declines in drug-related overdoses for the first time in ten years, from 807 in 2011 to 578 in 2012. A public safety official attributed the decline in part to increased use of Oklahoma's real-time PDMP.[44]
- Washington State also saw a reduction in prescription drug related deaths, down 27% from 2008 to 2012. Department of Health officials attribute the decline to state initiatives to address prescription drug abuse and overprescribing, including the PDMP.[45]
- A year after the inception of New York State's triplicate prescription program (its PDMP) in 1988, emergency department visits for drug overdoses involving benzodiazepines dropped by 48% in New York City and Buffalo.[24]
- A national evaluation comparing states with and without PDMPs and focusing primarily on Schedule II controlled substances (e.g., opioids such as oxycodone) found that proactive PDMPs were associated with lower rates of treatment admissions for abuse of these drugs.[36]
- A study comparing PDMP states with non-PDMP states found that PDMP states had decreases in admission rates to opioid addiction treatment programs.[37]
- An analysis of poison center data from 2003 to mid-2009 found that in states with PDMPs, calls concerning intentional exposures to opioids (an indicator of opioid abuse or misuse) increased just 0.2% per quarter, while in states without PDMPs these calls increased 1.9%.[46]

Reducing drug and medical costs related to inappropriate prescribing

- After New York State instituted its triplicate prescription program in 1988, the estimated savings due to the decline in benzodiazepine prescribing for New York's Medicaid program in 1989 and 1990 was $27 million.[24]
- A January 2013 report from the California's Workers' Compensation Institute estimates that the potential savings from enhanced opioid management controls made possible by California's PDMP

would be $57.2 million, with a return on investment estimated at $15.50 to $1.[47] Given the potential for PDMP data to reduce the costs of workers' compensation claims and lost productivity attributable to prescription drug abuse, the American Insurance Association recommends that "It is essential for there to be broad [third party payer] access to PDMP data."[48]

- WellPoint/Anthem Blue Cross Blue Shield of Virginia, a health insurance payer, estimated saving $333,418 in drug and medical claims by restricting 100 clients to one pharmacy who had been receiving multiple narcotic prescriptions from 5 or more sources over a 90-day period. PDMP data are essential for the identification of such clients, since they track filled prescriptions from all sources, not just those prescribed by providers within a health insurance network.[49]
- PDMP data identified 20 Medicaid clients appropriate for participation in Washington State's Medicaid "lock-in" program – the Patient Review and Coordination (PRC) program – which restricts at-risk Medicaid clients to one pharmacy and one prescriber for controlled substances. It is estimated that PRC participation results in a $6,000 savings per year per client. Since clients stay in lock-in between two and five years, depending on their compliance, savings for these 20 clients were estimated at over $400,000.[50]
- According to a report by the PDMP Center of Excellence at Brandeis, participants at a meeting on PDMPs and third party payers concluded that PDMP data would be of great value to workers compensation programs and other medical insurers since it supplies a complete picture of controlled substance prescribing, permitting more effective detection of doctor shopping, prescription fraud, and over-prescribing.[51]

Reducing diversion and drug investigation times

- A study of diversion rates for prescription opioids in Florida found significant declines for several drugs, including oxycodone, methadone and morphine, after the implementation of pill mill laws and the state's prescription monitoring program.[52]
- An evaluation of Virginia's PDMP found that investigation times were reduced by use of PDMP data.[53]
- In 2002, the Government Accounting Office reported that the average times for investigations of doctor shoppers in Kentucky dropped from 156 days to 16 days after implementation of its PDMP. The same report found that average investigation times for doctor shoppers dropped markedly following the implementation of Nevada's PDMP, from 120 days to 20 days, reducing expenses related to investigations.[54]
- A 2010 survey found that nearly three quarters (73%) of law enforcement officers who used Kentucky's PDMP (KASPER) strongly agreed that "KASPER is an excellent tool for obtaining evidence in the investigative process."[55]
- A case study of a Kentucky drug diversion investigator provides an example of PDMP data serving as important aids in increasing the efficiency of investigations.[56]

Monitoring compliance and abstinence

- Nevada's Pre-Criminal Intervention Program uses PDMP data to identify, enroll, and monitor individuals to help them stop doctor shopping, making law enforcement involvement unnecessary and saving taxpayers the cost of investigations, prosecutions and incarceration.[57]

- Drug courts in Kentucky use PDMP data to help monitor abstinence from prescription drugs, helping clients achieve sobriety and stability. This improves the court's ability to assure compliance and reduces costs related to drug diversion and abuse.[58]

Assisting in substance abuse treatment and medical examiner practice

- Substance abuse treatment programs in Maine consult PDMP data when admitting patients into treatment (patient consent required) to help validate patient self-reports on use of medications.[59]
- A report from the medical director of an opioid addiction treatment program indicates that PDMP data are an important clinical tool in monitoring use of controlled substances by patients addicted to opioids, keeping patients safe and increasing the effectiveness of treatment. [60] The Substance Abuse and Mental Health Services Administration has issued a policy advisory letter recommending use of PDMP data by opioid treatment programs. [61]
- Medical examiners in Virginia consult PDMP data as standard procedure in guiding autopsies and in conducting forensic investigations.[62]

Assisting in drug abuse prevention and surveillance efforts

- Project Lazarus, a comprehensive overdose prevention program in North Carolina, makes use of PDMP data in motivating and measuring community drug abuse prevention efforts, helping to reduce overdose deaths.[63]
- The Prescription Behavior Surveillance System (PBSS) collects and analyzes de-identified PDMP data from multiple states to track trends in prescribing, doctor shopping and problematic prescribing. Analyzes can identify longitudinal and geographic patterns in prescription behavior, as well as the characteristics and demographics of those most at risk for prescription drug abuse. Such surveillance can help state and community drug abuse prevention organizations target their interventions for maximum impact.[64]

Physicians express support for PDMPs [65]

- "This has been a huge benefit for our clinic and managing patients' narcotic use. It has improved our clinic and our time required for calling all the pharmacies in the area to find out if our patients are being compliant with medications and weed out those who are not, to provide for those patients who really need our care." – Mississippi Pain Management Specialist
- "We would like to take the time to express our gratitude for all your efforts in the CURES program. This program is a wonderful resource tool in tracking our controlled substance prescriptions and aiding in prevention of substance abuse." – California Pain Management Specialist.
- "As an emergency physician, I have found the OARRS program [Ohio's PDMP] extremely useful. I am shocked daily by the number of prescriptions and prescribers that some of my patients possess." - Ohio physician
- "I appreciate this website greatly!!! As a hospitalist it makes my life much easier to verify drug history and doctor shoppers." – Ohio physician
- "Instant access to controlled substance history is critical to safe management of patients." – Massachusetts physician[66]

Investigators find PDMPs an invaluable resource[67]

- "As far as enforcement of the Controlled Substance Act, the Prescription Monitoring Program is one of the best assets we have ever had. The countless hours saved by the agents being able to pull the profile compared to the way agents used to have to go to each pharmacy to get a profile have saved the state a large amount of money in salaries and vehicle expense." - Agent, Mississippi Bureau of Narcotics
- "This database is like cell phones and e-mail - what the heck did we do without it?" - Pharmacy Diversion Investigator, Ohio Narcotics Agency
- "... the monitoring system in [Mississippi] has been great. It has helped me identify alleged over prescribing registrants, possible doctor shopping patients, as well as possibly impaired practitioners writing prescriptions for themselves." - DEA Diversion Investigator
- "After receiving a complaint, I can request a report and know in just a few minutes if there is a case to investigate or not... I cannot say enough about KASPER and how valuable it is in my day to day investigations. If you, as an investigator, are not utilizing KASPER, you are limiting your resources and missing valuable information." – KY State police officer[68]

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Note: For inquiries concerning this report, please contact the PDMP Center of Excellence at http://www.pdmpexcellence.org or call 781-736-3909.

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DATA REQUESTOR NOTARY FORM

To be granted access to the AK PDMP database, you must register online and **fill out this form in its entirety and then be signed in front of a Notary Public.** You may then upload this form to your account. If you do not have access to a scanner to be able to upload it yourself, you may fax it to 907-269-6003. Once this form is uploaded, the AK PDMP office will verify your information. Completion of this form or your online registration does not guarantee approval.

I affirm that all information on my online data requestor registration is true and that all requests made pursuant to approval of this registration will be used for legitimate purposes outlined in Alaska Statute 17.30.200, 12 AAC 52.855 and 12 AAC 52.860. All data obtained from the site should be treated as Protected Health Information and handled in accordance with all federal and state laws regarding such. HIPAA and other privacy laws affect the disclosure of any data that is obtained. Additionally, I understand that inappropriate access or disclosure of patient profile information received from the AK PDMP database is a violation of state law, and may result in disciplinary action by my licensing board, criminal charges and/or revocation of my database access privileges.

After you receive your account information, you may begin requesting reports. **Be sure to keep your password in a safe place and *do not share* your login information with anyone.** If you have any questions or need assistance in accessing the AK PDMP system, please feel free to contact the AK PDMP support at 1-855-525-4767.

I declare under penalty of law that this application (including any accompanying documents) were examined by me, and to the best of my knowledge and belief, is a true, correct, and complete application.

Printed Name _____

User Email Address _____

This must be your own personal email account - delegate or staff emails are ***NOT*** allowed.

License Type (Circle One): **MD/DO PA PharmD/RPh APRN DDS/DMD VET DPM**

License #_____ **State:**_____ **Expiration Date** _____

SIGN HERE ➡ _____
Signature

_____
Date

(NOTARY SEAL)

SUBSCRIBED AND SWORN to before me,
a Notary Public, in and for the State of _____
this _____ day of _____, **20** _____.

NOTARY ➡ _____

My Commission Expires: _____

Disclaimer: The information in the AK PDMP database may contain errors resulting from the reporting of information received. Additional independent verification of patient profile information with pharmacies and prescribers may sometimes be prudent or necessary.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline

Thomas R. Frieden, M.D., M.P.H., and Debra Houry, M.D., M.P.H.

Deaths from prescription-opioid overdose have increased dramatically in the United States, quadrupling in the past 15 years. Efforts to improve pain management resulted in quadrupled rates of opioid prescribing, which propelled a tightly correlated epidemic of addiction, overdose, and death from prescription opioids that is now further evolving to include increasing use and overdoses of heroin and illicitly produced fentanyl.

The pendulum of opioid use in pain management has swung back and forth several times over the past 100 years. Beginning in the 1990s, efforts to improve treatment of pain failed to adequately take into account opioids' addictiveness, low therapeutic ratio, and lack of documented effectiveness in the treatment of chronic pain. Increased prescribing was also fueled by aggressive and sometimes misleading marketing of long-acting opioids to physicians.[1] It has become increasingly clear that opioids carry substantial risks and uncertain benefits, especially as compared with other treatments for chronic pain.

On March 15, 2016, the Centers for Disease Control and Prevention (CDC) released a "Guideline for Prescribing Opioids for Chronic Pain" to chart a safer, more effective course.[2] The guideline is designed to support clinicians caring for patients outside the context of active cancer treatment or palliative or end-of-life care. More research is needed to fill in critical evidence gaps regarding the effectiveness, safety, and economic efficiency of long-term opioid therapy. However, given what we know about the risks associated with long-term opioid therapy and the availability of effective nonpharmacologic and non-opioid pharmacologic treatment options, the guideline uses the best available scientific data to provide information and recommendations to support patients and clinicians in balancing the risks of addiction and overdose with the limited evidence of benefits of opioids for the treatment of chronic pain.

Most placebo-controlled, randomized trials of opioids have lasted 6 weeks or less, and we are aware of no study that has compared opioid therapy with other treatments in terms of long-term (more than 1 year) outcomes related to pain, function, or quality of life.[2] The few randomized trials to evaluate opioid efficacy for

longer than 6 weeks had consistently poor results. In fact, several studies have showed that use of opioids for chronic pain may actually worsen pain and functioning, possibly by potentiating pain perception. A 3-year prospective observational study of more than 69,000 postmenopausal women with recurrent pain conditions showed that patients who had received opioid therapy were less likely to have improvement in pain (odds ratio, 0.42; 95% confidence interval [CI], 0.36 to 0.49) and had worsened function (odds ratio, 1.25; 95% CI, 1.04 to 1.51).[3] An observational case–control study of patients undergoing orthopedic surgery showed that those receiving long-term opioid therapy had significantly higher levels of preoperative hyperalgesia.[4] After surgery, patients who had received long-term opioid therapy reported higher pain intensity (a rating of 7.6 vs. 5.5 out of 10) in the recovery room than patients who had not been taking opioids.

Whereas the benefits of opioids for chronic pain remain uncertain, the risks of addiction and overdose are clear. Although partial agonists such as buprenorphine may carry a lower risk of dependence, prescription opioids that are full mu-opioid–receptor agonists — nearly all the products on the market — are no less addictive than heroin. Although abuse-deterrent formulations may reduce the likelihood that patients will inject melted pills, these formulations are no less addictive and do not prevent opioid abuse or fatal overdose through oral intake.

The prevalence of opioid dependence may be as high as 26% among patients in primary care receiving opioids for chronic non–cancer-related pain.[2] Risk-stratification tools do not allow clinicians to predict accurately whether a patient will become addicted to opioids, although persons with a history of mental illness or addiction are at higher risk.[2] Overdose risk increases in a dose–response manner, at least doubling at 50 to 99 morphine milligram equivalents (MME) per day and increasing by a factor of up to 9 at 100 or more MME per day, as compared with doses of less than 20 MME per day.[2] Overall, 1 of every 550 patients started on opioid therapy died of opioid-related causes a median of 2.6 years after the first opioid prescription; the proportion was as high as 1 in 32 among patients receiving doses of 200 MME or higher.[5] We know of no other medication routinely used for a nonfatal condition that kills patients so frequently.

The new CDC guideline emphasizes both patient care and safety. We developed the guideline using a rigorous process that included a systematic review of the scientific evidence and input from hundreds of leading experts and practitioners, other federal agencies, more than 150 professional and advocacy organizations, a wide range of key patient and provider groups, a federal advisory committee, peer reviewers, and more than 4000 public comments.

Three key principles underlie the guideline's 12 recommendations (see box). First, nonopioid therapy is preferred for chronic pain outside the context of active cancer, palliative, or end-of-life care. Opioids should be added to other treatments for chronic pain only when their expected benefits for both pain and function are likely to outweigh the substantial risks inherent in this class of medication.

Nonpharmacologic therapies can ameliorate chronic pain while posing substantially less risk to patients. In some instances, other therapies result in better outcomes than opioids. These therapies include exercise therapy, weight loss, psychological therapies such as cognitive behavioral therapy, interventions to improve sleep, and certain procedures. The evidence review conducted in developing the guideline revealed that exercise therapy helped improve, and sustain improvements in, pain and function in patients with osteoarthritis. It did not find evidence that opioids were more effective for pain reduction than nonopioid treatments such as nonsteroidal anti-inflammatory drugs for low back pain or antidepressants for neuropathic pain, but it did find that nonopioid treatments could be better tolerated and superior for improving physical function while conferring little or no risk of addiction and substantially lower risks of overdose and death.[2]

Second, when opioids are used, the lowest possible effective dose should be prescribed to reduce the risks of opioid use disorder and overdose. Clinicians should carefully reassess individual benefits and risks when increasing a dose to 50 MME or more per day. Doses of 90 MME or more should be avoided, or the decision to titrate above this level should be carefully considered and justified. When prescribing opioids, the rule of thumb is to "start low and go slow."

Third, clinicians should exercise caution when prescribing

opioids and should monitor all patients closely. Prescribers should mitigate risk by, for example, avoiding concurrent use of benzodiazepines if possible, reviewing data from a prescription-drug monitoring program when deciding whether to start or continue opioid therapy, offering naloxone at least to patients who are at greater risk for overdose, having a clear "off-ramp" plan to taper and discontinue therapy, reevaluating the dosage and necessity of opioid treatment regularly, and obtaining urine toxicology screening at the initiation of treatment and, for some patients, periodically thereafter. For patients who become addicted to opioids, treatment with methadone, buprenorphine, or naltrexone improves outcomes.

Initiation of treatment with opioids is a momentous decision and should be undertaken only with full understanding by both the physician and the patient of the substantial risks involved. Clinicians need to recognize the risk associated with any treatment with opioids and should prescribe only the shortest course needed. Although the guideline addresses chronic pain, many patients become addicted to opioids after being treated for acute pain. Three days of treatment or less will often be sufficient; more than 7 days will rarely be required. Some trauma and surgery may require longer courses; treatment of postsurgical pain is beyond the scope of this guideline. Furthermore, it is important to discuss storage of opioids in a secure location to prevent diversion, as well as to counsel patients regarding the overdose risk posed to household members and other persons.

Management of chronic pain is an art and a science. The science of opioids for chronic pain is clear: for the vast majority of patients, the known, serious, and too-often-fatal risks far outweigh the unproven and transient benefits.

The CDC Opioid-Prescribing Guideline.

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and provider responsibilities for managing therapy.
4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME) per day, and should avoid increasing dosage to ≥90 MME per day or carefully justify a decision to titrate dosage to ≥90 MME per day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than 7 days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1–4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.
8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (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.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid-use disorder.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Centers for Disease Control and Prevention, Atlanta.

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1. Van Zee A. The promotion and marketing of oxycontin: commercial triumph, public health tragedy. Am J Public Health 2009; 99:221-7.
2. CDC guideline for prescribing opioids for chronic pain — United States, 2016. MMWR Recomm Rep 2016;65(RR-1):1-49.
3. Braden JB, Young A, Sullivan MD, Walitt B, Lacroix AZ, Martin L. Predictors of change in pain and physical functioning among postmenopausal women with recurrent pain conditions in the Women's Health Initiative observational cohort. J Pain 2012;13:64-72.
4. Hina N, Fletcher D, Poindessous-Jazat F, Martinez V. Hyperalgesia induced by low-dose opioid treatment before orthopaedic surgery: an observational case-control study. Eur J Anaesthesiol 2015;32:255-61.
5. Kaplovitch E, Gomes T, Camacho X, Dhalla IA, Mamdani MM, Juurlink DN. Sex differences in dose escalation and overdose death during chronic opioid therapy: a population-based cohort study. PLoS One 2015; 10(8):e0134550.

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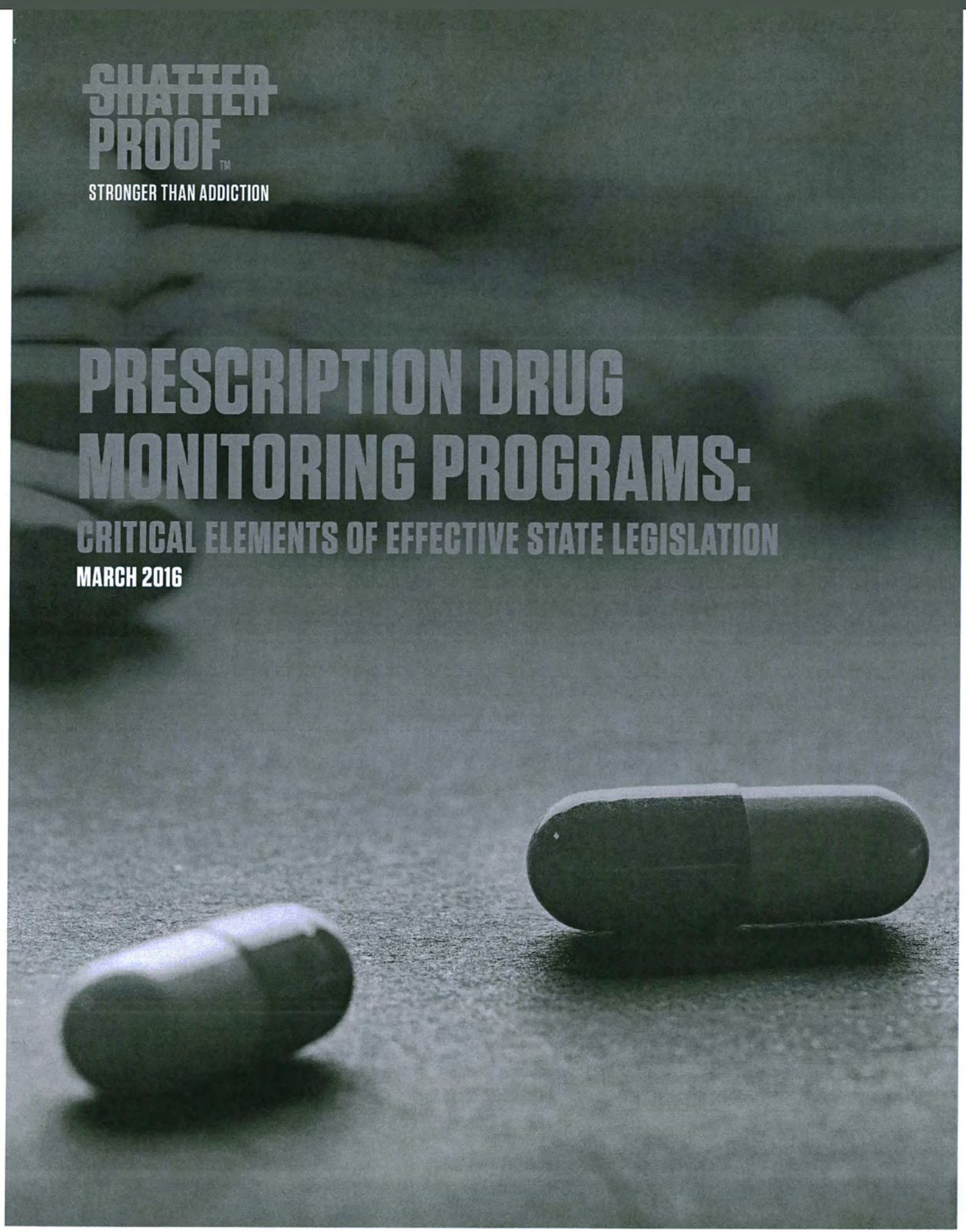
PRESCRIPTION DRUG MONITORING PROGRAMS:

CRITICAL ELEMENTS OF EFFECTIVE STATE LEGISLATION

MARCH 2016



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ABOUT SHATTERPROOF

Shatterproof is a national organization committed to preventing substance use disorder and facilitating access to evidence-based treatments without shame or stigma for those afflicted.

Shatterproof believes in the efficacy of PDMPs when used appropriately, and urges states to optimize the effectiveness of their PDMPs by adopting its Critical Elements of Effective State Legislation recommended in this document. PDMPs are essential tools in the quest to break the cycle of the misuse of prescription and illegal drugs that is devastating our families.

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PREFACE

As Shatterproof joins fellow stakeholders from around the country to convene for the 5th National Rx Drug Abuse & Heroin Summit, the shared sense of urgency is palpable. Collaboration across our communities, states and federal government is the single most powerful weapon within our grasp. However this collaboration is itself fueled by something far more individual, infinitely more intimate.

While we can certainly quantify the vastness of this epidemic and measure the effectiveness of solutions with various statistics, there is ultimately a single number that stands above all others as the driving force behind our collective purpose. That number is One. For me, the devastating loss of one life – my son – was a transformative event that redefined my sense of purpose. One life lost. One more hug I will never share. One family shattered, forever.

However, Jewish tradition has taught that when you save a single life, you've saved the whole world. Several months ago I received an email from a legislator with whom we worked in West Virginia to pass legislation to expand access to naloxone; "Tonight I watched naloxone save a life. Because of the availability of this medication a 24 year old young man will live to get another chance at life. Well done, well done." Save one life, save a whole world.

Since my journey began I have been honored and moved to be with other individuals with similar stories of purpose borne from grief. Our power of one is unleashed at the National Summit as we are here to understand what's working, and what gaps we must bridge to make more of a life-saving difference. To that end, I am proud to introduce the first edition of this important report about Prescription Drug Monitoring Programs (PDMPs). PDMPs can save a life; someone's son or daughter, brother or sister, father or mother.

The central question surrounding PDMPs is not whether they should exist or can save lives. The answer to both is a definitive yes. Rather, the question at hand is how quickly states will enact legislation that mandates participation. The fact that most do not is the gating factor that often prevents a life from being saved. And then another life.

This report provides compelling examples of states whose legislation has saved lives, and clear guidance for other states to achieve this. By summoning the political will of our leadership and inherent compassion of our citizenship, we can help make a life-saving difference in every community today. Save one life, save a whole world.

Gary Mendell

Founder, Chairman
Shatterproof...Stronger Than Addiction
March 28, 2016

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EXECUTIVE SUMMARY

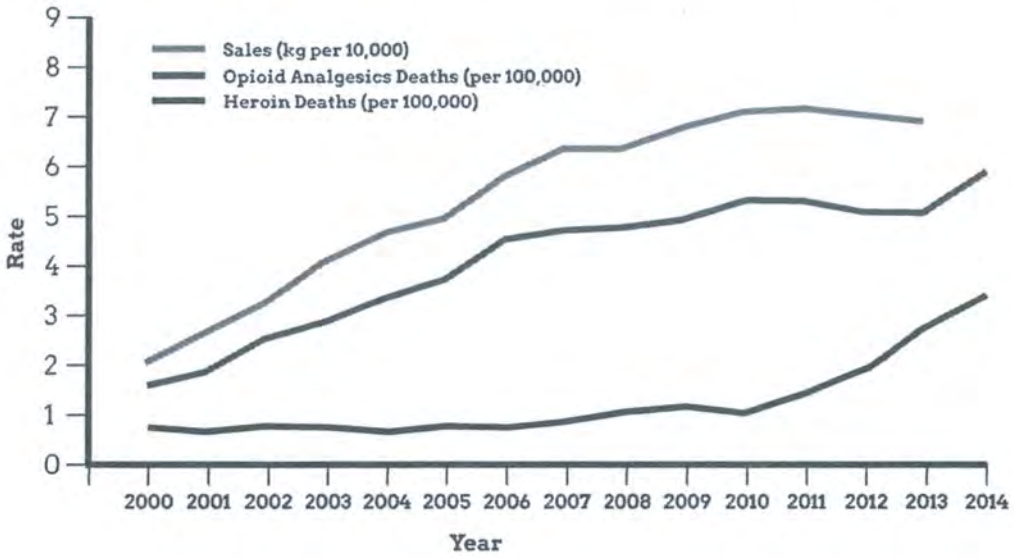
Tens of thousands of our sons, daughters, and loved ones die every year as a consequence of prescription opioid and heroin use. In 1999, death from opioid overdose claimed 6,000 American lives. By 2014, increasing 14% from 2013, this number spiked to nearly 30,000.[1] And this is not simply a number... It is real people with real names and real families.

Many in our society still associate substance use disorders mostly with heroin and other illicit drugs, and have dated socioeconomic stereotypes about those affected. However, this alarming escalation in loss of life and devastation to surviving families is most directly linked to the overprescribing of opioids that now routinely populate U.S. household medicine cabinets. These all-too-familiar instruments of death by overdose include medicines such as OxyContin, Vicodin and Percocet.

"Overall, 1 of every 550 patients started on opioid therapy died of opioid-related causes a median of 2.6 years after the first opioid prescription.[2] We know of no other medication routinely used for a nonfatal condition that kills patients so frequently."

- Dr. Thomas Frieden and Dr. Debra Houry for the CDC in the New England Journal of Medicine

PRESCRIPTION PAINKILLER SALES AND AGE-ADJUSTED RATES FOR DRUG-POISONING DEATHS, BY TYPE OF DRUG: UNITED STATES, 2000–2014

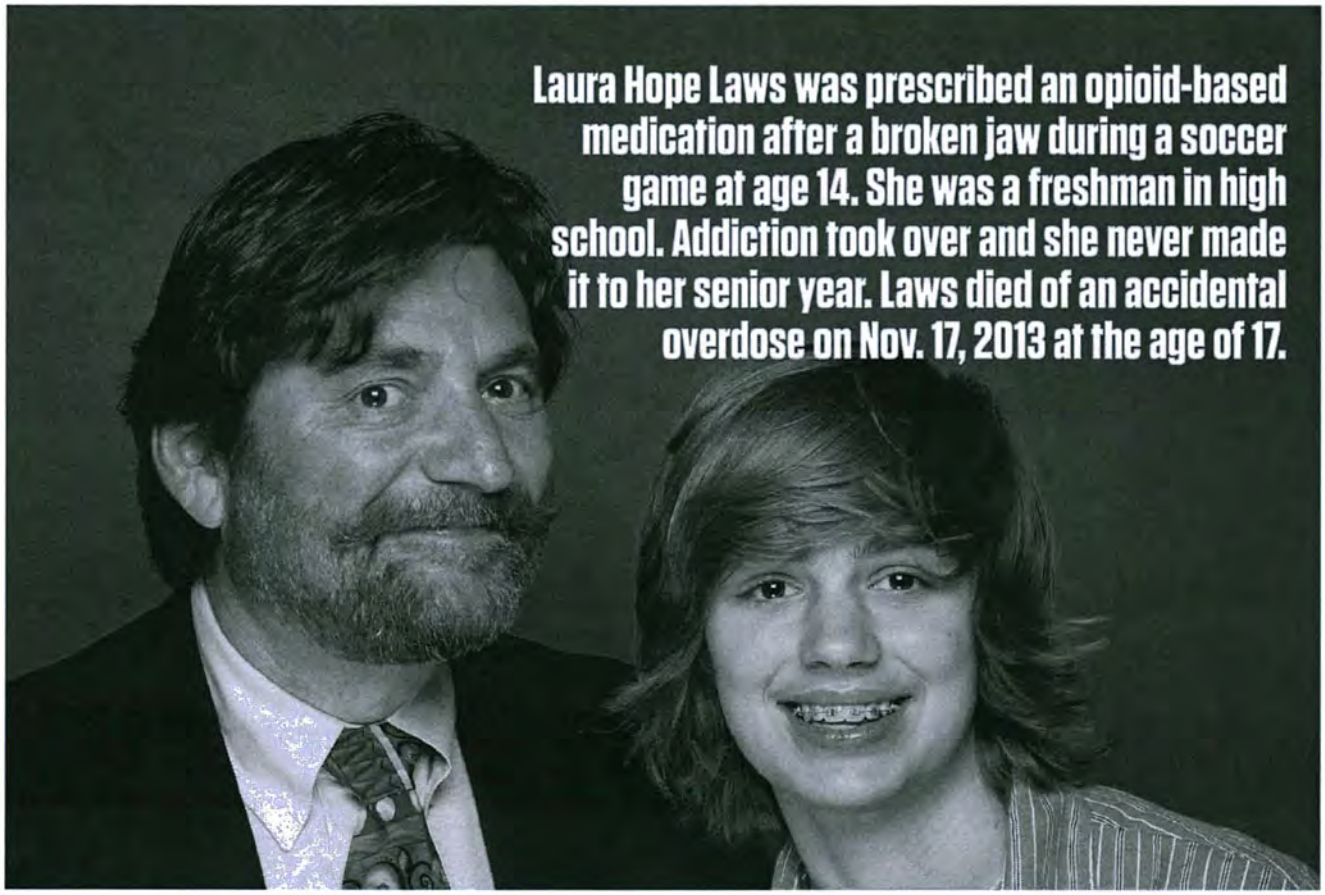


NOTES The number of drug-poisoning deaths in 2013 was 43,982, the number of drug-poisoning deaths involving opioid analgesics was 16,235, and the number of drug-poisoning deaths involving heroin was 8,257. A small subset of 1,342 deaths involved both opioid analgesics and heroin. Deaths involving both opioid analgesics and heroin are included in both the rate of deaths involving opioid analgesics and the rate of deaths involving heroin.

SOURCE: Center for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, Mortality File. (2015). Number and Age-Adjusted Rates of Drug-poisoning Deaths Involving Opioid Analgesics and Heroin: United States, 2000–2014. Atlanta, GA: Center for Disease Control and Prevention. Available at http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf.

[1] Prescription Drug Monitoring Programs. (2016). U.S. Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/drugoverdose/pdmp/

[2] Kaplovitch E, Gomes T, Camacho X, Dhalla IA, Mamdani MM, Juurlink DN. Sex differences in dose escalation and overdose death during chronic opioid therapy: a population-based cohort study. PLoS One 2015; 10(8): e0134550.



Since 1999, prescription opioid consumption in the U.S. has quadrupled.[3] We can no longer question a causal link between opioid overprescribing and opioid overdose deaths.

The impact of prescription painkillers on the size and scope of this crisis demands that evidence-based solutions available to prevent and treat this brain disease must be powerfully advocated for, established and enforced. One such solution is the design, enactment and effective utilization of Prescription Drug Monitoring Programs (PDMPs).

A PDMP employs a statewide electronic database that collects designated data on controlled substances dispensed within the state. When properly used, PDMPs identify and prevent drug misuse or diversion, identify polypharmacy, and offer treatment to patients in need of support, while ensuring the legitimate medical use of painkillers. The data collected can also be used more broadly to analyze prescribing patterns and trends in use, and ultimately inform patient-centered public health initiatives.

[3] Prescription drug monitoring frequently asked questions. Prescription Drug Monitoring Program Training and Technical Assistance Center. Retrieved from: http://www.pdmpassist.org/content/prescription-drug-monitoring-frequently-asked-questions-faq

Contrary to some concerns that have been raised about PDMPs, there is no evidence to suggest that mandating their use will limit appropriate access to prescription opioids for patients in need. The objective is to protect people from being prescribed opioids they either don't need, in volumes that are unnecessary, or in combination with benzodiazepines, thus minimizing the potential for developing an addiction and/or death from an overdose.

To date, 49 states and the District of Columbia have enacted legislation authorizing the creation and operation of a PDMP.[4] However, in the vast majority of states, PDMP participation by prescribers is extremely low, and the effectiveness of this clinical tool is therefore compromised. A 2015 study of primary care prescribers found that while a majority reported having obtained data from their PDMP at some point in time, prescribers consulted PDMP data in fewer than one-quarter of instances when they prescribed opioids to patients.[5] In a recent review of 2015 prescribing data in a sample of states where participation in the PDMP is voluntary, prescribers checked the patient history in the PDMP only 14% of the time before prescribing an opioid.[6]

State legislation mandating healthcare providers to record, consult and proactively monitor prescribing data will help reverse the current course of this tragic epidemic, reducing the enormous suffering and loss of life.

After knee surgery, Faye Roscoe's 23-year-old son Chris was prescribed Vicodin against her wishes. Chris had a history of drug issues, but she says that was overlooked. "Had stricter guidelines been in place, discussing other alternatives for pain medication, I believe Vicodin would not have been prescribed," Roscoe said.

Based on current program designs and successes, Shatterproof has analyzed PDMP practices and policies to identify a proven model that states can adopt. Herein are 12 guiding practices and recommended legislation to maximize the effectiveness of state-level PDMPs. By heeding this guidance, state leadership will be taking concrete action to save the lives of its residents by systematically preventing future overprescribing and dangerous co-prescribing of prescription painkillers.

[4] Prescription Drug Monitoring Program Training and Technical Assistance Center. Prescription Drug Monitoring Frequently Asked Questions. Retrieved from: http://www.pdmpassist.org/content/prescription-drug-monitoring-frequently-asked-questions-faq

[5] Rutkow, L. et al., Many primary care physicians are aware of prescription drug monitoring programs, but many find the data difficult to access. Health Affairs 34, No. 3 (2015): 484-492. Retrieved from: http://content.healthaffairs.org/content/34/3/484.abstract.

[6] Prescription Behavior Surveillance System (PBSS). Definitions of PBSS Measures. PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures.pdf

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CRITICAL ELEMENTS OF EFFECTIVE STATE LEGISLATION

1. DISPENSERS REPORT SPECIFIED INFORMATION EXPEDITIOUSLY
2. PRESCRIBERS QUERY PDMP BEFORE PRESCRIBING DRUGS IN SCHEDULES II, III AND IV
3. LICENSED PRESCRIBERS REGISTER WITH PDMP
4. ENABLE DELEGATION OF PDMP DATA QUERIES
5. AUTHORIZE SPECIFIED RECIPIENTS OF PDMP DATA
6. PROACTIVELY ANALYZE AND DISTRIBUTE PDMP DATA
7. REQUIRE INTERSTATE SHARING OF PDMP DATA
8. PROVIDE DE-IDENTIFIED INFORMATION
9. TAKE A COMMUNITY-BASED APPROACH TO PDMP DATA
10. LINK PDMP DATA TO PAIN AND ADDICTION TREATMENT
11. INSTITUTE CONFIDENTIALITY PROTECTIONS
12. TRACK AND REPORT EVALUATION MEASURES

OUR MOST URGENT HEALTH CRISIS

Opioids were collectively responsible for 29,467 deaths in 2014 alone, including 18,893 resulting from opioid pain relievers and 10,574 from heroin. Drug overdose death rates have increased more than five times since 1980.[7] In 2014, more Americans died of drug overdoses than car crashes, making drug overdose now the leading cause of accidental death in the United States.[8]

According to the United States Centers for Disease Control and Prevention (CDC), this is the "worst drug overdose epidemic in [U.S.] history."[9] The problem has grown so severe that, in 2014, the CDC added opioid overdose prevention to its list of top five public health challenges.[10]

While the rapidly escalating number of deaths in this country due to opioid overdose makes headlines, little is said about the sheer number of Americans across all demographics who continue to suffer from substance abuse disorders related to opioids. Today, it is estimated 4.5 million people in the U.S. are addicted to prescription opioids, and 467,000 to heroin.[11,12] These individuals struggle daily with a devastating cycle between managing their disorder and relapse.

It is estimated 4.5 million people in the U.S. are addicted to prescription opioids, and 467,000 to heroin.

These numbers do not account for the millions of family members fighting to understand this disease, struggling to steer their loved ones toward treatment and continuously waiting for that dreaded phone call letting them know that their child, parent or loved one has overdosed and died.

"The root cause of our nation's opioid epidemic is not unethical or illegal medical practice, but the well-intentioned yet tragically misguided practice of over-prescribing opioids for common conditions. To prevent new cases of opioid addiction clinicians must prescribe more cautiously. On March 15th the CDC took an enormous step in this regard by releasing the CDC Guideline for Prescribing Opioids for Chronic Pain. This report, Prescription Drug Monitoring Programs: Critical Elements of Effective State Legislation, is another vitally important step forward."

- Andrew Kolodny, MD, Executive Director of Physicians for Responsible Prescribing and Chief Medical Officer of Phoenix House Foundation and senior scientist at Brandeis University's Heller School for Social Policy and Management

[7] Addressing prescription drug abuse in the United States: Current activities and future opportunities. Developed by the Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee. US Department of Health and Human Services.

[8] CDC/NHS, National Vital Statistics System, Mortality File. Retrieved from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm

[9] Paulozzi LJ. 2010. The epidemiology of drug overdoses in the United States. Presented at Promis. Leg. Responses to the Epidemic of Prescr. Drug Overdoses in the U.S., Maimonides Med. Cent.Dep. Psychiatry, Dec. 2, Grand Rounds, Brooklyn

[10] CDC (Cent. Dis. Control Prev.). 2014. CDC's Top Ten: 5 Health Achievements in 2013 and 5 Health Threats in 2014. Atlanta, GA: CDC.

[11] Substance Abuse and Mental Health Services Administration, Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.

[12] Kolodny, A, et al. (2015). The prescription opioid and heroin crisis: A public health approach to an epidemic of addiction. Annual Review of Public Health. 36:559-574.

Opioid Use Disorder (OUD)

Opioids such as legally available pain relievers (e.g. oxycodone and hydrocodone) and heroin reduce the perception of pain but can also produce drowsiness, mental confusion, euphoria, nausea, constipation, and, depending upon the amount of drug taken, can depress respiration. If a person uses opioids for a long time, they develop physical dependence and tolerance, and require more of the drug to continue to get high. If a person stops or attempts to reduce using opioids after they become physically dependent on the drug, they will experience drug withdrawal symptoms which can include anxiety, irritability, muscle aches, vomiting, sweating and tremors.

Individuals who develop an OUD experience a strong desire for opioids. When prescription opioids are no longer available, many switch to heroin because it is less expensive and easier to obtain. Presently, four out of five of those who use heroin report that their use started with prescription painkillers. Because of variable purity and other chemicals and drugs mixed with heroin on the black market, this also increases risk of overdose.

The mother of Britt Doyle's children succumbed to a 15-year battle with addiction to opioids that began with her third c-section childbirth. Doyle says she was an extensive "doctor shopper." She told her family she was "following doctor's orders" by taking nearly 50 pills a day. She underwent 13 different treatment programs, but could not break the grasp of her addiction.

Opioid use disorders do not discriminate based on age, race, gender, or socioeconomic status. According to a recent report by the New York Times, drug overdoses are driving up the death rate of young white adults in the United States to levels not seen since the end of the AIDS epidemic more than two decades ago.[13]

Also tragic is the stigma related to addiction that pervades both public and self-perception, and is often a barrier to individuals getting necessary treatment. In a recent study, among those who needed and made an effort to get treatment, but did not receive it, 24% cited the reason as either possible negative effect on job prospects or concern that receiving treatment might cause neighbors/community to form a negative opinion.[14] On a broad scale, the perpetuation of stigma blocks acknowledgment of this public health crisis as a non-discriminatory killer. It is imperative that community members, law enforcement, and health care providers treat addiction as the disease that it is and put aside the unjust stigma and stereotypes.

Brian Mendell

Shatterproof founder Gary Mendell believes society must look inward, because pervasive stigmatization of addiction is as deadly as the neurological consequences of the disease his organization is driven to eradicate: "My son Brian did not die of an overdose. After not having used a substance for 13 months, he woke up on October 20th, 2011 and took his own life out of shame; stigma," Mendell states. "He told me often that he felt like an outcast, not a patient."

[13] http://www.nytimes.com/2016/01/17/science/drug-overdoses-propel-rise-in-mortality-rates-of-young-whiteshtml?action=click&contentCollection=Politics&module=RelatedCoverage%C2%AEion=Marginalia&pgtype=article

[14] Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health. (2015, September). Substance Abuse and Mental Health Services Administration.

DRIVERS OF THIS EPIDEMIC

While the true impact of this epidemic on the lives of individuals across our nation can only be estimated, its causes are well-known. Researchers and experts have identified several key drivers of this epidemic.[15]

PRESCRIBING TRENDS

Up until the late 20th Century, medical convention held that prescription opioids were only to be prescribed in rare instances involving acute pain (e.g. surgery), chronic pain from illnesses like cancer and in end of life care. Physicians were cautious about long-term opioid use given its linkage to addiction, tolerance and physiological dependence.[16]

In 2012, doctors wrote 259 million prescriptions for opioids – enough for every adult in the United States to have a bottle of pills for a month.

This prevailing thought was questioned in 1986 when a paper published in the journal Pain describing treatment of 38 chronic pain patients concluded that opioid painkillers could be prescribed safely on a long-term basis.[17] In 1996, the rate of opioid prescribing began to rapidly increase following the 1995 FDA approval of OxyContin.[18] The drug's manufacturer, Purdue Pharma, subsequently funded more than 20,000 pain-related educational programs through sponsorships or financial grants and launched a campaign to promote long-term use of opioid painkillers for chronic, non-cancer pain.[19]

[15] Addressing prescription drug abuse in the United States: Current activities and future opportunities. Developed by the Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee. US Department of Health and Human Services.

[16] Turk DC, Brody MC, Okifuji EA. 1994. Physicians' attitudes and practices regarding the long-term prescribing of opioids for non-cancer pain. Pain 59:201–8

[17] Portenoy RK, Foley KM. (1986). Chronic use of opioid analgesics in non-malignant pain. report of 38 cases. Pain 25:171–86

[18] The report of the International Narcotics Control Board for 2007. International Narcotics Control Board. Retrieved from: https://www.incb.org/incb/en/publications/annual-reports/annual-report-2007.html

[19] Prescription drugs: Oxycontin abuse and diversion and efforts to address the problem. (December 2003). Report to congressional requesters. United States General Accounting Office. Retrieved from: http://www.gao.gov/new.items/d04110.pdf

Growing concern about systemic under-treatment of pain galvanized physicians and pain societies to successfully lobby for increased use of opioids for all pain types, regardless of the patient's diagnosis.[20] In 1995, the American Pain Society introduced a campaign entitled, "Pain is the Fifth Vital Sign," championing the idea that clinicians should assess and treat pain with the same urgency as other vital signs and use opioids for non-cancer pain.[21] The Veterans Affairs health system and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), a group that accredits hospitals and health care organizations, endorsed this campaign to increase pain treatment with opioids.

In the 1990s and 2000s, physicians expanded their treatment of pain through use of the growing number of approved prescription opioids. Today, pain management is a fully actualized medical practice. Clinical inquiry about a patient's pain status is ubiquitous across the settings, specialties and continuum of healthcare. The therapeutic response too often involves opioid medication, with far-reaching, sometimes tragic consequences.

1983

Vicodin becomes available as a generic.

1986

Published paper concludes that opioid painkillers could be prescribed safely on a long-term basis.

1995

OxyContin receives approval from FDA.

American Pain Society introduces a campaign entitled, "Pain is the Fifth Vital Sign."

1996

Purdue Pharma begins multi-year educational programs promoting long-term use of opiod painkillers.

2000s

Physicians expand their treatment of pain through use of the growing number of approved prescription opioids.

Prescription painkillers flood the market

2014

4x annual increase in prescriptions from 1999 - 2014. 5x annual increase in overdose deaths related to opioids.

[20] A pain drug champion has second thoughts. Wall Street Journal Published Dec. 17, 2012. Retrieved from: http://www.wsj.com/news/articles/SB10001424127887324478304578173342657044604

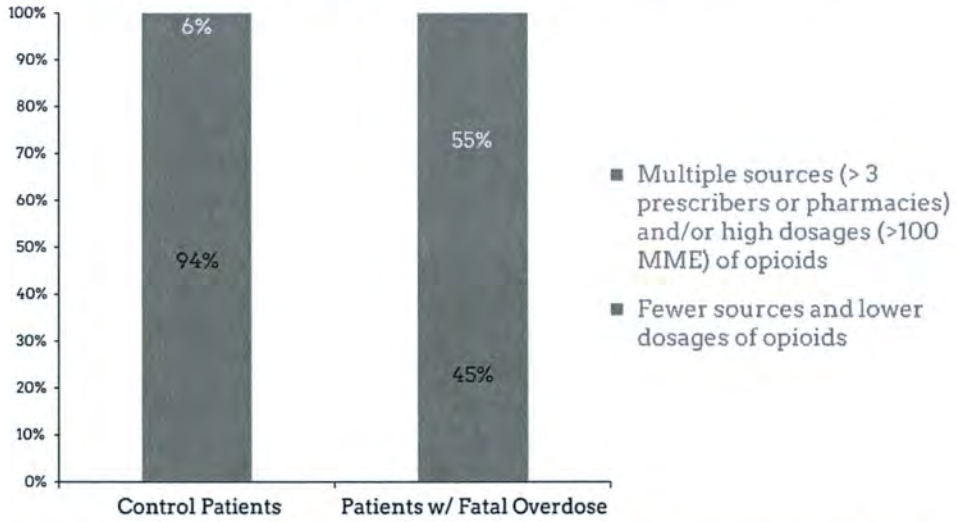
[21] Haddox JD, Joranson D, Angarola RT, Brady A, Carr DB, et al. (1997). The use of opioids for the treatment of chronic pain: a consensus statement from the American Academy of Pain Medicine and the American Pain Society. Clin. J. Pain 13:6–8

HIGH DOSAGE PRESCRIBING

With daily use of opioids, physiological dependence and tolerance set in rapidly. For patients to continue to achieve pain relief, dose increases are often required. Over time, the dose required to obtain an analgesic effect can approach the lethal dose that will cause respiratory depression. Studies indicate that as doses increase beyond the equivalent of 90mg of morphine, the risk of overdose increases exponentially.[22] High dose opioid therapy is also associated with other serious adverse effects including neuroendocrine suppression, cognitive impairment, and hyperalgesia (worsening of pain). For individuals who feign pain to obtain opioids to sell, high dose prescribing may also account for significant diversion on to the black market.

The average amount of opioid per prescription, in morphine milligram equivalents, increased 69.7 percent for oxycodone, 69.4 percent for hydrocodone, and 20.9 percent for fentanyl nationally between 2000 and 2009.[23]

MAJORITY OF OPIOID OVERDOSE DEATHS ASSOCIATED WITH MULTIPLE SOURCES AND/OR HIGH DOSAGES



Baumblatt JAG et al. High Risk Use by Patients Prescribed Opioids for Pain and its Role in Overdose Deaths. JAMA Intern Med 2014; 174: 796-801.

[22] Addressing prescription drug abuse in the United States: Current activities and future opportunities. Developed by the Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee. US Department of Health and Human Services.

[23] Addressing prescription drug abuse in the United States: Current activities and future opportunities. Developed by the Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee. US Department of Health and Human Services.

GENERAL PRESCRIBING

A majority of opioid analgesics in the US are prescribed by primary care physicians, dentists and internists, most of whom are not trained in pain management or addiction. Opioid analgesic sales increased four-fold between 1999 and 2010, and this was paralleled by an increase in opioid overdose deaths and substance abuse treatment admissions during the same time period.[24]

EMERGENCY DEPARTMENTS AND HOSPITAL PROVIDERS

Among people entering treatment for opioid abuse, 13% cite emergency departments as a source for drugs while 10% of opioid analgesic prescriptions for people ages 20-39 are written in emergency departments. Problematic prescribing practices in emergency departments include high daily doses of opioids, overlapping prescriptions for opioids or a combination of opioids and benzodiazepines, and receiving long-acting/extended release opioids for acute pain.[25]

INSURERS AND PHARMACY BENEFIT MANAGERS

Policies by insurers and pharmacy benefit managers contribute to abuse and overdose. Several examples include: covering methadone as a first-line agent for pain because it is inexpensive; not covering non-opioid and non-pharmacological therapies; and not reimbursing for screening and risk mitigation activities.[26] Additionally, prior authorization requirements for buprenorphine serve as a barrier to a first-line treatment for opioid use disorders.

CO-PRESCRIBING OPIOIDS AND BENZODIAZDEPINES

Not publicly well known is that the co-prescribing of opioids and benzodiazepines (a sedative) is also a significant contributor to the overdose crisis. Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Between 2005 and 2009 this combination was the most common cause of overdose deaths involving multiple drugs.[27]

Co-prescribing can arise when two providers treating the same patient for different problems unknowingly issue prescriptions for medicines whose combination is unsafe. Today, most of the attention is given to opioids classified within Schedules II and III by the Controlled Substances Act, however reporting of medications in Schedules II, III and IV to PDMPs will provide practitioners the information necessary to protect their patients' safety.

Without a mandate to check the PDMP before prescribing schedule IV drugs, which include sedatives, health care providers are unable to detect this potentially dangerous, and often fatal drug combination.

[24-26] Addressing prescription drug abuse in the United States: Current activities and future opportunities. Developed by the Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee. US Department of Health and Human Services.

[27] Calcaterra, S., Glanz, J., & Binswanger, I. (2013). National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999-2009. *Drug and Alcohol Dependence*. 131(3): 263–270.

EVIDENCE-BASED SOLUTIONS

The opioid epidemic is a multi-dimensional crisis requiring a multi-faceted response. Initiatives must be tightly coordinated across the full stakeholder spectrum including public health officials and researchers, clinicians, public safety organizations, patient and family advocates and legislators. Solutions must be evidence-based, and implemented and sustained across communities. Shatterproof and the cosigners of this report support the following solutions, which are based on the recommendations of federal and state agencies:

PUBLIC HEALTH SURVEILLANCE

Collection and analysis of data to determine design, target and evaluate public health initiatives.

COMMUNITY-BASED DRUG ABUSE PREVENTION PROGRAMS

Local educational initiatives that target families, schools, community venues and houses of worship.

NATIONAL PATIENT AND PUBLIC EDUCATION

Multi-media campaigns and ongoing access to educational materials provided by government institutions and their branches including HHS, FDA, CDC and NIH.

PROVIDER EDUCATION

Government initiatives to improve the training and education of healthcare providers about pain management and substance use disorder. Under HHS, for example, the NIH has developed five curriculum resources focusing on opioid misuse.

PRESCRIBING GUIDELINES

Addressing the need for opioid prescription guidelines, in March, 2016 the CDC issued the CDC Guideline for Prescribing Opioids for Chronic Pain to be used by primary care physicians. Guidelines need to be developed for prescribing opioids for acute pain, and for the use of all physicians and prescribers.

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

Establishing and maximizing the effectiveness of state-based electronic databases that enable health care providers, pharmacists, health officials and others to confidentially track the dispensing of controlled substance prescriptions in a coordinated fashion to eliminate overprescribing and inadvertent co-prescribing.

REGULATORY OVERSIGHT

Federal, state and local regulatory actions such as FDA oversight of drug approval and post-marketing activities and CMS's oversight of Medicaid and Medicare to impact behavior among patients and providers in terms of access to and use of opioids.

LEGISLATION ON PRESCRIBING

State adoption of rules governing prescribing, for example, specifying the maximum allowable number of days for initial opioid prescriptions.

Massachusetts has recently passed a 7 day maximum, consistent with CDC Guideline on opioid prescribing.

MEDICATION-ASSISTED TREATMENT (MAT)

The use of medications such as methadone, buprenorphine and naltrexone to treat substance use disorder and sustain recovery. Medication with psychosocial support is now considered the optimal evidenced-based approach.

OVERDOSE PREVENTION

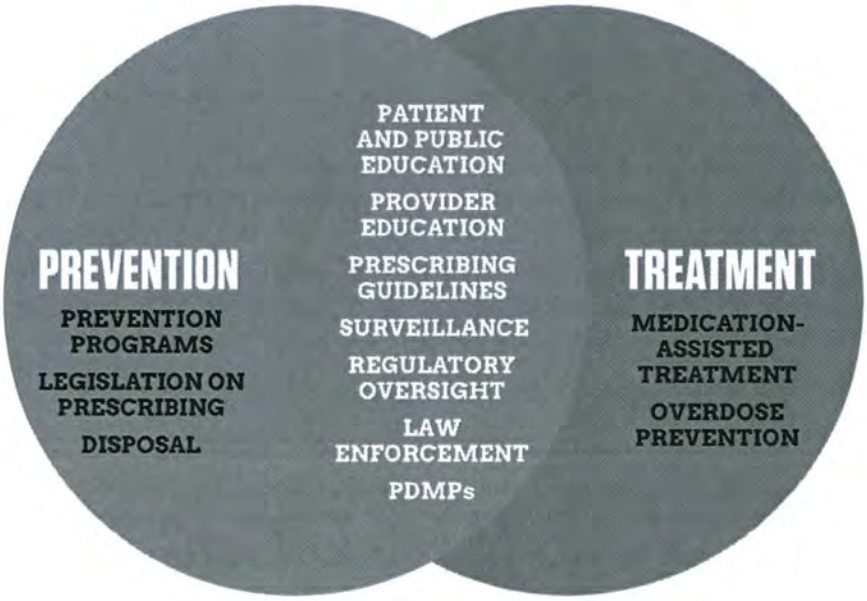
Programs focused on increasing access to naloxone to reverse the effects of overdose in emergency situations and granting immunity from prosecution to encourage people to seek help during an overdose emergency.

SAFE DISPOSAL OF MEDICATIONS AND TAKE-BACK PROGRAMS

The U.S. Drug Enforcement Administration (DEA) and local law enforcement periodically host collection events in communities for safe disposal of prescription drugs.

LAW ENFORCEMENT INVOLVEMENT

Aggressive law enforcement actions including efforts to address doctor shopping and pill mills to enforce compliance with state and national drug laws.



Important Update on Prescribing Guidelines

Improving the way painkillers are prescribed through clinical practice guidelines will ensure patients have access to effective pain treatments while reducing the rates of addiction and overdose.[28] On March 15, 2016, the CDC issued the Guideline for Prescribing Opioids for Chronic Pain, providing recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline includes 12 recommendations addressing 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use.[29] (Appendix D). The use of PDMP data is recommended to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk of an overdose.

In this report, we focus on one of the these evidence-based solutions; optimizing the effectiveness of Prescription Drug Monitoring Programs.

"Kentucky has seen, first-hand, the lifesaving power of legislation mandating physician participation in Prescription Drug Monitoring Programs (PDMPs). In 2012 Kentucky became the first state in the nation to pass legislation requiring doctors to check a patient's drug history before issuing new prescriptions for pain pills. Since that time we have seen a 13.4% decline in prescriptions of opioids dispensed, and a 25% decline in prescription opioid deaths. We still have an epidemic, but we've finally been able to make inroads into stemming the senseless opioid prescription growth that's cost so many lives in our state."

- Van Ingram, Executive Director of Kentucky Office of Drug Control Policy

[28] Prescription drug overdose. US Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/drugoverdose/prescribing/common-elements.html

[29] CDC guideline for prescribing opioids for chronic pain. (2016). US Centers for Disease control and Prevention. Retrieved from: http://www.cdc.gov/drugoverdose/prescribing/guideline.html

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

Prescription Drug Monitoring Programs (PDMPs) are state-run electronic databases that track the prescribing and dispensing of controlled prescription substances, and are among the most promising clinical tools to curb prescription opioid abuse. A PDMP is not just a monitoring system, but a dynamic, multi-stakeholder tool that has the potential to address the broader issues of prevention, identification, and treatment in real time. PDMPs can provide a prescriber or pharmacist with important information regarding a patient's prescription history, helping to identify patients who may be misusing medications and at risk for overdose due to co-prescribing.[30] PDMP data can help prescribers and pharmacists to identify high-risk patients who would benefit from early interventions and/or referral to treatment.[31] PDMPs also can help federal, state and local officials identify key trends in both legitimate and problematic prescribing and dispensing, critical for tackling this nationwide crisis.

BRIEF HISTORY

The concept of PDMPs was introduced in the 1930s as a paper-based database to track Schedule II drugs so that law enforcement officials could identify diversion. By 1992, 10 states had operational PDMPs.

Reflecting their locations primarily in state agencies concerned with public safety and drug enforcement, these early PDMPs all provided solicited reports and most provided unsolicited reports, to law enforcement personnel and regulatory agencies or professional licensing agencies. None provided reports to prescribers or pharmacists. The reports and, where relevant, PDMP investigations, focused on prescribers selling prescriptions, pharmacies selling controlled substances illegally, and organized doctor shopping rings.

With support from the U.S. Drug Enforcement Administration (DEA), in 1990 the existing PDMP administrators created the Alliance of States with Prescription Monitoring Programs (the "Alliance"). The Alliance was founded to provide a forum for support and information exchange among PDMPs, states where efforts were under way to establish a PDMP, and states where creation of a PDMP was being considered. At this time, PDMPs expanded data collection beyond Schedule II prescriptions. In the context of computer-based information technologies, a second generation of PDMPs came into existence that collected prescription information electronically. Examples included the Oklahoma PDMP in 1990, located in the Department of Public Safety, and the Massachusetts PDMP in 1992, located in the Department of Public Health.

The Nevada PDMP, implemented in 1997, ushered in a new era of PDMPs by providing data directly to prescribers and pharmacists. Initially, Nevada sent unsolicited reports to the health care practitioners who had issued and dispensed prescriptions to possible doctor shoppers—that is, individuals receiving multiple simultaneous prescriptions of commonly abused drugs. This resulted in a rapid demand for solicited reports, i.e. reports upon request.[32] While the reports initially were sent by fax, in 2001 Nevada developed an online system that began issuing

[30] What health care providers need to know about PDMP. (2016) US Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/drugoverdose/pdmp/providers.html

[31] Prescription drug monitoring programs. (2016). US Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/drugoverdose/pdmp/index.html

[32] Using PDMPs to improve medical care: Washington State's data sharing initiative with Medicaid and workers' compensation. Notes from the Field, NF 4.1, April 2013, PDMP Center of Excellence at Brandeis University

reports based upon users' direct inquiries. Kentucky soon followed Nevada's lead, developing online capabilities within a few years. In 1994, the Alliance initiated a process to help standardize electronic formats for data collection. This resulted in the publication of the American Society for Automation in Pharmacy's (ASAP) first version of guidelines for pharmacies to submit controlled substances prescription data to PDMPs. The standards have been updated frequently to incorporate enhancements in electronic system capabilities, and all PDMPs are now using a version of an ASAP standard.

In 2002 the federal government created the Harold Rogers Prescription Drug Monitoring Program Grant Program in the Department of Justice, Bureau of Justice Assistance (BJA), funded by a specific appropriation. In 2005, Congress passed the National All Schedules Prescription Electronic Reporting (NASPER) Act.

In 2008, in collaboration with the Alliance and the Heller School of Social Policy and Management at Brandeis University, BJA formed the PDMP Training and Technical Assistance Center, charged with assisting PDMPs in planning, implementing, and enhancing their programs. Two years later BJA funded the PDMP Center of Excellence (COE) at the Heller School in order to provide practice-relevant information, evaluation, and expertise to PDMPs and their stakeholders, including the development of best practices. BJA has maintained a focus on developing PDMP best practices and encouraging innovative applications of PDMP data. BJA has given priority funding consideration to states proposing to implement evidence-based practices that contribute to PDMP effectiveness.

Beginning in 2014, the Center for Disease Control and Prevention (CDC) began funding a Prevention Boost State Program to equip states with the resources and scientific assistance to prevent prescription opioid overdoses by addressing the inappropriate prescribing that fuels the epidemic. The funding supports three key areas, including maximizing PDMPs. For this federal fiscal year, BJA has allocated approximately $12 million for PDMPs while the CDC Prevention Boost has allocated approximately $70 million, a significant portion of which will go to PDMPs. With increasing grants in 2015 and 2016, the CDC is becoming the provider of the most funding support for PDMP enhancements and technical assistance.[33]

As a result of increased public and private support and the growing recognition of PDMPs' potential to address the prescription drug abuse epidemic, PDMPs have proliferated rapidly.

PDMPs are well positioned to serve the dual objectives of improving medical care and reducing diversion of these important medications. This is analogous to the collaboration of public health and law enforcement agencies in reducing automobile accidents, injuries, and fatalities.

EFFECTIVENESS

Evidence indicates PDMPs are effective in addressing the opioid epidemic shattering our families.[34] PDMP data are irreplaceable in identifying questionable activity with respect to prescription drugs, such as doctor and pharmacy shopping, prescription fraud, and problematic

[33] CDC-Drug overdose prevention. US Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/injury/pdfs/budget/fy2016_pres_budget_final_drug-overdose-prevention.pdf

[34] Briefing on PDMP effectiveness. (2013, April). PDMP Center of Excellence, Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/briefing_PDMP_effectiveness_april_2013.pdf

prescribing. No other system exists that can compile all controlled substances prescriptions, regardless of who is issued the prescription, which pharmacy dispensed it, or the source of payment. According to surveys of PDMP users and a study of emergency department doctors, PDMPs are an important tool in making sound clinical decisions when prescribing or dispensing controlled substances. [35]

PDMP data can also be used to track emerging trends in legitimate prescribing, to evaluate efforts to improve prescribing practices, such as provider education initiatives, and epidemiological surveillance and early warning systems. Several additional studies further suggest a connection between PDMP utilization or particular PDMP practices and positive outcomes related to improving, prescribing, and reducing prescription drug misuse and substance abuse disorder.[36]

THE TRAGEDY: A VASTLY UNDERUTILIZED CLINICAL TOOL

Although 49 states and the District of Columbia have legislation authorizing the creation and operation of PDMPs, in the vast majority of our states this effective clinical tool is significantly underutilized. A 2015 study of primary care prescribers found that while a majority reported having obtained data from their PDMP at some point in time, prescribers consulted PDMP data in fewer than one-quarter of instances when they prescribed opioids to patients. In a recent review of 2015 prescribing data in a sample of states where prescriber's have discretion of whether to request patient information from their state PDMP prior to considering issuing a prescription for an opioid, prescribers did so only 14% of the time before prescribing an opioid.[37] **These facts clearly indicate that state legislation which mandates that prescribers view PDMP data before making a decision to prescribe is the single most critical success factor for the effectiveness of PDMPs to save lives of citizens.**

"Having been a public health professional for 46 years and in leadership in preventing prescription drug misuse and abuse for 31 of those years, I am very impressed with the work Shatterproof has done to put together this document and their on-the-ground advocacy in states. This organization understands the vitally important role of PDMPs in helping stop the prescription opioid overdose epidemic and in reversing the role those drugs play in driving new heroin use. This document provides solid recommendations for every state. Governors and state legislatures will be very wise if they adopt all of them."

- John Eadie, Public Health and PDMP Project Coordinator, National Emerging Threat Initiative of the National High Intensity Drug Trafficking Areas (HIDTA) Assistance Center and former Director, PDMP Center of Excellence at Brandeis University

[35] ASPMP, 2007; Kentucky Cabinet for Health and Family Services, 2010; Baehren, 2010

[36] Pearson et al., 2006; Pradel et al., 2009; Reisman et al., 2009; Wang & Christo, 2009; Paulozzi & Stier, 2010; Fisher et al. 2011b; LeMire et al., 2012; Reifler et al., 2012

[37] The prescription opioid epidemic: An evidence-based approach. (2015, November) Johns Hopkins Bloomberg School of Public Health. Retrieved from: http://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/opioid-epidemic-town-hall-2015/2015-prescription-opioid-epidemic-report.pdf

CRITICAL ELEMENTS OF EFFECTIVE STATE LEGISLATION

Shatterproof holds that PDMPs are key tools in the fight against prescription drug misuse and addiction. Their effectiveness is maximized by the adoption of proven best practices, including mandates for prescribers to view PDMP data before making the decision to prescribe all drugs within Schedules II, III and IV of the federal Controlled Substances Act.

The following pages highlight recommendations for legislation that will optimize PDMPs so that their full potential is achieved in saving lives that would otherwise be lost to the opioid epidemic.

OVERARCHING PRINCIPLES:

Shatterproof holds that there are three principals that states need to adopt in order to address the prescription opioid overdose epidemic that transcend the legislative language of specific sections of PDMP authorization. These are:

I. PDMPs require sufficient funding to carry out the functions described in this paper. Each state must assure that its PDMP receives adequate funding. In addition to state funds, federal funds that may be available include funding through the Centers for Disease Control and Prevention and the Harold Rogers PDMP Grant Program administered by the Bureau of Justice Assistance.

II. States need to assure that prescribers, dispensers and other healthcare professionals fully understand the appropriate uses of prescription controlled substances and the risks of misuse, abuse, addiction, overdoses and deaths involving these medications, how to intervene with persons who may be addicted, and how to refer such persons into treatment.

III. The CDC issued the Guideline for prescribing of opioids for treatment of chronic pain. States should assure that healthcare professional licensing boards adopt these guidelines, that prescribers use these guidelines in their practices, and that the guidelines become the standard of care.

1. DISPENSERS REPORT SPECIFIED INFORMATION EXPEDITIOUSLY

RECOMMENDED LEGISLATION

1.1. Dispensers required to input the information listed in Appendix C ("Data Elements") to the PDMP on all controlled substances in Schedules II – V in the federal Controlled Substances Act (Appendix A, B) and any drugs the state has specifically scheduled or designated as drugs of concern.[38]

1.2. Dispensers required to submit prescription information to the PDMP within 10 minutes of dispensing, or at a maximum, no later than within 24 hours of dispensing (or by close of next business day).

1.3. Dispensers required to inspect the photo identification of each person picking up the prescription and, if that person is not the patient for whom the prescription was written, report to the PDMP the name, address, date of birth, gender and the relationship of that person to the patient.[39]

1.4. Dispensers required to report the source of payment for the prescription.

RATIONALE

1.1. Inputting information to the PDMP database on all controlled substances in Schedules II – V in the Controlled Substances Act will allow health care providers to see a more comprehensive list of prescription information and make better informed clinical prescribing decisions.

1.2. Timely data entry ensures health care providers are receiving up-to-date information regarding prescribing information on patients.

1.3. Entering information on the individual who physically obtains the prescription medication will allow for authorized recipients of the data collected (physicians, nurses or law enforcement officials) to detect any potential patterns of misuse or abuse. When a PDMP examined prescriptions for Schedule II drugs, it found that 38% were picked up by someone other than the patient. If the person picking up the medication is not identified, the state is making it easy for persons with substance use disorder to obtain drugs undetected and criminal elements to divert medications into drug trafficking.

1.4. Entering information on the source of payment will allow for authorized recipients of the data collected (physicians, nurses or law enforcement officials) to detect potential problematic patterns such as frequent payments in cash.[40] Persons trying to obtain drugs for illegal use often pay in cash to hide what they are doing from being observed by Medicaid, Medicare and health insurance carriers.

[38] Controlled Substances Act. (2009) US Food and Drug Administration. Retrieved from: http://www.fda.gov/regulatoryinformation/legislation/ucm148726.htm#cntlsbb

[39] As of 1/11/2016 the American Society for Automation in Pharmacy standard 4.2 for pharmacies to transmit controlled substances data to PDMPs has fields for information on the person dropping off or picking up the prescription if other than the patient (i.e. data fields AIR03 through AIR08). Included are the person's first and last names, the relationship to the patient, and an ID number. Should state legislation also require, the address, date of birth and gender, the ASAP standard will need to be modified, which can be done.

[40] For a description of PDMP measures indicative of possible at-risk prescribing, see Definitions of Prescription Behavior Surveillance System (PBSS) Measures, Section 5: Pill Mill Measures, pp. 4-7, http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures%20112113.docx

2. PRESCRIBERS QUERY PDMP BEFORE PRESCRIBING DRUGS IN SCHEDULES II, III AND IV

RECOMMENDED LEGISLATION

2.1. Prescribers or their delegates required to request and review a patient's previous twelve-month prescription history report prior to prescribing any drug included in Schedules II through IV of the Controlled Substances Act.

Exceptions may be permitted for:

- Terminally ill patients under the supervised care of a hospice program
- Prescriptions of three days or less supply with no refills
- Rare instances when it is impossible to query the PDMP in a timely manner due to an emergency situation or if the program is not operational due to technological or electrical failure or natural disaster
- Patient is in a long-term care facility where medication orders are filled by its own pharmacy or hospital pharmacy
- Patients being administered methadone or buprenorphine for treatment of opioid addiction – if drug is dispensed, cannot be exempted

RATIONALE

2.1 Not all enrolled prescribers regularly use PDMPs. Less than half of states with PDMPs legally mandate prescribers to query the system before writing for controlled substances with recognized potential for abuse or dependence or that pose danger to patients when used concurrently with existing prescriptions. As a result, prescribers are solely reliant on information shared by patients to inform clinical decision-making. This practice is fraught with risk because a patient who is misusing opioid medications or has an opioid use disorder may be motivated to conceal prescription history, or alternatively, a patient's memory or understanding of their own drug intake may be inaccurate or incomplete.

Medications that are classified in Schedule I by the Controlled Substances Act, or drugs that currently have no accepted medical use in the U.S., are not prescribed for or dispensed to patients. Without mandated reporting of medications that are classified in Schedules II through IV, which can be prescribed and dispensed by healthcare providers, the prescribers do not know if a drug can be safely prescribed and how much. Prescribers are unable to detect prescription drug misuse and may unintentionally expose patients to dangerous and sometimes fatal drug quantities or combinations. Controlled substances in Schedules II, III and IV contain opioids, sedatives/tranquilizers, and stimulants which are subject to misuse, substance use disorder, overdose, injury and death. Schedule II and III substances include frequently prescribed painkillers including oxycodone and hydrocodone; Schedule IV prescriptions include central nervous system depressants, including Benzodiazepines like Xanax or Valium, that when mixed with Schedule II and III substances can be fatal. Mandated PDMP-generated intelligence on a patient's current or past Schedule II and III substance history offers health care providers vital, and sometimes life-saving, background information to inform sound clinical and prescribing decisions. It will also deter "doctor shoppers" from asking for medications within Schedules II thru IV, with potentially fatal outcomes.

WHY SCHEDULE IV?

The dangers of opioids are beginning to become well known. And in this regard, policy makers are beginning to legislate that prescribers check a patient's prescribing history before considering prescribing an opioid.

So if most opioids are listed in Schedule's II and III, why do the Shatterproof recommendations include a prescriber checking a patient's history before considering prescribing drugs listed in Schedule's II, III and IV?

The most important reason is that Schedule IV includes benzodiazepines, which if taken concurrently with an opioid can be extremely dangerous. In fact, Guideline #11 in the recently released CDC Guideline for Prescribing Opioids for Chronic Pain states:

"Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible."

FURTHER BACKGROUND IN THE GUIDELINE STATES:

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. One case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants.

Recent data confirms that both overdoses and deaths involving combinations of opioid analgesics and benzodiazepines are rising:

A 2016 study published in the American Journal of Public Health found that in 2013 22,767 people died of an overdose involving prescription drugs in the United States. Benzodiazepines were involved in 31% of these fatal overdoses.

- A 2015 study published in the British Medical Journal found approximately 50% of the veterans who died from drug overdose between 2004 and 2009 were prescribed opioids and benzodiazepines at the same time. Those at highest risk of death were those receiving the larger quantities of benzodiazepines.[41]
- Beyond benzodiazepines, Schedules II, III and IV controlled substances contain sedatives/tranquilizers, and stimulants which are subject to abuse, addiction and death.
- For further information on drugs that are contained in each of Schedules II, III and IV, see Appendix A, B.

[41] Park, T.W., Saitz, R., Ganoczy, D., Ilgen, M.A., & Bohnert, A.S.B. (2015). Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ*. Retrieved from: http://www.bmj.com/content/bmj/350/bmj.h2698.full.pdf

3. LICENSED PRESCRIBERS REGISTER WITH PDMP

RECOMMENDED LEGISLATION

3.1. All prescribers with a U.S. Drug Enforcement Administration (DEA) or state-controlled substance registration number and all state-licensed pharmacists should be required to register with the PDMP upon the initial registration or renewal of the prescriber's professional license or certification. This can be accomplished automatically by the board or agency responsible for licensing, registering, or certifying the prescriber, or can be incorporated into the licensing, registering, or certifying process to be completed by the prescriber at the time s/he applies for initial registration, licensure, certification or renewal.

RATIONALE

3.1 PDMP registration in conjunction with license registration and renewal will ensure prescriber compliance and reinforce the importance of the program. It also makes it possible for these healthcare providers to request data from their state's PDMP.

4. ENABLE DELEGATION OF PDMP DATA QUERIES

RECOMMENDED LEGISLATION

4.1. Allow prescribers and dispensers to designate individuals to act as an agent of said prescriber or dispenser for the purposes of obtaining data from the PDMP. Delegates must be:

- Licensed or registered health care professionals overseen by a professional licensing board, such as a physician assistant, registered nurse, resident physician or pharmacy technician.
- Other employees who report directly to the prescriber or dispenser

In all cases, each delegate must be directly supervised by the prescriber or dispenser and such prescriber or dispenser must be held accountable for the delegate's actions.

RATIONALE

4.1 Prescribers have reported that the time required to obtain PDMP reports is the major obstacle to using the PDMP.[42] Allowing them to delegate this activity to staff removes this obstacle. Enlisting delegates such as nurses, physician assistants, resident physicians or other individuals among the team of health care providers and pharmacy staff, can not only benefit patient care and safeguard prescribing and dispensing activities, but can also save doctors' time.

[42] Rutkow L, Turner L, Lucas, E, et al. (2015). Most primary care physicians are aware of prescription drug monitoring programs, but many find the data difficult to access. *Health Affairs*. 34(3): 484–492. Retrieved from: http://content.healthaffairs.org/content/34/3/484.full.html

5. AUTHORIZE SPECIFIED RECIPIENTS OF PDMP DATA

RECOMMENDED LEGISLATION

5.1. The individuals or officials given direct access must include:

- Prescribers and their designees, including those practicing in Veterans Affairs (VA), Department of Defense (DOD) and Indian Health Service (IHS) facilities and in other states.
- Dispensers and their designees, including those located in VA, DOD and IHS facilities and in other states.
- The state department of public health for purposes of public health research, education, disease intervention, and evaluation of the quality of healthcare provided by healthcare facilities under its regulatory authority.
- Local public health departments for purposes of public health research, education, and disease intervention.
- Professional licensing or certification boards or agencies for prescribers and dispensers who are specifically designated, trained, and supervised for specific investigations.
- Medical examiners, county coroners or others authorized under law to investigate causes of deaths.
- Licensed healthcare professionals at drug and alcohol addiction treatment programs, including individuals licensed or certified to provide substance abuse treatment services.
- Drug court judges and their designees.
- Representatives from the state Medicaid or other state-administered health insurance program.

5.2. Individuals allowed to request specific data from the PDMP database will include:

- Licensed healthcare professional supervisors from Medicare, health insurers, workers compensation programs/insurers for persons enrolled in or covered by their programs, and prescription benefit managers (PBMs) as agents of the third party payers for whom they manage benefits;[43] the above representatives must be authorized to request and receive data for all of the persons enrolled in or covered by their programs.[44]
- Licensed healthcare professional supervisors of VA, DOD and IHS facilities must be authorized to access data regarding individuals enrolled in their healthcare programs as well as the prescribers and dispensers who work for them; the above representatives must be authorized to request and receive data for their systems' prescribers and dispensers and all persons enrolled in or covered by their programs.[45]

[43] PDMPs and third party payers meeting: Report of proceedings. (2014, April) PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_COE_PDMP_3rd_pty_payer_mtg_rpt.pdf

[44] Using PDMPs to improve medical care: Washington State's data sharing initiative with Medicaid and workers' compensation. Notes from the Field, NF 4.1, April 2013, PDMP Center of Excellence at Brandeis University.

[45] Using PDMPs to improve medical care: Washington State's data sharing initiative with Medicaid and workers' compensation. Notes from the Field, NF 4.1, April 2013, PDMP Center of Excellence at Brandeis University.

- Peer review committees in hospitals and other healthcare facilities so they can assess quality of care being provided by healthcare professionals to patients.
- Patients and parents of patients who are minor children.
- Local, state and federal law enforcement and prosecutorial officials as part of an ongoing investigation.

RATIONALE

5.1 Physicians, health care providers and insurers play a key role in addressing prescription drug abuse, and access to PDMP data is key to an effective response. Insurers, while not direct health care providers, do not have a complete understanding of the scope or type of prescribing actually provided to their enrollees without access to PDMP data.[46] With proper guidelines in place to regulate legitimate use of prescription history information, patient confidentiality, and data security, third party payers can become a strategic partner in preventing and identifying abuse.

5.2. Confidential access to data in the PDMP for third party payers and their prescription benefit managers (PBMs), as agents of the third party payers, can improve clinical decision-making and patient health care and safety. PBMs manage the pharmacy benefits for health plans and large employers and possess members' claims data for prescription drugs, and at times, other healthcare goods and services. PBMs do not have visibility of prescriptions paid with cash or those paid by another insurer. The fact that PBMs lack a comprehensive view of an individual patient's prescription history makes it essential for them to be able to request information in the PDMPs for all of the persons enrolled in or covered by their programs.

Software algorithms can be used to identify individuals, pharmacies and prescribers that are potentially using or dispensing controlled substances fraudulently. In addition, PBMs' prescription claims surveillance and prescriber intervention programs often use retrospective analysis to identify members meeting excessive controlled substance use criteria, such as some combination of the use of multiple prescribers, multiple dispensing pharmacies, exceeding a threshold of morphine milligram equivalent (MME) dose, or multiple controlled substance claims over a period of three-to-six months. Prescriber letter interventions through PBMs have been shown to decrease members' controlled substance score and controlled substance drug claims.[47,48] These programs could be enhanced if the PBM has the complete controlled substance prescription history, including cash claims, through access to states' PDMPs.[49]

[46] PDMPs and third party payers meeting: December 2012. (2014, April). Prescription Drug Monitoring Program Center of Excellence at Brandeis. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_COE_PDMP_3rd_pty_payer_mtg_rpt.pdf

[47] Gonzalez A.M., Kolbasovsky A.(2012) Impact of a managed controlled-opioid prescription monitoring program on care coordination. American Journal of Managed Care. 18(9):516-24.

[48] Daubresse M., Gleason P.P., Peng Y., Shah N.D., Ritter S.T., & Alexander C.G. (2014) Impact of a drug utilization review program on high-risk use of prescription controlled substances. Pharmacoepidemiology Drug Safety. 23:419-427.

[49] The prescription opioid epidemic: An evidence-based approach. (2015, November) Johns Hopkins Bloomberg School of Public Health. Retrieved from: http://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/opioid-epidemic-town-hall-2015/2015-prescription-opioid-epidemic-report.pdf

CASE STUDY

The health insurer Aetna reported in 2014 that its PBM "Pharmacy Misuse, Waste and Abuse" program monitors access to opioids through precertification and reviews of pharmacy and medical claims and quantity limits to find patterns of above-normal use. Further, members who have had frequent emergency room visits are identified. Other signs, and suspicion of developing substance abuse problems or a history of controlled substance abuse, also are noted. The program reduced opioid prescriptions among 4.3 million members by 14 percent between January 2010 and January 2012.[50]

In addition to improving the quality of care, allowing third party payer access can provide significant savings to workers compensation claims. According to predictive data from the California Workers Compensation Institute, expanding PDMP access to third party payers in California would have yielded savings of $57 million (4%) in 2011 in claims alone.[51]

[50] Aetna helps members fight prescription drug abuse. (2014, January). Aetna. http://news.aetna.com/news-releases/aetnahelps-members-fight-prescription-drug-abuse/. (Accessed February 3, 2015).

[51] Briefing on PDMP effectiveness. (2013, April). PDMP Center of Excellence, Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/briefing_PDMP_effectiveness_april_2013.pdf

6. PROACTIVELY ANALYZE AND DISTRIBUTE PDMP DATA

RECOMMENDED LEGISLATION

6.1. The PDMP should be required to proactively analyze its data to identify persons who may be using, prescribing, or dispensing prescription controlled substances in a manner that puts patients at risk of injury, overdose, or death or that violates laws or practice standards.

Analyses should measure data against criteria indicative of high-risk drug use or illegal activities.[52]

When probable high-risk behavior is identified, the PDMP should distribute unsolicited reports to the party best able to address it.

State statutes should direct PDMPs to analyze data and send out reports regarding:

- Data regarding patients.
- Data regarding prescribers.
- Data regarding dispensers.

For patients, an example is the State of California that launched its rebuilt PDMP system in December 2015. As each prescriber signs into his/her PDMP account, the account dashboard lists his/her patients who:[53]

- Are currently prescribed more than 100 morphine milligram equivalents per day.
- Have obtained prescriptions from six or more prescribers or six or more pharmacies during the last year.
- Are currently prescribed more than 40 milligrams of methadone daily.
- Have been prescribed opioids for more than 90 consecutive days.
- Are prescribed benzodiazepines and opioids concurrently.

For prescribers, examples include:

- Multiple patients who travel long distances to the prescriber and general practitioners prescribing high dosages or high-risk drug combinations to multiple patients.[54,55]

[52] Prescription Behavior Surveillance System (PBSS). Definitions of PBSS Measures. PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures.pdf

[53] CURES 2.0: Prescription Drug Monitoring Program. California Department of Justice. September 2015-power point slide presentation

[54] Kolodny, A, et al. (2015). The prescription opioid and heroin crisis: A public health approach to an epidemic of addiction. Annual Review of Public Health. 36:559-574.

[55] Fulton-Kehoe, D., Sullivan, M.D., Turner, J.A., et. al. (2015). Opioid poisonings in Washington State Medicaid: Trends, dosing, and guidelines. *Medical Care*. 53(8): 679-685.

For dispensers, examples include:

- Quantities of drugs purchased by the pharmacy (as reported to state and DEA) should be equivalent to quantities dispensed.
- Pharmacies that regularly dispense prescriptions issued by prescribers who appear to be engaged in high-risk prescribing or "pill mill" activity.

The parties to whom PDMPs should distribute unsolicited reports when probable high-risk behavior is identified include:

- For patients at risk of addiction, injury, overdose or death, the patients' prescribers and dispensers should be notified so that they may intervene and, if necessary, refer patients to appropriate treatment.
- When a patient's activity appears to be criminal in nature, such as organized doctor shopping to obtain drugs for street sale, law enforcement should receive a report.
- For prescribers and dispensers, if questionable prescribing or possible mis-prescribing, mis-dispensing or self-misuse is identified, the applicable professional licensure board should receive a report.
- If practitioner criminal behavior is identified, such as "pill mill operation," law enforcement should receive a report.

RATIONALE

6.1 Because they collect a constant stream of comprehensive data, PDMPs are uniquely positioned to identify inappropriate prescribing and misuse patterns among physicians and patients, respectively, as those behaviors emerge. PDMP-generated reports can notify prescribers and dispensers that patients may be misusing or diverting medications, and law enforcement agencies and prescriber licensing boards of questionable activity among prescribers and dispensers.

A 2014 study that surveyed more than 300 physicians in Massachusetts after they received unsolicited reports found that only 8 percent were aware of most, all, or nearly all other prescribers. Nearly 44 percent indicated having sufficient knowledge to determine whether the prescriptions were medically necessary after reviewing the reports, of whom nearly 70 percent felt the prescriptions were unwarranted. A majority of the physicians found the report useful to their practice.[56]

Multiple state-level experiences have shown that a minority of prescribers are responsible for problematic behavior, which PDMPs can detect when proactively monitored. In Florida in 2012, 60 percent of opioid prescriptions originated from the top 10 percent of prescribers in the state. While prescribing frequency and dosage alone do not necessarily denote inappropriate prescribing practices, when brought to light by PDMPs, they provide data points for further law enforcement agency or prescriber licensing board investigation.

[56] Thomas, C.P., Kim, M., Nikitin, R.V., et al. (2014). Prescriber response to unsolicited prescription drug monitoring program reports in Massachusetts. *Pharmacoepidemiology and Drug Safety.* DOI: 10.1002/pds

Additionally, proactive PDMP reporting can allow for early identification of intentional misuse practices. Data identifiable in PDMPs is capable of pinpointing possible patient misuse or substance use disorder by alerting authorities to concerning patterns, such as medical practices that attract a high proportion of possible doctor shoppers and pharmacies that dispense a large volume of prescriptions paid for in cash.[57]

Proactive reporting to law enforcement agencies and prescriber licensing boards concerning questionable activity by patients and prescribers, respectively, can also help reduce drug diversion.[58]

[57] Data from the Prescription Behavior Surveillance System (PBSS) as presented by Dr. Len Paulozzi at the 2013 Harold Rogers PDMP National Meeting, see http://www.pdmpassist.org/pdf/PPTs/National2013/26-8-A%20Paulozzi.pdf slide 21.

[58] Guidance on PDMP Best Practices. Options for Unsolicited Reporting. Prescription Drug Monitoring Program Center of Excellence at Brandeis. Published January 2014. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_COE_Guidance_on_Unsolicited_Reporting_final.pdf

7. REQUIRE INTERSTATE SHARING OF PDMP DATA

RECOMMENDED LEGISLATION

7.1 Each state with a PDMP must provide for appropriate interstate sharing of PDMP data with other states' PDMPs by statute, regulation, or interstate agreement.

7.2 Users of PDMP data from the sending state through the receiving state's PDMP must include all users with direct access to PDMP data in the sending state, but at minimum:

- Prescribers & dispensers.
- When part of an ongoing investigation, trained and supervised law enforcement and professional licensing board investigators.
- PDMP officials, or other specified authorities.

7.3 Upon receipt of requests from prescribers and dispensers for patient prescription histories, PDMPs should routinely request data from all adjoining states as well as providing data from within the PDMP's own database.

RATIONALE

7.1. Current PDMPs are limited within state lines and may not be able to detect cases of individuals who filled prescriptions in other states.

7.2. Permitting interstate sharing of information will help providers more quickly identify cases of doctor shopping, where patients may have gone out of state for an opioid prescription. In addition, frequently a college student will have a doctor prescribing medication in his or her home state and then another doctor at college. To protect the health of this student, interstate sharing of information is a must.

7.3. Prescribers and dispensers need the full prescription history for each patient for clinical evaluation prior to issuing or dispensing prescriptions. Yet patients may also obtain prescriptions from others. PDMP data show that while a large majority of prescriptions dispensed in a state were issued by prescribers in that state, 5% or more are issued by prescribers in adjoining states. That leaves about 1% to 2% issued by prescribers in the rest of the US and its territories. Thus, if the PDMP routinely requests data from the adjoining states, they can provide to the requesting prescribers and dispensers all or almost all of the prescriptions they need to see. The requesters are also able to specify the additional state or territory from which they request data, should they be aware of a patient's travel to those locations.

8. PROVIDE DE-IDENTIFIED INFORMATION

RECOMMENDED LEGISLATION

8.1 PDMP administrator authorized to disclose de-identified data for statistical, public research, public policy, or educational purposes. Prior to disclosure, the PDMP administrator should remove information that identifies, or could reasonably be used to identify, the patient, prescriber, dispenser, or other person who is the subject of the information. For purposes of epidemiological use, the dates of birth and the zip codes should be left unchanged in the data whenever feasible. States may opt to charge for the provision of this information to apply toward the costs associated with sharing this information.

RATIONALE

8.1. Current means of obtaining data do not allow proper assessments of PDMPs and accurate measurement of their success against the growing use and abuse of prescription painkillers. By allowing the use of de-identified data to be shared with researchers and other authorized personnel, patterns and trends may be identified that could aid in the effort to end addiction on a broad scale. In particular, the CDC and the FDA fund a Prescription Behavior Surveillance System (PBSS) at the PDMP Center of Excellence (COE) at Brandeis University. States participate in this system by providing quarterly de-identified data to the PDMP COE. In return, the states receive back reports of analyzed data using 43 trend measures that permit states to understand the level of the epidemic, identify the rates of doctor shopping and other signs of high risk danger in prescription patterns, and evaluate effectiveness of interventions.

9. TAKE A COMMUNITY-BASED APPROACH TO PDMP DATA

RECOMMENDED LEGISLATION

9.1. PDMPs required to work with their states' Departments of Public Health and Substance Abuse Services to utilize their epidemiological capabilities to identify community hot spots, target prevention programs, assign resources for substance abuse treatment, and assist in interventions to address overprescribing, such as sending letters to the top prescribers in each therapeutic category of controlled substances.

9.2. Using de-identified data, PDMPs required to work with law enforcement to track the intersection of prescription opioid overprescribing, misuse and overdoses with heroin trafficking in order to warn communities of increasing heroin risks. Since four out of five heroin users begin using heroin following nonmedical use of prescription opioids,[59] communities where opioids are most used and misused would appear to be at highest risk for increases in heroin use.

To facilitate this type of work, states should consider joining the Prescription Behavior Surveillance System.[60] In addition, technical assistance is available from the PDMP Center of Excellence on using PDMP data for these purposes.

RATIONALE

9.1. PDMPs can serve a wider purpose than data records for prescribers and dispensers. When properly used, PDMPs have the potential to offer additional stakeholders in the fight against the opioid epidemic, essential information which could help assist in prevention and treatment of substance use disorders. Data from PDMPs identify the levels of persons in need of prevention and treatment so states can target limited resources to the communities with the greatest problems. As the number of substance use disorders moves up or down within communities or between communities, states should routinely review the PDMP data to monitor these changes and make adjustments in assignment of resources as needed.

9.2. State governments and law enforcement can and should consider PDMP data an early warning system for communities, and leverage the data to help address the epidemic on a community level.

[59] Volkow, N.D. (2014). America's addiction to opioids: Heroin and prescription drug abuse. Presented May 14, 2014. Retrieved from: https://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2016/americas-addiction-to-opioids-heroin-prescription-drug-abuse

[60] Prescription Behavior Surveillance System (PBSS). Definitions of PBSS Measures. PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Definitions%20of%20PBSS%20Measures.pdf

10. LINK PDMP DATA TO PAIN AND ADDICTION TREATMENT

RECOMMENDED LEGISLATION

10.1. PDMPs required to assist prescribers and dispensers in referring patients to pain and substance use disorder treatment.

State statutes should:

- Direct PDMPs to provide prescribers and dispensers links to pain and substance use disorder professionals and treatment centers as well as guidelines for intervening with persons with possible substance use disorders on their web pages.
- Direct PDMP administrators to refer prescribers and dispensers whom the data indicate may be impaired to the appropriate professional licensing or certification agency for investigation and referral to impaired professionals associations, as appropriate.

RATIONALE

10.1 Raw data spotting potential opioid abuse and misuse has limited value if it does not effectively foster intervention. Beyond identifying individuals who may have substance use disorders, PDMPs should assist prescribers in establishing linkages between these individuals and pain and substance use disorder treatment professionals.

Additionally, enabling PDMP administrators to take action and report at-risk prescribers can be an effective action. Kentucky's PDMP sends reports on prescribers to investigators at the state's Drug Enforcement and Professional Practices Branch (DEPPB). From July 2012 (the start of this initiative) to November 2013, DEPPB received 95 cases for review.[61] Actions thus far have resulted in retirements, agreed orders setting out sanctions and terms to be imposed upon the prescriber, and controlled substance license revocations.[62]

[61] Data from DEPPB provided courtesy of KASPER.

[62] Using PDMP Data to Guide Interventions with Possible At-Risk Prescribers. (2014, October). PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Using_PDMP_Data_Guide_Interventions_at_Risk_Prescribers.pdf

11. INSTITUTE CONFIDENTIALITY PROTECTIONS

RECOMMENDED LEGISLATION

11.1. Requirement that PDMP law or other state law that applies to the PDMP require confidentiality protections from improper use of the system or of information from the PDMP. These are important statutory and programmatic provisions.

- PDMP data should not be subject to public or open records laws, civil subpoena or disclosure or be discoverable, compelled to be produced in any civil proceeding, nor deemed admissible as evidence in any civil proceeding where a prescriber or dispenser is not a named party.
- The enabling statute for the PDMP or other statute applicable to the PDMP should include civil and criminal penalties for knowingly disclosing, using or obtaining information other than as authorized by law.
- The PDMP administering agency should be required to maintain procedures to protect the privacy and confidentiality of patients and to ensure that data collected, recorded, transmitted, and maintained pursuant to the PDMP law is not disclosed or used except as authorized by the law.
- The law should mandate that auditable records are kept of every release of identified data.
- While PDMPs should provide patients and parents access to the data held by the database (as above under item 2), PDMPs should be exempted from state information practices acts that require the PDMP to reveal to an individual his/her prescription records and, when demanded, correct those records. The pharmacy that dispensed each prescription and submitted the information to the PDMP is the only party that should make such correction.

RATIONALE

11.1 Data held by PDMPs is confidential health information that should only be accessed and used by persons and organizations expressly authorized for that purpose by state law and regulation. To assure that the data is restricted to these authorized users and uses, states must provide statutory protections to the data and penalties if someone violates those protections. To ensure consistent use and acceptance of PDMP practices, it is critical that this confidentiality be clearly communicated and uniformly enforced.

12. ESTABLISH BASELINE EVALUATION MEASURES

RECOMMENDED LEGISLATION

12.1 Requirement to report basic measures of PDMP registration, utilization, prescribing, and patient risk measures. Using these data, produce quarterly and annual reports that can be used to track trends in controlled substance use and assess the PDMP's performance and impact. The reports should contain data from prior quarters and/or years to allow trend analysis by comparing the most recent time period to previous time periods. Provide such reports to the Governor, legislature, other key stakeholders and post them on the PDMPs' websites and a website open to the public. Areas that should be described in reports include:

- Registrations with the PDMP, including but not limited to:
  - Number of prescribers, by type of practice, e.g. physician, dentist, nurse practitioner, physician assistant, podiatrist, optometrist, veterinarian, and dispensers who have registered with the PDMP.
  - For each type of prescriber and dispenser, the percentage registered of all in-state practitioners who have a DEA registration.
  - Numbers of law enforcement and professional licensing board investigators registered with the PDMP.
- Use of PDMP Data, including but not limited to:
  - Number of requests for PDMP reports made by prescribers, dispensers, law enforcement, professional licensing boards and other users.
  - The ratio of requests to volume of prescriptions, for each category of user above.
  - At least annually, calculate the ratio of requests by each type of prescriber, i.e., number of requests made by physicians, dentists, nurse practitioners, physician assistants, podiatrists, and others divided by number of prescriptions issued by each group.
  - Number of unsolicited reports/alerts provided, by category of recipient, i.e. prescribers, dispensers, law enforcement, professional licensing boards and other users.
  - At least annually, the ratio of unsolicited reports sent to each category of user divided by the number of users in each category should be calculated, including by each type of prescriber.
  - Comparison of a state's use of data to other states.

- At least annually, prescribers' compliance with mandate to review PDMP data, including but not limited to:
  - Collect audit data on each prescriber's queries to the PDMP.
  - Calculate each prescriber's ratio of data requests to number of prescriptions issued by that prescriber that required pre-check with the PDMP.
  - Prescribers with low ratios can be sent letters by state health departments, professional licensing boards, or the PDMP, encouraging better compliance with the mandate.
  - For prescribers with the very lowest ratios and/or those who previously received letters but made no change in practice, investigations and, if necessary, proceedings should be undertaken by professional licensing boards.
- Changes in prescribing and risk measures over multiple quarters and years, including but not limited to:
  - Total prescriptions by therapeutic category, and by specific drug
  - Geographical distribution of prescribed drugs by county or municipal area, by total and by therapeutic category (can be done by mapping)
  - Number of prescriptions per 100,000 population
  - Number of dosage units per 100,000 population
  - Number of morphine milligram equivalents (for opioids) per 100,000 population
- Changes in patients' risk measures, for example, including but not limited to:
  - Number of individuals meeting threshold for multiple provider episodes.
  - Number of patients being prescribed over 100 morphine milligram equivalents.
  - Number of patients being prescribed opioids and benzodiazepines during the same time period.

RATIONALE

12.1 One of the key uses for PDMPs is the ability to measure success of the programs in order to evolve and improve upon the process. However, there is currently no protocol in place to formally track data to report basic measures of PDMP registration, utilization, prescribing, and patient risk measures. Putting in place a system and reporting structure for evaluating the success of PDMPs will enable more uniform assessment of PDMP success.

SHATTERPROOF
STRONGER THAN ADDICTION

STRONG STATE LEADERSHIP: SAVING THE LIVES OF THEIR RESIDENTS

It requires strong leadership by state elected officials to stop the epidemic of prescription drug overdoses and death. Recognizing that discretionary use of PDMPs is not effective in maximizing the benefits of PDMPs, elected leadership in several states began passing legislation in 2012 requiring various aspects related to utilizing its PDMPs.

Shatterproof applauds the leadership in the following seven states for passing legislation that captures most of the elements in *Shatterproof's Critical Elements of Effective State Legislation:*

Kentucky	New York	Tennessee	Connecticut	Ohio	Wisconsin	Massachusetts
2012	2013	2013	2015	2015	2016	2016

Stories of Success

Three states passed legislation in 2012 and 2013 which included many of the elements in *Shatterproof's Critical Elements of Effective State Legislation.* It is important to note that as a result these states are seeing significant increases in PDMP use simultaneous with decreases in key indicators including doctor shopping, prescriptions for the most misused drugs, co-prescribing of opioids and benzodiazepines, and high risk prescribing of large dose opioids. At the same time, prescribing of buprenorphine, a medication used to help treat OUD, has increased.

Summarized on the following pages are the experiences of these states.

KENTUCKY

THE LEGISLATION

- Enacted April, 2012. Effective July 2012.
- First state in the nation to mandate comprehensive PDMP use.

RECOMMENDATIONS INCLUDED*

1. Dispensers Reporting of Information	24 Hour Reporting
2. Prescriber Query	Schedule II, III and IV – First time, every 3 months in most situations
3. Prescriber Registration	All Shatterproof Recommendations
4. Delegates	All Shatterproof Recommendations
5. Authorized Recipients	Most Shatterproof Recommendations

6. Proactive Analysis	Most Shatterproof Recommendations
7. Interstate Sharing	Most Shatterproof Recommendations
8. De-Identified Information	All Shatterproof Recommendations
11. Confidentiality	Most Shatterproof Recommendations
12. Evaluation	Most Shatterproof Recommendations

THE RESULTS

- 13.4% decline in prescriptions of opioids dispensed (twelve months prior to June 2015 compared to twelve months prior to June 2012). [63]
- 17.7% decline in prescriptions of sedatives dispensed (twelve months prior to June 2015 compared to twelve months prior to June 2012). [63]
- 26% decline in prescription overdose hospitalizations after the program's inception.[64,65]
- 25% decline in prescription opioid deaths, the first decline in a decade.[66]
- Nearly 90% increase in prescriptions for buprenorphine, a medication used to treat opioid addiction.[67]
- 465% increase in prescriber's average requests for reports (2011 to 2013).[68]

Every 1% reduction in opioids prescribed for chronic pain will result in an approximate 1% - 1.2% reduction in overdose deaths.

[63] Kentucky Office of Drug Control Policy.

[64] PDMP Center of Excellence at Brandeis University. Bureau of Justice Assistance Prescription Drug Monitoring Program Performance Measures Report: January 2009 through June 2012. Revised 2014. Available at: http://www.pdmpexcellence.org/sites/all/pdfs/BJA_PDMP_Performance_Measures_1_09_6_12_fdbk.pdf.

[65] The prescription opioid epidemic: An evidence-based approach. (2015, November) Johns Hopkins Bloomberg School of Public Health. Retrieved from: http://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/opioid-epidemic-town-hall-2015/2015-prescription-opioid-epidemic-report.pdf

[66] Ingram V, Kentucky Executive Director, Office of Drug Control Policy. Email correspondence to Eadie, JL. 6 March 2015 and 12 March 2015.

[67] The prescription opioid epidemic: An evidence-based approach. (2015, November) Johns Hopkins Bloomberg School of Public Health. Retrieved from: http://www.jhsph.edu/research/centers-and-institutes/center-for-drug-safety-and-effectiveness/opioid-epidemic-town-hall-2015/2015-prescription-opioid-epidemic-report.pdf

[68] Mandating PDMP participation by medical providers: current status and experience in selected states. (2014, February). PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/COE%20briefing%20on%20mandates%20revised_a.pdf

*As two of the twelve recommendations are new to the field, they have been excluded from this analysis

SHATTERPROOF
STRONGER THAN ADDICTION

NEW YORK

THE LEGISLATION

- Enacted June 2013; effective August 2013.
- First state to require prescribers request and review a patient's prescription history prior to prescribing any drug included in Schedules II through IV.

RECOMMENDATIONS INCLUDED*

1. Dispensers Reporting of Information	24 Hour Reporting
2. Prescriber Query	Schedule II, III and IV – Every time
3. Prescriber Registration	Does not require
4. Delegates	All Shatterproof Recommendations
5. Authorized Recipients	Many Shatterproof Recommendations
6. Proactive Analysis	Most Shatterproof Recommendations
7. Interstate Sharing	Most Shatterproof Recommendations
8. De-Identified Information	Most Shatterproof Recommendations
11. Confidentiality	Most Shatterproof protections in place
12. Evaluation	Some Shatterproof Recommendations

THE RESULTS

Between Q4 2012 and Q4 2013:

- 9% decline in the number of opioid painkillers prescribed
- 75% decline in patients' seeing multiple prescribers for the same drugs
- 15% increase in the number of buprenorphine prescriptions (medication used to treat opioid addiction)
- 11,400% increase in requests for PDMP reports[69]

Every 1% reduction in opioids prescribed for chronic pain will result in an approximate 1% - 1.2% reduction in overdose deaths.

[69] Mandating PDMP participation by medical providers: current status and experience in selected states. (2014, February). PDMP Center of Excellence at Brandeis University. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/COE%20briefing%20on%20mandates%20revised_a.pdf

*As two of the twelve recommendations are new to the field, they have been excluded from this analysis

TENNESSEE

THE LEGISLATION

- Effective April 2013.

RECOMMENDATIONS INCLUDED*

1. Dispensers Reporting of Information	24 Hour Reporting
2. Prescriber Query	Opioids, Benzodiazepines. First time, Annually
3. Prescriber Registration	All Shatterproof Recommendations
4. Delegates	All Shatterproof Recommendations
5. Authorized Recipients	Most Shatterproof Recommendations
6. Proactive Analysis	Most Shatterproof Recommendations
7. Interstate Sharing	Most Shatterproof Recommendations
8. De-Identified Information	Area for improvement
11. Confidentiality	Most Shatterproof Recommendations
12. Evaluation	Some Shatterproof Recommendations

THE RESULTS

From 2012 to 2014:

- 7% decline in the number of opioid prescriptions
- 36% decline in persons involved in multiple provider episodes[70]
- 405% increase in requests for PDMP reports in first year[71]

Every 1% reduction in opioids prescribed for chronic pain will result in an approximate 1% - 1.2% reduction in overdose deaths.

[70] PDMP Center of Excellence at Brandeis University. Mandating PDMP participation by medical providers: current status and experience in selected states. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/COE%20briefing%20on%20mandates%20revised_a.pdf

[71] Controlled substance monitoring database: 2015 report to the 109th Tennessee General Assembly. (2015, February). Tennessee Department of Health: Health Licensure & Regulation, Controlled Substance Monitoring Database Committee.

*As two of the twelve recommendations are new to the field, they have been excluded from this analysis

Inspired by this and other compelling evidence of the effectiveness of PDMP legislation, in 2015 and 2016, leadership from the states of Connecticut, Massachusetts, Ohio and Wisconsin each drove enactment of PDMP legislation requiring many of the components of *Shatterproof's Critical Elements of Effective State Legislation*. These states and their leadership are true pioneers in the mission to protect the lives of their residents.

CONCLUSION

Shatterproof, in conjunction with leaders in substance use disorder treatment across the country, believes strongly that PDMPs can and will be a key piece of the puzzle in solving our national health crisis. However, we cannot make this happen alone, and the support of state governors and legislators is required.

Together, we can reduce the number of our loved ones who become addicted to opioids and the tragic shattering of lives caused by this preventable epidemic.

APPENDIX A

FEDERAL CONTROLLED SUBSTANCES ACT

Schedules I-V of Controlled Substances (Federal Controlled Substances Act)

- Schedule I
  - (A) The drug or other substance has a high potential for abuse.
  - (B) The drug or other substance has no currently accepted medical use in treatment in the United States.
  - (C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.
- Schedule II
  - (A) The drug or other substance has a high potential for abuse.
  - (B) The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.
  - (C) Abuse of the drug or other substances may lead to severe psychological or physical dependence.
- Schedule III
  - (A) The drug or other substance has a potential for abuse less than the drugs or other substances in schedules I and II.
  - (B) The drug or other substance has a currently accepted medical use in treatment in the United States.
  - (C) Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence.
- Schedule IV
  - (A) The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III.
  - (B) The drug or other substance has a currently accepted medical use in treatment in the United States.
  - (C) Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

- Schedule V
  - (A) The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV.
  - (B) The drug or other substance has a currently accepted medical use in treatment in the United States.
  - (C) Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.

APPENDIX B

SCHEDULED CONTROLLED SUBSTANCES: THERAPEUTIC CATEGORIES & EXAMPLES OF EACH WITH GENERIC AND (BRAND) NAMES

Schedules	Opioids	Sedatives & Tranquilizers	Stimulants	Other
II	Fentanyl (Duragesic) Hydrocodone (Lortabs) Morphine (MS Contin) Oxycodone (OxyContin)	Amobarbital (Amytal Sodium) Secobarbital (Seconal)	Dextroamphetamine (Adderall) Methamphetamine (Desoxyn) Methylphenidate (Ritalin)	
III	Buprenorphine (Bupranex) Codeine (Empirin with Codeine)	Butabarbital (Busodium) Butalbital (Fioranol)	Benzpheatmine (Didrex) Phendimetrazine (Phendiet)	Muscle relaxants: Carisoprodol (Soma) Anabolic Steroids: Testosterone (Androderm)
IV	Propoxyphene (Darvon) Tramadol (Ultram)	Benzodiazepines: Alprazolam (Xanax) Diazepam (Valium) Triazolam (Halcion)	Mefenorex (Rondimen) Phentermine (Obenix)	

APPENDIX C
DATA ELEMENTS

List of data elements dispensers should submit to PDMPs for each prescription.

1. (I) Dispenser identification number.
2. (II) Date prescription filled.
3. (III) Prescription number.
4. (IV) Prescription is new or is a refill.
5. (V) NDC code for drug dispensed.
6. (VI) Quantity dispensed.
7. (VII) Days' supply dispensed
8. (VIII) Number of refills ordered
9. (IX) Patient identification number.
10. (X) Patient name.
11. (XI) Patient address.
12. (XII) Patient date of birth.
13. (XIII) Patient gender
14. (XIV) Prescriber identification number.
15. (XV) Date prescription issued by prescriber.
16. (XVI) Person who receives the prescription from the dispenser, if other than the patient, including name, address, date of birth, gender and the relationship of that person to the patient.
17. (XVII) Source of payment for prescription.
18. (XVIII) State issued serial number [if state chooses to establish a serialized prescription system].

APPENDIX D
CDC GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

SHATTERPROOF
STRONGER THAN ADDICTION

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC's *Guideline for Prescribing Opioids for Chronic Pain* is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

CLINICAL REMINDERS

- **Opioids are not first-line or routine therapy for chronic pain**
- **Establish and measure goals for pain and function**
- **Discuss benefits and risks and availability of nonopioid therapies with patient**

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LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

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OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

CLINICAL REMINDERS

- **Use immediate-release opioids when starting**
- **Start low and go slow**
- **When opioids are needed for acute pain, prescribe no more than needed**
- **Do not prescribe ER/LA opioids for acute pain**
- **Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if needed**

4 When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5 When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

6 Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7 Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

8 Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9 Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (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.

10 When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11 Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12 Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

CLINICAL REMINDERS

- **Evaluate risk factors for opioid-related harms**
- **Check PDMP for high dosages and prescriptions from other providers**
- **Use urine drug testing to identify prescribed substances and undisclosed use**
- **Avoid concurrent benzodiazepine and opioid prescribing**
- **Arrange treatment for opioid use disorder if needed**

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

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CONTENTS

Disclosure of Relationship

The Core Expert Group (CEG) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Pam Archer discloses authorship of the Oklahoma Emergency Department and Urgent Care Clinic Opioid Prescribing Guidelines and the Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office Based Setting; Bonnie Burman discloses authorship of the Ohio Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain; Jane Ballantyne discloses that she has served as a paid consultant to Cohen Milstein Sellers & Toll, PLLC, and has special advisory committee responsibilities on the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategies committee; Phillip Coffin discloses that in 2012 he provided expert testimony to the California State Assembly regarding a bill to expand naloxone access and reports that he is the principal investigator on a research study of methamphetamine dependence that receives donated injectable naltrexone from Alkermes, Inc.; Gary Franklin discloses authorship of the AMDG Interagency Guideline on Prescribing Opioids for Pain; Erin Krebs discloses that she represented the American College of Physicians at a 2014 Food and Drug Administration meeting on Abuse Deterrent Opioid Formulations; Lewis Nelson discloses his ad-hoc membership on the FDA Drug Safety and Risk Management Advisory Committee; Trupti Patel discloses authorship of the Arizona Opioid Prescribing Guidelines; Robert "Chuck" Rich discloses that he was an author of the 2013 American Academy of Family Physicians position paper on opioids and pain management; Joanna Starrels discloses that she received honoraria from the Betty Ford Institute; Thomas Tape discloses that he was an author of the 2013 American College of Physicians policy position paper on prescription drug abuse. CDC provided 100% of the funding for the supplemental evidence review tasks and meeting support. No foundation or industry support was accepted.

The Opioid Guideline Workgroup (OGW) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Anne Burns discloses that she participated in a congressional briefing sponsored by Reps. Carter and DeSaulnier on the pharmacist's role of furnishing Naloxone and that she participates on the National Advisory Board for the Prescription Drug Abuse and Heroin Summit. Chinazo Cunningham discloses that her husband is employed by Quest Diagnostics and Dr. Cunningham was recused from any discussion related to urine drug testing. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Erin Krebs discloses that she served on the CDC Opioid Prescribing Guideline CEG. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG. Greg Terman discloses that he serves as the President of the American Pain Society. Mark Wallace discloses that he served on a Kempharma advisory panel for an abuse-deterrent hydrocodone formulation to treat acute postoperative pain and Dr. Wallace was recused form any discussion related to abuse-deterrent drugs.

The NCIPC Board of Scientific Counselors (BSC) members disclose that they have no financial conflicts of interest. Two BSC members, Traci Green and Christina Porucznik, served on the Opioid Guideline Workgroup. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG.

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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Summary

This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.

Introduction

Background

Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (*1*). In 2012, health care providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (*2*). Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties (*3*). Rates of opioid prescribing vary greatly across states in ways that cannot be explained by the underlying health status of the population, highlighting the lack of consensus among clinicians on how to use opioid pain medication (*2*).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment (*4*). Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care (*4*). Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.

Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing (*5*). Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (*4*). Estimates of the prevalence of chronic pain vary, but it is clear that the number of persons experiencing chronic pain in the United States is substantial. The 1999–2002 National Health and Nutrition Examination Survey estimated that 14.6% of adults have current widespread or localized pain lasting at least 3 months (*6*). Based on a survey conducted during 2001–2003 (*7*), the overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) was estimated at 43% among adults in the

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United States, although minimum duration of symptoms was not specified. Most recently, analysis of data from the 2012 National Health Interview Study showed that 11.2% of adults report having daily pain (*8*). Clinicians should consider the full range of therapeutic options for the treatment of chronic pain. However, it is hard to estimate the number of persons who could potentially benefit from opioid pain medication long term. Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks (*9,10*), and patients receiving opioid therapy for chronic pain report some pain relief when surveyed (*11–13*). However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later (*14*). On the basis of data available from health systems, researchers estimate that 9.6–11.5 million adults, or approximately 3%–4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005 (*15*).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States (*16*). In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly (*17*). Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths (*18*). The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (*19*). Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home (*20*). This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder. In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million persons abused or were dependent on prescription opioid pain medication (*21*). Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder (*22–24*), highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15–64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that one in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and one in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (*25*).

This guideline provides recommendations for the prescribing of opioid pain medication by primary care clinicians for chronic pain (i.e., pain conditions that typically last >3 months or past the time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care. Although the guideline does not focus broadly on pain management, appropriate use of long-term opioid therapy must be considered within the context of all pain management strategies (including nonopioid pain medications and nonpharmacologic treatments). CDC's recommendations are made on the basis of a systematic review of the best available evidence, along with input from experts, and further review and deliberation by a federally chartered advisory committee. The guideline is intended to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes such as reduced pain and improved function, and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs. Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient's clinical situation, functioning, and life context. The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care.

Rationale

Primary care clinicians report having concerns about opioid pain medication misuse, find managing patients with chronic pain stressful, express concern about patient addiction, and report insufficient training in prescribing opioids (*26*). Across specialties, physicians believe that opioid pain medication can be effective in controlling pain, that addiction is a common consequence of prolonged use, and that long-term opioid therapy often is overprescribed for patients with chronic noncancer pain (*27*). These attitudes and beliefs, combined with increasing trends in opioid-related overdose, underscore the need for better clinician guidance on opioid prescribing. Clinical practice guidelines focused on prescribing can improve clinician knowledge, change prescribing practices (*28*), and ultimately benefit patient health.

Professional organizations, states, and federal agencies (e.g., the American Pain Society/American Academy of Pain Medicine, 2009; the Washington Agency Medical Directors Group, 2015; and the U.S. Department of Veterans Affairs/Department of Defense, 2010) have developed guidelines for opioid prescribing (*29–31*). Existing guidelines share some common elements, including dosing thresholds, cautious titration, and risk mitigation strategies such as using risk assessment tools, treatment agreements, and urine drug testing. However, there is considerable variability in the specific recommendations (e.g., range of dosing thresholds of 90 MME/day to 200 MME/day), audience (e.g., primary care clinicians versus specialists), use of evidence (e.g., systematic review, grading of evidence and recommendations, and role of expert opinion), and rigor of methods for addressing conflict of interest (*32*). Most guidelines, especially those that are not based on evidence from scientific studies published in 2010 or later, also do not reflect the most recent scientific evidence about risks related to opioid dosage.

This CDC guideline offers clarity on recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input. Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain) (*24,33,34*). Using guidelines to address problematic prescribing has the potential to optimize care and improve patient safety based on evidence-based practice (*28*), as well as reverse the cycle of opioid pain medication misuse that contributes to the opioid overdose epidemic.

Scope and Audience

This guideline is intended for primary care clinicians (e.g., family physicians and internists) who are treating patients with chronic pain (i.e., pain lasting >3 months or past the time of normal tissue healing) in outpatient settings. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians has been above average (*3*). Primary care clinicians include physicians as well as nurse practitioners and physician assistants. Although the focus is on primary care clinicians, because clinicians work within team-based care, the recommendations refer to and promote integrated pain management and collaborative working relationships with other providers (e.g., behavioral health providers, pharmacists, and pain management specialists). Although the transition from use of opioid therapy for acute pain to use for chronic pain is hard to predict and identify, the guideline is intended to inform clinicians who are considering prescribing opioid pain medication for painful conditions that can or have become chronic.

This guideline is intended to apply to patients aged ≥18 years with chronic pain outside of palliative and end-of-life care. For this guideline, palliative care is defined in a manner consistent with that of the Institute of Medicine as care that provides relief from pain and other symptoms, supports quality of life, and is focused on patients with serious advanced illness. Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms (*35*). End-of-life care is defined as care for persons with a terminal illness or at high risk for dying in the near future in hospice care, hospitals, long-term care settings, or at home. Patients within the scope of this guideline include cancer survivors with chronic pain who have completed cancer treatment, are in clinical remission, and are under cancer surveillance only. The guideline is not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care because of the unique therapeutic goals, ethical considerations, opportunities for medical supervision, and balance of risks and benefits with opioid therapy in such care.

The recommendations address the use of opioid pain medication in certain special populations (e.g., older adults and pregnant women) and in populations with conditions posing special risks (e.g., a history of substance use disorder). The recommendations do not address the use of opioid pain medication in children or adolescents aged <18 years. The available evidence concerning the benefits and harms of long-term opioid therapy in children and adolescents is limited, and few opioid medications provide information on the label regarding safety and effectiveness in pediatric patients. However, observational research shows significant increases in opioid prescriptions for pediatric populations from 2001 to 2010 (*36*), and a large proportion of adolescents are commonly prescribed opioid pain medications for conditions such as headache and sports injuries (e.g., in one study, 50% of adolescents presenting with headache received a prescription for an opioid pain medication [*37,38*]). Adolescents who misuse opioid pain medication often misuse medications from their own previous prescriptions (*39*), with an estimated 20% of adolescents with currently prescribed opioid medications reporting using them intentionally to get high or increase the effects of alcohol or other drugs (*40*). Use of prescribed opioid pain medication before high school graduation is associated with a 33% increase in the risk of later opioid misuse (*41*). Misuse of opioid pain medications in adolescence strongly predicts later onset of heroin use (*42*). Thus, risk of opioid medication use in pediatric populations is of great concern. Additional clinical trial and observational research is needed,

and encouraged, to inform development of future guidelines for this critical population.

The recommendations are not intended to provide guidance on use of opioids as part of medication-assisted treatment for opioid use disorder. Some of the recommendations might be relevant for acute care settings or other specialists, such as emergency physicians or dentists, but use in these settings or by other specialists is not the focus of this guideline. Readers are referred to other sources for prescribing recommendations within acute care settings and in dental practice, such as the American College of Emergency Physicians' guideline for prescribing of opioids in the emergency department (*43*); the American Society of Anesthesiologists' guideline for acute pain management in the perioperative setting (*44*); the Washington Agency Medical Directors' Group Interagency Guideline on Prescribing Opioids for Pain, Part II: Prescribing Opioids in the Acute and Subacute Phase (*30*); and the Pennsylvania Guidelines on the Use of Opioids in Dental Practice (*45*). In addition, given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease (*46*).

Guideline Development Methods

Guideline Development Using the Grading of Recommendations Assessment, Development, and Evaluation Method

CDC developed this guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method (http://www.gradeworkinggroup.org). This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method has been adapted by the CDC Advisory Committee on Immunization Practices (ACIP) (*47*). CDC has applied the ACIP translation of the GRADE framework in this guideline. Within the ACIP GRADE framework, the body of evidence is categorized in a hierarchy. This hierarchy reflects degree of confidence in the effect of a clinical action on health outcomes. The categories include type 1 evidence (randomized clinical trials or overwhelming evidence from observational studies), type 2 evidence (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 evidence (observational studies or randomized clinical trials with notable limitations), and type 4 evidence (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). Type of evidence is categorized by study design as well as limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and a constellation of plausible biases that could change observations of effects. Type 1 evidence indicates that one can be very confident that the true effect lies close to that of the estimate of the effect; type 2 evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; type 3 evidence means that confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect; and type 4 evidence indicates that one has very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of the effect (*47*,*48*). When no studies are present, evidence is considered to be insufficient. The ACIP GRADE framework places recommendations in two categories, Category A and Category B. Four major factors determine the category of the recommendation: the quality of evidence, the balance between desirable and undesirable effects, values and preferences, and resource allocation (cost). Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so clinicians must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations (*47*). According to the GRADE methodology, a particular quality of evidence does not necessarily imply a particular strength of recommendation (*48–50*). Category A recommendations can be made based on type 3 or type 4 evidence when the advantages of a clinical action greatly outweigh the disadvantages based on a consideration of benefits and harms, values and preferences, and costs. Category B recommendations are made when the advantages and disadvantages of a clinical action are more balanced. GRADE methodology is discussed extensively elsewhere (*47*,*51*). The U.S. Preventive Services Task Force (USPSTF) follows different methods for developing and categorizing recommendations (http://www.uspreventiveservicestaskforce.org). USPSTF recommendations focus on preventive services and are categorized as A, B, C, D, and I. Under the Affordable Care Act, all "nongrandfathered" health plans (that is, those health plans not in existence prior to March 23, 2010 or those with significant changes to their coverage) and expanded Medicaid plans are required to cover

preventive services recommended by USPSTF with a category A or B rating with no cost sharing. The coverage requirements went into effect September 23, 2010. Similar requirements are in place for vaccinations recommended by ACIP, but do not exist for other recommendations made by CDC, including recommendations within this guideline.

A previously published systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness and risks of long-term opioid treatment of chronic pain (*14,52*) initially served to directly inform the recommendation statements. This systematic clinical evidence review addressed the effectiveness of long-term opioid therapy for outcomes related to pain, function, and quality of life; the comparative effectiveness of different methods for initiating and titrating opioids; the harms and adverse events associated with opioids; and the accuracy of risk-prediction instruments and effectiveness of risk mitigation strategies on outcomes related to overdose, addiction, abuse, or misuse. For the current guideline development, CDC conducted additional literature searches to update the evidence review to include more recently available publications and to answer an additional clinical question about the effect of opioid therapy for acute pain on long-term use. More details about the literature search strategies and GRADE methods applied are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026). CDC developed GRADE evidence tables to illustrate the quality of the evidence for each clinical question.

As identified in the AHRQ-sponsored clinical evidence review, the overall evidence base for the effectiveness and risks of long-term opioid therapy is low in quality per the GRADE criteria. Thus, contextual evidence is needed to provide information about the benefits and harms of nonpharmacologic and nonopioid pharmacologic therapy and the epidemiology of opioid pain medication overdose and inform the recommendations. Further, as elucidated by the GRADE Working Group, supplemental information on clinician and patient values and preferences and resource allocation can inform judgments of benefits and harms and be helpful for translating the evidence into recommendations. CDC conducted a contextual evidence review to supplement the clinical evidence review based on systematic searches of the literature. The review focused on the following four areas: effectiveness of nonpharmacologic and nonopioid pharmacologic treatments; benefits and harms related to opioid therapy (including additional studies not included in the clinical evidence review such as studies that evaluated outcomes at any duration or used observational study designs related to specific opioid pain medications, high-dose opioid therapy, co-prescription of opioids with other controlled substances, duration of opioid use, special populations, risk stratification/mitigation approaches, and effectiveness of treatments for addressing potential harms of opioid therapy); clinician and patient values and preferences; and resource allocation. CDC constructed narrative summaries of this contextual evidence and used the information to support the clinical recommendations. More details on methods for the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

On the basis of a review of the clinical and contextual evidence (review methods are described in more detail in subsequent sections of this report), CDC drafted recommendation statements focused on determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. To help assure the draft guideline's integrity and credibility, CDC then began a multistep review process to obtain input from experts, stakeholders, and the public to help refine the recommendations.

Solicitation of Expert Opinion

CDC sought the input of experts to assist in reviewing the evidence and providing perspective on how CDC used the evidence to develop the draft recommendations. These experts, referred to as the "Core Expert Group" (CEG) included subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline development methodology.* CDC identified subject matter experts with high scientific standing; appropriate academic and clinical training and relevant clinical experience; and proven scientific excellence in opioid prescribing, substance use disorder treatment, and pain management. CDC identified representatives from leading primary care professional organizations to represent the audience for this guideline. Finally, CDC identified state agency officials and representatives based on their experience with state guidelines for opioid prescribing that were developed with multiple agency stakeholders and informed by scientific literature and existing evidence-based guidelines.

Prior to their participation, CDC asked potential experts to reveal possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Experts could not serve if they had conflicts that might have a direct and predictable effect on the recommendations. CDC excluded experts who had a financial or promotional relationship with a company

* A list of the members appears at the end of this report. The recommendations and all statements included in this guideline are those of CDC and do not necessarily represent the official position of any persons or organizations providing comments on the draft guideline.

that makes a product that might be affected by the guideline. CDC reviewed potential nonfinancial conflicts carefully (e.g., intellectual property, travel, public statements or positions such as congressional testimony) to determine if the activities would have a direct and predictable effect on the recommendations. CDC determined the risk of these types of activities to be minimal for the identified experts. All experts completed a statement certifying that there was no potential or actual conflict of interest. Activities that did not pose a conflict (e.g., participation in Food and Drug Administration [FDA] activities or other guideline efforts) are disclosed.

CDC provided to each expert written summaries of the scientific evidence (both the clinical and contextual evidence reviews conducted for this guideline) and CDC's draft recommendation statements. Experts provided individual ratings for each draft recommendation statement based on the balance of benefits and harms, evidence strength, certainty of values and preferences, cost, recommendation strength, rationale, importance, clarity, and ease of implementation. CDC hosted an in-person meeting of the experts that was held on June 23–24, 2015, in Atlanta, Georgia, to seek their views on the evidence and draft recommendations and to better understand their premeeting ratings. CDC sought the experts' individual opinions at the meeting. Although there was widespread agreement on some of the recommendations, there was disagreement on others. Experts did not vote on the recommendations or seek to come to a consensus. Decisions about recommendations to be included in the guideline, and their rationale, were made by CDC. After revising the guideline, CDC sent written copies of it to each of the experts for review and asked for any additional comments; CDC reviewed these written comments and considered them when making further revisions to the draft guideline. The experts have not reviewed the final version of the guideline.

Federal Partner Engagement

Given the scope of this guideline and the interest of agencies across the federal government in appropriate pain management, opioid prescribing, and related outcomes, CDC invited its National Institute of Occupational Safety and Health and CDC's federal partners to observe the expert meeting, provide written comments on the full draft guideline after the meeting, and review the guideline through an agency clearance process; CDC reviewed comments and incorporated changes. Interagency collaboration will be critical for translating these recommendations into clinical practice. Federal partners included representatives from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, FDA, the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Office of the National Coordinator for Health Information Technology, the Centers for Medicare and Medicaid Services, the Health Resources and Services Administration, AHRQ, and the Office of National Drug Control Policy.

Stakeholder Comment

Given the importance of the guideline for a wide variety of stakeholders, CDC also invited review from a Stakeholder Review Group (SRG) to provide comment so that CDC could consider modifications that would improve the recommendations' specificity, applicability, and ease of implementation. The SRG included representatives from professional organizations that represent specialties that commonly prescribe opioids (e.g., pain medicine, physical medicine and rehabilitation), delivery systems within which opioid prescribing occurs (e.g., hospitals), and representation from community organizations with interests in pain management and opioid prescribing.* Representatives from each of the SRG organizations were provided a copy of the guideline for comment. Each of these representatives provided written comments. Once input was received from the full SRG, CDC reviewed all comments and carefully considered them when revising the draft guideline.

Constituent Engagement

To obtain initial perspectives from constituents on the recommendation statements, including clinicians and prospective patients, CDC convened a constituent engagement webinar and circulated information about the webinar in advance through announcements to partners. CDC hosted the webinar on September 16 and 17, 2015, provided information about the methodology for developing the guideline, and presented the key recommendations. A fact sheet was posted on the CDC Injury Center website (http://www.cdc.gov/injury) summarizing the guideline development process and clinical practice areas addressed in the guideline; instructions were included on how to submit comments via email. CDC received comments during and for 2 days following the first webinar. Over 1,200 constituent comments were received. Comments were reviewed and carefully considered when revising the draft guideline.

Peer Review

Per the final information quality bulletin for peer review (https://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf), peer review requirements applied to this guideline because it provides influential

scientific information that could have a clear and substantial impact on public- and private-sector decisions. Three experts independently reviewed the guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations.* CDC selected peer reviewers based on expertise, diversity of scientific viewpoints, and independence from the guideline development process. CDC assessed and managed potential conflicts of interest using a process similar to the one as described for solicitation of expert opinion. No financial interests were identified in the disclosure and review process, and nonfinancial activities were determined to be of minimal risk; thus, no significant conflict of interest concerns were identified. CDC placed the names of peer reviewers on the CDC and the National Center for Injury Prevention and Control Peer Review Agenda websites that are used to provide information about the peer review of influential documents. CDC reviewed peer review comments and revised the draft guideline accordingly.

Public Comment

To obtain comments from the public on the full guideline, CDC published a notice in the *Federal Register* (80 FR 77351) announcing the availability of the guideline and the supporting clinical and contextual evidence reviews for public comment. The comment period closed January 13, 2016. CDC received more than 4,350 comments from the general public, including patients with chronic pain, clinicians, families who have lost loved ones to overdose, medical associations, professional organizations, academic institutions, state and local governments, and industry. CDC reviewed each of the comments and carefully considered them when revising the draft guideline.

Federal Advisory Committee Review and Recommendation

The National Center for Injury Prevention and Control (NCIPC) Board of Scientific Counselors (BSC) is a federal advisory committee that advises and makes recommendations to the Secretary of the Department of Health and Human Services, the Director of CDC, and the Director of NCIPC.* The BSC makes recommendations regarding policies, strategies, objectives, and priorities, and reviews progress toward injury and violence prevention. CDC sought the BSC's advice on the draft guideline. BSC members are special government employees appointed as CDC advisory committee members; as such, all members completed an OGE Form 450 to disclose relevant interests. BSC members also reported on their disclosures during meetings. Disclosures for the BSC are reported in the guideline.

To assist in guideline review, on December 14, 2015, via Federal Register notice, CDC announced the intent to form an Opioid Guideline Workgroup (OGW) to provide observations on the draft guideline to the BSC. CDC provided the BSC with the draft guideline as well as summaries of comments provided to CDC by stakeholders, constituents, and peer reviewers, and edits made to the draft guideline in response. During an open meeting held on January 7, 2016, the BSC recommended the formation of the OGW. The OGW included a balance of perspectives from audiences directly affected by the guideline, audiences that would be directly involved with implementing the recommendations, and audiences qualified to provide representation. The OGW comprised clinicians, subject matter experts, and a patient representative, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, substance abuse treatment, pharmacy, patients, and research.* Additional sought-after attributes were appropriate academic and clinical training and relevant clinical experience; high scientific standing; and knowledge of the patient, clinician, and caregiver perspectives. In accordance with CDC policy, two BSC committee members also served as OGW members, with one serving as the OGW Chair. The professional credentials and interests of OGW members were carefully reviewed to identify possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Only OGW members whose interests were determined to be minimal were selected. When an activity was perceived as having the potential to affect a specific aspect of the recommendations, the activity was disclosed, and the OGW member was recused from discussions related to that specific aspect of the recommendations (e.g., urine drug testing and abuse-deterrent formulations). Disclosures for the OGW are reported. CDC and the OGW identified ad-hoc consultants to supplement the workgroup expertise, when needed, in the areas of pediatrics, occupational medicine, obstetrics and gynecology, medical ethics, addiction psychiatry, physical medicine and rehabilitation, guideline development methodology, and the perspective of a family member who lost a loved one to opioid use disorder or overdose.

The BSC charged the OGW with reviewing the quality of the clinical and contextual evidence reviews and reviewing each of the recommendation statements and accompanying rationales. For each recommendation statement, the OGW considered the quality of the evidence, the balance of benefits and risks, the values and preferences of clinicians and patients, the cost feasibility, and the category designation

of the recommendation (A or B). The OGW also reviewed supplementary documents, including input provided by the CEG, SRG, peer reviewers, and the public. OGW members discussed the guideline accordingly during virtual meetings and drafted a summary report of members' observations, including points of agreement and disagreement, and delivered the report to the BSC.

NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, 2015. The BSC met on January 28, 2016, to discuss the OGW report and deliberate on the draft guideline itself. Members of the public provided comments at this meeting. After discussing the OGW report, deliberating on specific issues about the draft guideline identified at the meeting, and hearing public comment, the BSC voted unanimously: to support the observations made by the OGW; that CDC adopt the guideline recommendations that, according to the workgroup's report, had unanimous or majority support; and that CDC further consider the guideline recommendations for which the group had mixed opinions. CDC carefully considered the OGW observations, public comments, and BSC recommendations, and revised the guideline in response.

Summary of the Clinical Evidence Review

Primary Clinical Questions

CDC conducted a clinical systematic review of the scientific evidence to identify the effectiveness, benefits, and harms of long-term opioid therapy for chronic pain, consistent with the GRADE approach (*47*,*48*). Long-term opioid therapy is defined as use of opioids on most days for >3 months. A previously published AHRQ-funded systematic review on the effectiveness and risks of long-term opioid therapy for chronic pain comprehensively addressed four clinical questions (*14*,*52*). CDC, with the assistance of a methodology expert, searched the literature to identify newly published studies on these four original questions. Because long-term opioid use might be affected by use of opioids for acute pain, CDC subsequently developed a fifth clinical question (last in the series below), and in collaboration with a methodologist conducted a systematic review of the scientific evidence to address it. In brief, five clinical questions were addressed:

- The effectiveness of long-term opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for long term (≥1 year) outcomes related to pain, function, and quality of life, and how effectiveness varies according to the type/cause of pain, patient demographics, and patient comorbidities (Key Question [KQ] 1).
- The risks of opioids versus placebo or no opioids on abuse, addiction, overdose, and other harms, and how harms vary according to the type/cause of pain, patient demographics, patient comorbidities, and dose (KQ2).
- The comparative effectiveness of opioid dosing strategies (different methods for initiating and titrating opioids; immediate-release versus ER/LA opioids; different ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled, continuous versus as-needed dosing; dose escalation versus dose maintenance; opioid rotation versus maintenance; different strategies for treating acute exacerbations of chronic pain; decreasing opioid doses or tapering off versus continuation; and different tapering protocols and strategies) (KQ3).
- The accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse; the effectiveness of risk mitigation strategies (use of risk prediction instruments); effectiveness of risk mitigation strategies including opioid management plans, patient education, urine drug testing, prescription drug monitoring program (PDMP) data, monitoring instruments, monitoring intervals, pill counts, and abuse-deterrent formulations for reducing risk for opioid overdose, addiction, abuse, or misuse; and the comparative effectiveness of treatment strategies for managing patients with addiction (KQ4).
- The effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on long-term use (KQ5).

The review was focused on the effectiveness of long-term opioid therapy on long-term (>1 year) outcomes related to pain, function, and quality of life to ensure that findings are relevant to patients with chronic pain and long-term opioid prescribing. The effectiveness of short-term opioid therapy has already been established (*10*). However, opioids have unique effects such as tolerance and physical dependence that might influence assessments of benefit over time. These effects raise questions about whether findings on short-term effectiveness of opioid therapy can be extrapolated to estimate benefits of long-term therapy for chronic pain. Thus, it is important to consider studies that provide data on long-term benefit. For certain opioid-related harms (overdose, fractures, falls, motor vehicle crashes), observational studies were included with outcomes measured at shorter intervals because such outcomes can occur early during opioid therapy, and such harms are not captured well in short-term clinical trials. A detailed listing of the key questions is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Clinical Evidence Systematic Review Methods

Complete methods and data for the 2014 AHRQ report, upon which this updated systematic review is based, have been published previously (*14,52*). Study authors developed the protocol using a standardized process (*53*) with input from experts and the public and registered the protocol in the PROSPERO database (*54*). For the 2014 AHRQ report, a research librarian searched MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL for English-language articles published January 2008 through August 2014, using search terms for opioid therapy, specific opioids, chronic pain, and comparative study designs. Also included were relevant studies from an earlier review (*10*) in which searches were conducted without a date restriction, reference lists were reviewed, and ClinicalTrials.gov was searched. CDC updated the AHRQ literature search using the same search strategies as in the original review including studies published before April, 2015. Seven additional studies met inclusion criteria and were added to the review. CDC used the GRADE approach outlined in the ACIP Handbook for Developing Evidence-Based Recommendations (*47*) to rate the quality of evidence for the full body of evidence (evidence from the 2014 AHRQ review plus the update) for each clinical question. Evidence was categorized into the following types: type 1 (randomized clinical trials or overwhelming evidence from observational studies), type 2 (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 (observational studies, or randomized clinical trials with notable limitations), or type 4 (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). When no studies were present, evidence was considered to be insufficient. Per GRADE methods, type of evidence was categorized by study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects. Results were synthesized qualitatively, highlighting new evidence identified during the update process. Meta-analysis was not attempted due to the small numbers of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of the studies. More detailed information about data sources and searches, study selection, data extraction and quality assessment, data synthesis, and update search yield and new evidence for the current review is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Summary of Findings for Clinical Questions

The main findings of this updated review are consistent with the findings of the 2014 AHRQ report (*14*). In summary, evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited, with insufficient evidence to determine long-term benefits versus no opioid therapy, though evidence suggests risk for serious harms that appears to be dose-dependent. These findings supplement findings from a previous review of the effectiveness of opioids for adults with chronic noncancer pain. In this previous review, based on randomized trials predominantly ≤12 weeks in duration, opioids were found to be moderately effective for pain relief, with small benefits for functional outcomes; although estimates vary, based on uncontrolled studies, a high percentage of patients discontinued long-term opioid use because of lack of efficacy and because of adverse events (*10*).

The GRADE evidence summary with type of evidence ratings for the five clinical questions for the current evidence review are outlined (Table 1). This summary is based on studies included in the AHRQ 2014 review (35 studies) plus additional studies identified in the updated search (seven studies). Additional details on findings from the original review are provided in the full 2014 AHRQ report (*14,52*). Full details on the clinical evidence review findings supporting this guideline are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Effectiveness

For KQ1, no study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence for KQ1 is rated as insufficient (0 studies contributing) (*14*).

Harms

For KQ2, the body of evidence is rated as type 3 (12 studies contributing; 11 from the original review plus one new study). One fair-quality cohort study found that long-term opioid therapy is associated with increased risk for an opioid abuse or dependence diagnosis (as defined by ICD-9-CM codes) versus no opioid prescription (*22*). Rates of opioid abuse or dependence diagnosis ranged from 0.7% with lower-dose (≤36 MME) chronic therapy to 6.1% with higher-dose (≥120 MME) chronic therapy, versus 0.004% with no opioids prescribed. Ten fair-quality uncontrolled studies reported estimates of opioid abuse, addiction, and related outcomes (*55–65*). In primary care settings, prevalence of opioid dependence

(using DSM-IV criteria) ranged from 3% to 26% (*55,56,59*). In pain clinic settings, prevalence of addiction ranged from 2% to 14% (*57,58,60,61,63–65*).

Factors associated with increased risk for misuse included history of substance use disorder, younger age, major depression, and use of psychotropic medications (*55,62*). Two studies reported on the association between opioid use and risk for overdose (*66,67*). One large fair-quality retrospective cohort study found that recent opioid use was associated with increased risk for any overdose events and serious overdose events versus nonuse (*66*). It also found higher doses associated with increased risk. Relative to 1–19 MME/day, the adjusted hazard ratio (HR) for any overdose event (consisting of mostly nonfatal overdose) was 1.44 for 20 to 49 MME/day, 3.73 for 50–99 MME/day, and 8.87 for ≥100 MME/day. A similar pattern was observed for serious overdose. A good-quality population-based, nested case-control study also found a dose-dependent association with risk for overdose death (*67*). Relative to 1–19 MME/day, the adjusted odds ratio (OR) was 1.32 for 20–49 MME/day, 1.92 for 50–99 MME/day, 2.04 for 100–199 MME/day, and 2.88 for ≥200 MME/day.

Findings of increased fracture risk for current opioid use, versus nonuse, were mixed in two studies (*68,69*). Two studies found an association between opioid use and increased risk for cardiovascular events (*70,71*). Indirect evidence was found for endocrinologic harms (increased use of medications for erectile dysfunction or testosterone from one previously included study; laboratory-defined androgen deficiency from one newly reviewed study) (*72,73*). One study found that opioid dosages ≥20 MME/day were associated with increased odds of road trauma among drivers (*74*).

Opioid Dosing Strategies

For KQ3, the body of evidence is rated as type 4 (14 studies contributing; 12 from the original review plus two new studies). For initiation and titration of opioids, the 2014 AHRQ report found insufficient evidence from three fair-quality, open-label trials to determine comparative effectiveness of ER/LA versus immediate-release opioids for titrating patients to stable pain control (*75,76*). One new fair-quality cohort study of Veterans Affairs patients found initiation of therapy with an ER/LA opioid associated with greater risk for nonfatal overdose than initiation with an immediate-release opioid, with risk greatest in the first 2 weeks after initiation of treatment (*77*).

For comparative effectiveness and harms of ER/LA opioids, the 2014 AHRQ report included three randomized, head-to-head trials of various ER/LA opioids that found no clear differences in 1-year outcomes related to pain or function (*78–80*) but had methodological shortcomings. A fair-quality retrospective cohort study based on national Veterans Health Administration system pharmacy data found that methadone was associated with lower overall risk for all-cause mortality versus morphine (*81*), and a fair-quality retrospective cohort study based on Oregon Medicaid data found no statistically significant differences between methadone and long-acting morphine in risk for death or overdose symptoms (*82*). However, a new observational study (*83*) found methadone associated with increased risk for overdose versus sustained-release morphine among Tennessee Medicaid patients. The observed inconsistency in study findings suggests that risks of methadone might vary in different settings as a function of different monitoring and management protocols, though more research is needed to understand factors associated with safer methadone prescribing.

For dose escalation, the 2014 AHRQ report included one fair-quality randomized trial that found no differences between more liberal dose escalation and maintenance of current doses after 12 months in pain, function, all-cause withdrawals, or withdrawals due to opioid misuse (*84*). However, the difference in opioid dosages prescribed at the end of the trial was relatively small (mean 52 MME/day with more liberal dosing versus 40 MME/day). Evidence on other comparisons related to opioid dosing strategies (ER/LA versus immediate-release opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled continuous dosing versus as-needed dosing; or opioid rotation versus maintenance of current therapy; long-term effects of strategies for treating acute exacerbations of chronic pain) was not available or too limited to determine effects on long-term clinical outcomes. For example, evidence on the comparative effectiveness of opioid tapering or discontinuation versus maintenance, and of different opioid tapering strategies, was limited to small, poor-quality studies (*85–87*).

Risk Assessment and Mitigation

For KQ4, the body of evidence is rated as type 3 for the accuracy of risk assessment tools and insufficient for the effectiveness of use of risk assessment tools and mitigation strategies in reducing harms (six studies contributing; four from the original review plus two new studies). The 2014 AHRQ report included four studies (*88–91*) on the accuracy of risk assessment instruments, administered prior to opioid therapy initiation, for predicting opioid abuse or misuse. Results for the Opioid Risk Tool (ORT) (*89–91*) were extremely inconsistent; evidence for other risk assessment instruments was very sparse, and studies had serious methodological shortcomings. One additional fair-quality (*92*) and one poor-quality (*93*) study identified for this update compared the predictive accuracy of the ORT, the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), and the Brief Risk Interview.

For the ORT, sensitivity was 0.58 and 0.75 and specificity 0.54 and 0.86; for the SOAPP-R, sensitivity was 0.53 and 0.25 and specificity 0.62 and 0.73; and for the Brief Risk Interview, sensitivity was 0.73 and 0.83 and specificity 0.43 and 0.88. For the ORT, positive likelihood ratios ranged from noninformative (positive likelihood ratio close to 1) to moderately useful (positive likelihood ratio >5). The SOAPP-R was associated with noninformative likelihood ratios (estimates close to 1) in both studies.

No study evaluated the effectiveness of risk mitigation strategies (use of risk assessment instruments, opioid management plans, patient education, urine drug testing, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations) for improving outcomes related to overdose, addiction, abuse, or misuse.

Effects of Opioid Therapy for Acute Pain on Long-Term Use

For KQ5, the body of evidence is rated as type 3 (two new studies contributing). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain associated with greater likelihood of long-term use. One study evaluated opioid-naïve patients who had undergone low-risk surgery, such as cataract surgery and varicose vein stripping (*94*). Use of opioids within 7 days of surgery was associated with increased risk for use at 1 year. The other study found that among patients with a workers' compensation claim for acute low back pain, compared to patients who did not receive opioids early after injury (defined as use within 15 days following onset of pain), patients who did receive early opioids had an increased likelihood of receiving five or more opioid prescriptions 30–730 days following onset that increased with greater early exposure. Versus no early opioid use, the adjusted OR was 2.08 (95% CI = 1.55–2.78) for 1–140 MME/day and increased to 6.14 (95% confidence interval [CI] = 4.92–7.66) for ≥450 MME/day (*95*).

Summary of the Contextual Evidence Review

Primary Areas of Focus

Contextual evidence is complementary information that assists in translating the clinical research findings into recommendations. CDC conducted contextual evidence reviews on four topics to supplement the clinical evidence review findings:

- Effectiveness of nonpharmacologic (e.g., cognitive behavioral therapy [CBT], exercise therapy, interventional treatments, and multimodal pain treatment) and nonopioid pharmacologic treatments (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, and anticonvulsants), including studies of any duration.
- Benefits and harms of opioid therapy (including additional studies not included in the clinical evidence review, such as studies that were not restricted to patients with chronic pain, evaluated outcomes at any duration, performed ecological analyses, or used observational study designs other than cohort and case-cohort control studies) related to specific opioids, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and potential usefulness of risk stratification/mitigation approaches, in addition to effectiveness of treatments associated with addressing potential harms of opioid therapy (opioid use disorder).
- Clinician and patient values and preferences related to opioids and medication risks, benefits, and use.
- Resource allocation including costs and economic efficiency of opioid therapy and risk mitigation strategies.

CDC also reviewed clinical guidelines that were relevant to opioid prescribing and could inform or complement the CDC recommendations under development (e.g., guidelines on nonpharmacologic and nonopioid pharmacologic treatments and guidelines with recommendations related to specific clinician actions such as urine drug testing or opioid tapering protocols).

Contextual Evidence Review Methods

CDC conducted a contextual evidence review to assist in developing the recommendations by providing an assessment of the balance of benefits and harms, values and preferences, and cost, consistent with the GRADE approach. Given the public health urgency for developing opioid prescribing recommendations, a rapid review was required for the contextual evidence review for the current guideline. Rapid reviews are used when there is a need to streamline the systematic review process to obtain evidence quickly (*96*). Methods used to streamline the process include limiting searches by databases, years, and languages considered, and truncating quality assessment and data abstraction protocols. CDC conducted "rapid reviews" of the contextual evidence on nonpharmacologic and nonopioid pharmacologic treatments, benefits and harms, values and preferences, and resource allocation.

Detailed information about contextual evidence data sources and searches, inclusion criteria, study selection, and

data extraction and synthesis are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). In brief, CDC conducted systematic literature searches to identify original studies, systematic reviews, and clinical guidelines, depending on the topic being searched. CDC also solicited publication referrals from subject matter experts. Given the need for a rapid review process, grey literature (e.g., literature by academia, organizations, or government in the forms of reports, documents, or proceedings not published by commercial publishers) was not systematically searched. Database sources, including MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews, varied by topic. Multiple reviewers scanned study abstracts identified through the database searches and extracted relevant studies for review. CDC constructed narrative summaries and tables based on relevant articles that met inclusion criteria, which are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Findings from the contextual reviews provide indirect evidence and should be interpreted accordingly. CDC did not formally rate the quality of evidence for the studies included in the contextual evidence review using the GRADE method. The studies that addressed benefits and harms, values and preferences, and resource allocation most often employed observational methods, used short follow-up periods, and evaluated selected samples. Therefore the strength of the evidence from these contextual review areas was considered to be low, comparable to type 3 or type 4 evidence. The quality of evidence for nonopioid pharmacologic and nonpharmacologic pain treatments was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines (e.g., for treatment of chronic neuropathic pain, low back pain, osteoarthritis, and fibromyalgia). Similarly, the quality of evidence on pharmacologic and psychosocial opioid use disorder treatment was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines.

Summary of Findings for Contextual Areas

Full narrative reviews and tables that summarize key findings from the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Effectiveness of Nonpharmacologic and Nonopioid Pharmacologic Treatments

Several nonpharmacologic and nonopioid pharmacologic treatments have been shown to be effective in managing chronic pain in studies ranging in duration from 2 weeks to 6 months. For example, CBT that trains patients in behavioral techniques and helps patients modify situational factors and cognitive processes that exacerbate pain has small positive effects on disability and catastrophic thinking (*97*). Exercise therapy can help reduce pain and improve function in chronic low back pain (*98*), improve function and reduce pain in osteoarthritis of the knee (*99*) and hip (*100*), and improve well-being, fibromyalgia symptoms, and physical function in fibromyalgia (*101*). Multimodal and multidisciplinary therapies (e.g., therapies that combine exercise and related therapies with psychologically based approaches) can help reduce pain and improve function more effectively than single modalities (*102,103*). Nonopioid pharmacologic approaches used for pain include analgesics such as acetaminophen, NSAIDs, and cyclooxygenase 2 (COX-2) inhibitors; selected anticonvulsants; and selected antidepressants (particularly tricyclics and serotonin and norepinephrine reuptake inhibitors [SNRIs]). Multiple guidelines recommend acetaminophen as first-line pharmacotherapy for osteoarthritis (*104–109*) or for low back pain (*110*) but note that it should be avoided in liver failure and that dosage should be reduced in patients with hepatic insufficiency or a history of alcohol abuse (*109*). Although guidelines also recommend NSAIDs as first-line treatment for osteoarthritis or low back pain (*106,110*), NSAIDs and COX-2 inhibitors do have risks, including gastrointestinal bleeding or perforation as well as renal and cardiovascular risks (*111*). FDA has recently strengthened existing label warnings that NSAIDs increase risks for heart attack and stroke, including that these risks might increase with longer use or at higher doses (*112*). Several guidelines agree that first- and second-line drugs for neuropathic pain include anticonvulsants (gabapentin or pregabalin), tricyclic antidepressants, and SNRIs (*113–116*). Interventional approaches such as epidural injection for certain conditions (e.g., lumbar radiculopathy) can provide short-term improvement in pain (*117–119*). Epidural injection has been associated with rare but serious adverse events, including loss of vision, stroke, paralysis, and death (*120*).

Benefits and Harms of Opioid Therapy

Balance between benefits and harms is a critical factor influencing the strength of clinical recommendations. In particular, CDC considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches. Additional information on benefits and harms of long-term opioid therapy from studies meeting rigorous selection criteria is provided in the clinical evidence review (e.g., see KQ2). CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting

from opioids, and numbers affected by opioid-related harms. A review of these data is presented in the background section of this document, with detailed information provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder).

Regarding specific opioids and formulations, as noted by FDA, there are serious risks of ER/LA opioids, and the indication for this class of medications is for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain (*121*). Time-scheduled opioid use was associated with substantially higher average daily opioid dosage than as-needed opioid use in one study (*122*). Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (*123*).

Regarding high-dose therapy, several epidemiologic studies that were excluded from the clinical evidence review because patient samples were not restricted to patients with chronic pain also examined the association between opioid dosage and overdose risk (*23,24,124–126*). Consistent with the clinical evidence review, the contextual review found that opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. Two of these studies (*23,24*), as well as the two studies in the clinical evidence review (*66,67*), evaluated similar MME/day dose ranges for association with overdose risk. In these four studies, compared with opioids prescribed at <20 MME/day, the odds of overdose among patients prescribed opioids for chronic nonmalignant pain were between 1.3 (*67*) and 1.9 (*24*) for dosages of 20 to <50 MME/day, between 1.9 (*67*) and 4.6 (*24*) for dosages of 50 to <100 MME/day, and between 2.0 (*67*) and 8.9 (*66*) for dosages of ≥100 MME/day. Compared with dosages of 1–<20 MME/day, absolute risk difference approximation for 50–<100 MME/day was 0.15% for fatal overdose (*24*) and 1.40% for any overdose (*66*), and for ≥100 MME/day was 0.25% for fatal overdose (*24*) and 4.04% for any overdose (*66*). A recent study of Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages (mean: 98 MME/day; median: 60 MME/day) than controls (mean: 48 MME/day, median: 25 MME/day) (*127*). Finally, another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (*128*). A listing of common opioid medications and their MME equivalents is provided (Table 2).

Regarding coprescription of opioids with benzodiazepines, epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (*67,128,129*). In one of these studies (*67*), among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids.

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time (*130*). Patients who do not experience clinically meaningful pain relief early in treatment (i.e., within 1 month) are unlikely to experience pain relief with longer-term use (*131*).

Regarding populations potentially at greater risk for harm, risk is greater for patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders. Interpretation of clinical data on the effects of opioids on sleep-disordered breathing is difficult because of the types of study designs and methods employed, and there is no clear consensus regarding association with risk for developing obstructive sleep apnea syndrome (*132*). However, opioid therapy can decrease respiratory drive, a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index (*133*), opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients, and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (*31*). Reduced renal or hepatic function can result in greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs (*134*). Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease (*135*), result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose. Older adults might also be at increased risk for falls and fractures related to opioids (*136–138*). Opioids used

in pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects (*139,140*), congenital heart defects (*140*), and gastroschisis (*140*); preterm delivery (*141*), poor fetal growth (*141*), and stillbirth (*141*). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (*142*). Patients with mental health comorbidities and patients with histories of substance use disorders might be at higher risk than other patients for opioid use disorder (*62,143,144*). Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts (*145*). In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (12% versus 6% [*66*], 40% versus 10% [*24*], and 26% versus 9% [*23*]).

Regarding risk stratification approaches, limited evidence was found regarding benefits and harms. Potential benefits of PDMPs and urine drug testing include the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder, and help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. For example, one study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information, multiple prescribers and high total daily opioid dosage, both important risk factors for overdose (*124,146*) that are available to prescribers in the PDMP (*124*). However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (*28*). Potential harms of risk stratification include underestimation of risks of opioid therapy when screening tools are not adequately sensitive, as well as potential overestimation of risk, which could lead to inappropriate clinical decisions.

Regarding risk mitigation approaches, limited evidence was found regarding benefits and harms. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (*147*).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids (*148*) or interference with appropriate pain treatment (*149*). With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use (*150*), CDC did not identify studies evaluating these potential outcomes.

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin (*151–153*). Although findings are mixed, some studies suggest that effectiveness is enhanced when psychosocial treatments (e.g., contingency management, community reinforcement, psychotherapeutic counseling, and family therapy) are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (*154,155*).

Clinician and Patient Values and Preferences

Clinician and patient values and preferences can inform how benefits and harms of long-term opioid therapy are weighted and estimate the effort and resources required to effectively provide implementation support. Many physicians lack confidence in their ability to prescribe opioids safely (*156*), to predict (*157*) or detect (*158*) prescription drug abuse, and to discuss abuse with their patients (*158*). Although clinicians have reported favorable beliefs and attitudes about improvements in pain and quality of life attributed to opioids (*159*), most consider prescription drug abuse to be a "moderate" or "big" problem in their community, and large proportions are "very" concerned about opioid addiction (55%) and death (48%) (*160*). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as PDMPs (*161,162*), urine drug testing (*163*), and opioid treatment agreements (*164*). This is likely due in part to challenges related to registering for PDMP access and logging into the PDMP (which can interrupt normal clinical workflow if data are not integrated into electronic health record systems) (*165*), competing clinical demands, perceived inadequate time to discuss the rationale for urine drug testing and to order confirmatory testing, and feeling unprepared to interpret and address results (*166*).

Many patients do not have an opinion about "opioids" or know what this term means (*167*). Most are familiar with the term "narcotics." About a third associated "narcotics" with addiction or abuse, and about half feared "addiction" from long-term "narcotic" use (*168*). Most patients taking opioids experience side effects (73% of patients taking hydrocodone for noncancer pain [*11*], 96% of patients taking opioids for chronic pain [*12*]), and side effects, rather than pain relief,

have been found to explain most of the variation in patients' preferences related to taking opioids (*12*). For example, patients taking hydrocodone for noncancer pain commonly reported side effects including dizziness, headache, fatigue, drowsiness, nausea, vomiting, and constipation (*11*). Patients with chronic pain in focus groups emphasized effectiveness of goal setting for increasing motivation and functioning (*168*). Patients taking high dosages report reliance on opioids despite ambivalence about their benefits (*169*) and regardless of pain reduction, reported problems, concerns, side effects, or perceived helpfulness (*13*).

Resource Allocation

Resource allocation (cost) is an important consideration in understanding the feasibility of clinical recommendations. CDC searched for evidence on opioid therapy compared with other treatments; costs of misuse, abuse, and overdose from prescription opioids; and costs of specific risk mitigation strategies (e.g., urine drug testing). Yearly direct and indirect costs related to prescription opioids have been estimated (based on studies published since 2010) to be $53.4 billion for nonmedical use of prescription opioids (*170*); $55.7 billion for abuse, dependence (i.e., opioid use disorder), and misuse of prescription opioids (*171*); and $20.4 billion for direct and indirect costs related to opioid-related overdose alone (*172*). In 2012, total expenses for outpatient prescription opioids were estimated at $9.0 billion, an increase of 120% from 2002 (*173*). Although there are perceptions that opioid therapy for chronic pain is less expensive than more time-intensive nonpharmacologic management approaches, many pain treatments, including acetaminophen, NSAIDs, tricyclic antidepressants, and massage therapy, are associated with lower mean and median annual costs compared with opioid therapy (*174*). COX-2 inhibitors, SNRIs, anticonvulsants, topical analgesics, physical therapy, and CBT are also associated with lower median annual costs compared with opioid therapy (*174*). Limited information was found on costs of strategies to decrease risks associated with opioid therapy; however, urine drug testing, including screening and confirmatory tests, has been estimated to cost $211–$363 per test (*175*).

Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (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.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

*All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

BOX 2. Interpretation of recommendation categories and evidence type

Recommendation Categories

Based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type

Based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

Determining When to Initiate or Continue Opioids for Chronic Pain

1. **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).**

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98,101*). Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111,112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110,179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110,179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. **Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).**

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.

- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).
- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent

opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the trial.) At the same time, risks for serious harms

related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage. Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is

now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

6. **Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).**

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192–194*) and other settings (*195,196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. **Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).**

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30,201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

Assessing Risk and Addressing Harms of Opioid Use

8. **Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (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 (recommendation category: A, evidence type: 4).

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.
- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should

use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently

whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213,214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151–153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154,155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216,217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220,221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in nonpregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a

checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

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TABLE 1. Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness and comparative effectiveness (KQ1)							
Effectiveness of long-term opioid therapy versus placebo or no opioid therapy for long-term (≥1 year) outcomes							
Pain, function, and quality of life	None	—[†]	—	—	Insufficient	—	No evidence
Harms and adverse events (KQ2)							
Risks of opioids versus placebo or no opioids on opioid abuse, addiction, and related outcomes; overdose; and other harms							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found long-term use of prescribed opioids associated with an increased risk of abuse or dependence diagnosis versus no opioid use (adjusted OR ranged from 14.9 to 122.5, depending on dose).
Abuse or addiction	10 uncontrolled studies (n = 3,780)	Very serious limitations	Very serious inconsistency	No imprecision	4	None identified	In primary care settings, prevalence of opioid abuse ranged from 0.6% to 8% and prevalence of dependence from 3% to 26%. In pain clinic settings, prevalence of misuse ranged from 8% to 16% and addiction from 2% to 14%. Prevalence of aberrant drug-related behaviors ranged from 6% to 37%.
Overdose	1 cohort study (n = 9,940)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Current opioid use associated with increased risk of any overdose events (adjusted HR 5.2, 95% CI = 2.1–12) and serious overdose events (adjusted HR 8.4, 95% CI = 2.5–28) versus current nonuse.
Fractures	1 cohort study (n = 2,341) and 1 case–control study (n = 21,739 case patients)	Serious limitations	No inconsistency	No imprecision	3	None identified	Opioid use associated with increased risk of fracture in 1 cohort study (adjusted HR 1.28, 95% CI = 0.99–1.64) and 1 case-control study (adjusted OR 1.27, 95% CI = 1.21–1.33).
Myocardial infarction	1 cohort study (n = 426,124) and 1 case–control study (n = 11,693 case patients)	No limitations	No inconsistency	No imprecision	3	None identified	Current opioid use associated with increased risk of myocardial infarction versus nonuse (adjusted OR 1.28, 95% CI = 1.19–1.37 and incidence rate ratio 2.66, 95% CI = 2.30–3.08).
Endocrinologic harms	1 cross-sectional study (n = 11,327)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Long-term opioid use associated with increased risk for use of medications for erectile dysfunction or testosterone replacement versus nonuse (adjusted OR 1.5, 95% CI = 1.1–1.9).
How do harms vary depending on the opioid dose used?							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found higher doses of long-term opioid therapy associated with increased risk of opioid abuse or dependence than lower doses. Compared to no opioid prescription, the adjusted odds ratios were 15 (95% CI = 10–21) for 1 to 36 MME/day, 29 (95 % CI = 20–41) for 36 to120 MME/day, and 122 (95 % CI = 73–205) for ≥120 MME/day.
Overdose	1 cohort study (n = 9,940) and 1 case–control study (n = 593 case patients in primary analysis)	Serious limitations	No inconsistency	No imprecision	3	Magnitude of effect, dose response relationship	Versus 1 to <20 MME/day, one cohort study found an adjusted HR for an overdose event of 1.44 (95% CI = 0.57–3.62) for 20 to <50 MME/day that increased to 8.87 (95% CI = 3.99–19.72) at ≥100 MME/day; one case-control study found an adjusted OR for an opioid-related death of 1.32 (95% CI = 0.94–1.84) for 20 to 49 MME/day that increased to 2.88 (95% CI = 1.79–4.63) at ≥200 MME/day.
Fractures	1 cohort study (n = 2,341)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Risk of fracture increased from an adjusted HR of 1.20 (95% CI = 0.92–1.56) at 1 to <20 MME/day to 2.00 (95% CI = 1.24–3.24) at ≥50 MME/day; the trend was of borderline statistical significance.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Myocardial infarction	1 cohort study (n = 426,124)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Relative to a cumulative dose of 0 to 1,350 MME during a 90-day period, the incidence rate ratio for myocardial infarction for 1350 to <2700 MME was 1.21 (95% CI = 1.02–1.45), for 2,700 to <8,100 MME was 1.42 (95% CI = 1.21–1.67), for 8,100 to <18,000 MME was 1.89 (95% CI = 1.54–2.33), and for ≥18,000 MME was 1.73 (95% CI = 1.32–2.26).
Motor vehicle crash injuries	1 case–control study (n = 5,300 case patients)	No limitations	Unknown (1 study)	No imprecision	3	None identified	No association between opioid dose and risk of motor vehicle crash injuries even though opioid doses >20 MME/day were associated with increased odds of road trauma among drivers.
Endocrinologic harms	1 cross-sectional study (n = 11,327) New for update: 1 additional cross-sectional study (n=1,585)	Serious limitations	Consistent	No imprecision	3	None identified	Relative to 0 to <20 MME/day, the adjusted OR for ≥120 MME/day for use of medications for erectile dysfunction or testosterone replacement was 1.6 (95% CI = 1.0–2.4). One new cross-sectional study found higher-dose long-term opioid therapy associated with increased risk of androgen deficiency among men receiving immediate-release opioids (adjusted OR per 10 MME/day 1.16, 95% CI = 1.09–1.23), but the dose response was very weak among men receiving ER/LA opioids.
Dosing strategies (KQ3)							
Comparative effectiveness of different methods for initiating opioid therapy and titrating doses							
Pain	3 randomized trials (n = 93)	Serious limitations	Serious inconsistency	Very serious imprecision	4	None identified	Trials on effects of titration with immediate-release versus ER/LA opioids reported inconsistent results and had additional differences between treatment arms in dosing protocols (titrated versus fixed dosing) and doses of opioids used.
Overdose	New for update: 1 cohort study (n = 840,606)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One new cross-sectional study found initiation of therapy with an ER/LA opioid associated with increased risk of overdose versus initiation with an immediate-release opioid (adjusted HR 2.33, 95% CI = 1.26–4.32).
Comparative effectiveness of different ER/LA opioids							
Pain and function	3 randomized trials (n = 1,850)	Serious limitations	No inconsistency	No imprecision	3	None identified	No differences
All-cause mortality	1 cohort study (n = 108,492) New for update: 1 cohort study (n = 38,756)	Serious limitations	Serious inconsistency	No imprecision	4	None identified	One cohort study found methadone to be associated with lower all-cause mortality risk than sustained-release morphine in a propensity-adjusted analysis (adjusted HR 0.56, 95% CI = 0.51–0.62) and one cohort study among Tennessee Medicaid patients found methadone to be associated with higher risk of all-cause mortality than sustained-release morphine (adjusted HR 1.46, 95% CI = 1.17–1.73).
Abuse and related outcomes	1 cohort study (n = 5,684)	Serious limitations	Unknown (1 study)	Serious imprecision	4	None identified	One cohort study found some differences between ER/LA opioids in rates of adverse outcomes related to abuse, but outcomes were nonspecific for opioid-related adverse events, precluding reliable conclusions.
ER/LA versus immediate-release opioids							
Endocrinologic harms	New for update: 1 cross-sectional study (n = 1,585)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One cross-sectional study found ER/LA opioids associated with increased risk of androgen deficiency versus immediate-release opioids (adjusted OR 3.39, 95% CI = 2.39–4.77).

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Dose escalation versus dose maintenance or use of dose thresholds							
Pain, function, or withdrawal due to opioid misuse	1 randomized trial (n = 140)	Serious limitations	Unknown (1 study)	Very serious imprecision	3	None identified	No difference between more liberal dose escalation versus maintenance of current doses in pain, function, or risk of withdrawal due to opioid misuse, but there was limited separation in opioid doses between groups (52 versus 40 MME/day at the end of the trial).
Immediate-release versus ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled and continuous versus as-needed dosing of opioids; or opioid rotation versus maintenance of current therapy							
Pain, function, quality of life, and outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of decreasing or tapering opioid doses versus continuation of opioid therapy							
Pain and function	1 randomized trial (n = 10)	Very serious limitations	Unknown (1 study)	Very serious imprecision	4	None identified	Abrupt cessation of morphine was associated with increased pain and decreased function compared with continuation of morphine.
Comparative effectiveness of different tapering protocols and strategies							
Opioid abstinence	2 nonrandomized trials (n = 150)	Very serious limitations	No inconsistency	Very serious imprecision	4	None identified	No clear differences between different methods for opioid discontinuation or tapering in likelihood of opioid abstinence after 3–6 months
Risk assessment and risk mitigation strategies (KQ4)							
Diagnostic accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse among patients with chronic pain being considered for long-term opioid therapy							
Opioid risk tool	3 studies of diagnostic accuracy (n = 496) New for update: 2 studies of diagnostic accuracy (n = 320)	Serious limitations	Very serious inconsistency	Serious imprecision	4	None identified	Based on a cutoff score of >4 (or unspecified), five studies (two fair-quality, three poor-quality) reported sensitivity that ranged from 0.20 to 0.99 and specificity that ranged from 0.16 to 0.88.
Screener and Opioid Assessment for Patients with Pain, Version 1	2 studies of diagnostic accuracy (n = 203)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of ≥8, sensitivity was 0.68 and specificity was 0.38 in one study, for a positive likelihood ratio of 1.11 and a negative likelihood ratio of 0.83. Based on a cutoff score of >6, sensitivity was 0.73 in one study.
Screener and Opioid Assessment for Patients with Pain-Revised	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of >3 or unspecified, sensitivity was 0.25 and 0.53 and specificity was 0.62 and 0.73 in two studies, for likelihood ratios close to 1.
Brief Risk Interview	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a "high risk" assessment, sensitivity was 0.73 and 0.83 and specificity was 0.43 and 0.88 in two studies, for positive likelihood ratios of 1.28 and 7.18 and negative likelihood ratios of 0.63 and 0.19.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Comparative effectiveness of treatment strategies for managing patients with addiction to prescription opioids							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of opioid therapy for acute pain on long-term use (KQ5)							
Long-term opioid use	New for update: 2 cohort studies (n = 399,852)	Serious limitations	No inconsistency	No imprecision	3	None identified	One study found use of opioids within 7 days of low-risk surgery associated with increased likelihood of opioid use at 1 year (adjusted OR 1.44, 95% CI = 1.39–1.50), and one study found use of opioids within 15 days of onset of low back pain among workers with a compensation claim associated with increased risk of late opioid use (adjusted OR 2.08, 95% CI = 1.55–2.78 for 1 to 140 MME/day and OR 6.14, 95% CI = 4.92–7.66 for ≥450 MME/day).

Abbreviations: CI = confidence interval; ER/LA = extended release/long-acting; HR = hazard ratio; MME = morphine milligram equivalents; OR = odds ratio.
* Ratings were made per GRADE quality assessment criteria; "no limitations" indicates that limitations assessed through the GRADE method were not identified.
† Not applicable as no evidence was available for rating.

TABLE 2. Morphine milligram equivalent (MME) doses for commonly prescribed opioids

Opioid	Conversion factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20 mg/day	4
21–40 mg/day	8
41–60 mg/day	10
≥61–80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol†	0.4

Source: Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Washington State Interagency Guideline on Prescribing Opioids for Pain (http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf).

* Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs. For example, tablets containing hydrocodone 5 mg and acetaminophen 300 mg taken four times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone 10mg and taken twice a day would contain a total of 20mg of oxycodone daily, equivalent to 30 MME daily. The following cautions should be noted: 1) All doses are in mg/day except for fentanyl, which is mcg/hr. 2) Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. 3) Do not use the calculated dose in MMEs to determine the doses to use when converting opioid to another; when converting opioids the new opioid is typically dosed at substantially lower than the calculated MME dose to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. 4) Use particular caution with methadone dose conversions because the conversion factor increases at higher doses. 5) Use particular caution with fentanyl since it is dosed in mcg/hr instead of mg/day, and its absorption is affected by heat and other factors.

† Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists.

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THE STATE of ALASKA
GOVERNOR BILL WALKER

Controlled Substances Advisory Committee

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January 29, 2016

Honorable Bill Walker
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Dear Governor Walker:

The Controlled Substances Advisory Committee (CSAC), created under AS 11.71.100, is an advisory board made up of various subject-matter experts in the field of controlled substances, with expertise in medicine, law enforcement, and citizenry. One of the duties of the CSAC is to recommend regulatory changes to the Board of Pharmacy regarding the prevention of "excessive prescribing of controlled substances and the diversion of prescription drugs into illicit channels." *See* AS 11.71.110(2). According to the Alaska Division of Public Health, 54 Alaskans died of prescription opioid overdose in 2015 and an additional 33 died of heroin overdose. A significant percentage of heroin users become dependent on opioids through the use of prescription drugs. As discussed in more detail below, the CSAC has concluded that Alaska's Prescription Drug Monitoring Program (PDMP), as currently enacted, faces unnecessary limitations in its effort to respond to the opioid epidemic currently being seen in Alaska.

Due to the fact that the committee's recommended modifications require a statutory change – as opposed to a regulatory change – the CSAC is advising you of its proposed modifications. The reasons and rationale for the proposed modifications are set forth in the attached white paper entitled, "*Increasing the Effectiveness of Alaska's Prescription Drug Monitoring Program (Alaska's PDMP)*".

In short, Alaska's PDMP, managed by the Board of Pharmacy, is a statutorily created electronic controlled substance database designed to enhance patient care and reduce misuse, abuse, and diversion of controlled substances. Over the past several months, the CSAC has reviewed Alaska's PDMP and discovered several areas that limit the overall effectiveness of the PDMP. In the opinion of the committee, those limitations are easily addressed, and in so doing, would increase the effectiveness of the PDMP and reduce the recurring opioid abuse occurring in Alaska. Specifically, the CSAC recommends nine modifications to Alaska's PDMP:

1. Require all prescribers and all pharmacists to register with the Alaska PDMP.
2. Require prescribers and pharmacists to review the PDMP database when prescribing or dispensing a controlled substance to a patient.
3. Authorize prescribers and pharmacists to delegate database access to supervised employees or clinical staff.

4. Authorize the Board of Pharmacy to forward unsolicited notifications to prescribers and dispensers database information about patients who may be obtaining controlled substances inconsistent with generally recognized standards of care.
5. Collect dispensing data and updating the PDMP database weekly.
6. Authorize PDMP database access to the State of Alaska Medicaid Pharmacy Program.
7. Authorize PDMP database access to the State of Alaska Medicaid Drug Utilization Review Committee.
8. Authorize PDMP database access to the State of Alaska Medical Examiner.
9. Authorize de-identified PDMP data access to the State of Alaska Department of Health and Social Services (Alaska DHSS) Division of Public Health.

These modifications are consistent with national recommendations of the American Medical Association's Task Force to Reduce Opioid Abuse, which urges states and providers to utilize prescription drugs monitoring programs to reduce prescription drug misuse, overdose, and death. The effects of heroin and opiate abuse in Alaska are well-documented. The CSAC recommends that action be taken to strengthen one of Alaska's most important tools in combating this epidemic – the PDMP.

Sincerely,

Robert E. Henderson
Chief Assistant Attorney General
Chair, Controlled Substance Advisory Committee

Enclosures as stated

cc: CSAC members (*via* email)

State of Alaska

Controlled Substances Advisory Committee

White Paper

Increasing the Effectiveness of Alaska's Prescription Drug Monitoring Program (Alaska's PDMP)

January 29, 2016

1. **Deaths from opiates and heroin are increasing in the U.S.**
   - Since 1990, the annual death rate from drug overdose has more than tripled.[1]
   - Since 2000, the age-adjusted death rate from drug overdose has more than doubled.[2]
   - From 2000 to 2014, almost 500,000 people have died from drug overdoses.[2]
   - Opiates, primarily prescription pain relievers and heroin, are the main drugs associated with overdose deaths.[2]
   - In 2006, the total cost of nonmedical use of prescription opiates was $53.4 billion.[3]
   - Between 2007 and 2013, the prevalence of heroin addiction almost doubled.[4]
   - In 2010, drug related poisoning was the leading cause of unintentional death.[3]
   - Since 2010, heroin death rates have more than tripled.[2]
   - Between 2011 and 2013, 45% of people who used heroin were addicted to prescription opiates.[4]
   - From 2013 to 2014, heroin overdose death rates increased 26%.[2]
   - In 2014, 61% of drug overdose deaths involved some type of opiate, including heroin.[2]
   - In 2014, more persons died from drug overdoses than during any previous year on record.[2]
   - In 2014, there were approximately one and a half times more deaths from drug overdoses than deaths from motor vehicle accidents.[2]
   - Forty-four (44) people die every day from prescription opiate overdoses.[5]

2. **Deaths from opiates and heroin are increasing in Alaska**
   - In 2008, Alaska ranked 5th for highest rate of drug overdose death (18.1 per 100,000).[1]
   - Between 2002 and 2013, the Substance Abuse and Mental Health Services Administration (SAMHSA) estimated that the annual average number of people using heroin increased four-fold (4x) and the annual average number of people with heroin addiction doubled (2x).[6]
   - Between 2008 and 2013, the incidence of heroin-associated deaths more than tripled.[6]
   - Between 2008 and 2013, there were more deaths by prescription opiate overdose and heroin overdose than by motor vehicle accident.[7]

3. **Other public health evidence of opiate and heroin use increasing in Alaska**
   - Between 2004 to 2013, Alaska Medicaid payment requests for heroin poisoning increased almost ten-fold (10x).[6]
   - From 2009 to 2013, substance treatment admissions for Alaskans 21-29 years of age with primary heroin use disorders increased 74% and heroin arrests increased 140%.[6,8]
   - Between 2010 and 2012, inpatient hospital discharge rates for heroin poisoning increased almost six-fold (6x).[6]

4. Outbreak of HIV and Hepatitis C in Indiana

Sharing syringes and injection paraphernalia increase the risk of being exposed to HIV and viral hepatitis.[9] Austin, Indiana (population 4,300) experienced an outbreak of HIV and Hepatitis C in 2015.[7] The majority of new cases (more than 170) were due to syringe sharing among individual who had injected the prescription oral opiate oxymorphone.[10] The lifelong medical care costs for treating the new cases of HIV and Hepatitis C will be more than $80 million (more than $470,000/new case).[10]

5. What is the link between heroin and prescription opiates?[11]

- Ninety-six percent (96%) of people who use heroin use at least one other drug in the past year with sixty-one percent (61%) using at least three other drugs.
- Misusing a prescription opiate is the strongest risk factor for a heroin use disorder.
- People who abuse or are dependent on prescription opiates are forty times (40x) more likely to use heroin than people who do not misuse prescription opiates.
- People who abuse or are dependent on:
    - alcohol are two times (2x) more likely to use heroin.
    - marijuana are three times (3x) more likely to use heroin.
    - cocaine are fifteen times (15x) more likely to use heroin.

6. How do people who misuse prescription opiates obtain prescription opiates?[1]

- Less than five percent (5%) obtain them from a stranger or "drug dealer."
- More than seventeen percent (17%) obtain them from one health care provider.
- More than seventy percent (70%) obtain them from a friend or relative.

7. Who is at highest risk for prescription opiate overdose?[1]

People at highest risk for prescription opiate overdose include:

- People who obtain multiple controlled substance prescriptions from multiple providers.
- People who take high daily doses of prescription opiates.
- People who misuse multiple abuse-prone prescription medications.
- People with substance use disorders or a history of substance use disorders.
- People with mental illness.
- People on Medicaid.

8. What can be done to reduce hospitalizations and deaths from prescription opiate and heroin overdose?

Several public health measures reduce the risk of opiate prescription misuse, heroin use, and overdose death:

- Increase medical professional training regarding pain management and the risks associated with opiate medications.
- Increase screening for and access to treatment for opiate and heroin addiction, including medication-assisted treatment (MAT).
- Improve recognition and management of acute opiate and heroin overdoses: the physical effects of these overdoses can be reversed with the drug naloxone (Narcan). Increasing the availability of naloxone can reduce the risk of death after overdose.

- Maximize PDMP database utilization to identify:
    - Prescription opiate misuse such as high dose opiate prescribing without medical justification.
    - Prescription opiate misuse such as long-term opiate therapy that may be inappropriate or outside commonly recognized standards of care.
    - Prescription opiate abuse.
    - Prescription opiate diversion.
    - Prescriptions for other controlled substances (medications) that may be inappropriate or outside commonly recognized standards of care.

9. What is a prescription drug-monitoring program (PDMP)?

- A PDMP is a state public health effort to facilitate appropriate prescribing and dispensing of controlled substances. A PDMP includes a centralized electronic database of prescribed and dispensed controlled substances (medications).
- PDMPs improve clinical decision-making, reduce "doctor shopping," reduce controlled substance (medication) misuse, and help identify controlled substance (medication) diversion.[3]
- Several states established PDMPs beginning in the 1990s. Currently, forty-nine (49) states have operational PDMPs.[3]
- In an impact survey of the Indiana PDMP, ninety percent (90%) of medical professionals who responded, prescribed fewer controlled substances (medications) and fifty percent (50%) reported the PDMP was the primary reason for the decrease.[3]
- In an impact survey of the Maine PDMP, ninety-seven percent (97%) of prescribers and dispensers who responded, rated the PDMP useful in monitoring medication prescriptions and identifying and reducing doctor shopping.[3]
- Kentucky, Florida, Oklahoma, and Washington all reported decreased opiate overdose death rates, at least partially attributable to requiring prescriber PDMP registration and utilization.[3]

10. Does Alaska have a PDMP?

Yes, the Alaska Prescription Drug Monitoring Program (Alaska PDMP) was established in 2008 (AS 17.30.200). The Board of Pharmacy manages the Alaska PDMP. Alaska's PDMP goals are to identify:

1. Prescribing and dispensing practices and patterns regarding controlled substances (Alaska Schedule IA-VA and Federal Schedule I-V medications).*

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* Pursuant to AS 17.30.200, Alaska's PDMP gathers prescription information for every prescription for a "schedule I, II, III, IV, or V controlled substance under federal law." The committee recognizes that federal schedule I controlled substances are defined as drugs with "no currently accepted medical use in treatment" and have "a high potential for abuse." Accordingly, such drugs are not monitored within the PDMP. However, in an effort to ensure consistency with the enabling statute, the committee has mirrored the language of AS 17.30.200 with regard to the monitored controlled substances.

2. Practitioners who prescribe controlled substances in an unprofessional or unlawful manner.
3. Individuals who receive prescriptions from licensed practitioners and who obtain controlled substances from a dispenser or pharmacy in quantities or frequencies inconsistent with generally recognized standards.
4. Individuals who present forged, false, or altered prescriptions for controlled substances.

Alaska's PDMP has a centralized electronic database containing the following information:

1. Name and federal Drug Enforcement Administration (DEA) registration number of the prescriber (MD, DO, ANP, RNA, PA, DDS, DVM, and DPM).
2. Date the prescription was ordered.
3. Date the prescription was filled and dispensed.
4. Name, address, and date of birth of the person for whom the prescription was ordered.
5. Name, strength, and quantity of the controlled substance dispensed.
6. Dispensing practitioner (most commonly RPh) and the location where dispensed.
7. The patient's method of payment.

All pharmacies and dispensing practitioners are required to report the controlled substance dispensing information to the PDMP by no later than the fifth day of each month. The Board of Pharmacy or licensing board may take disciplinary action against a dispenser failing to submit information to the PDMP database as required.

Federal funding from the Substance Abuse and Mental Health Services Administration (SAMHSA) began supporting the Alaska PDMP in 2015. Federal funding may increase if PDMP utilization increases.

11. Who uses Alaska PDMP data?

- Only licensed prescribers (most commonly MD, DO, ANP, PA, DDS) and licensed dispensers (most commonly Pharmacists) who have registered with the Alaska PDMP may access the Alaska PDMP database. Both registering and reviewing controlled substance prescription information within the Alaska PDMP is voluntary.
- Approximately 13.5% of prescribers are registered with the PDMP. These prescribers review the database regarding specific patients in their care.
- Approximately 40% of dispensers (pharmacists) are registered with PDMP. These dispensers (pharmacists) review the PDMP database regarding patient specific prescriptions for controlled substance (medication) before dispensing.
- Information in the database is confidential and not subject to public disclosure. Unauthorized access and disclosure of PDMP database information is unlawful.
- Federal, state, and local law enforcement authorities must obtain a search warrant, subpoena, or court order prior to obtaining Alaska PDMP data.
- The Alaska Legislature receives non-clinical Alaska PDMP performance measures annually.

Dispensers and practitioners may not be held civilly liable for damages for accessing or not accessing information in the PDMP database.

A person with authority to access the PDMP database who knowingly accesses information in the database beyond the scope of that person's authority commits a class A misdemeanor. A person with authority to access the PDMP database who knowingly accesses information in the database and recklessly discloses the information to a person not entitled to access or to receive the information commits a class C felony. A person who knowingly allows another person who is not authorized to access the PDMP database to access the database commits a class C felony. A person without authority to access the PDMP database who knowingly accesses the database or knowingly receives database information from another person commits a class C felony.

12. What is the Controlled Substances Advisory Committee (CSAC)?

The CSAC was established in 1982 (AS 11.71.100-11.71.120). CSAC goals are to:

1. Advise the governor about adding, deleting, and rescheduling controlled substances.
2. Recommend regulations to the Board of Pharmacy regarding the prevention of excessive prescribing and the diversion of controlled substances.
3. Evaluate the effectiveness of treatment resources for persons with controlled substance use disorders.
4. Evaluate the enforcement policies and practices regarding crimes involving controlled substances.
5. Review budget requests and recommend appropriations regarding:
    a. Enforcing criminal laws pertaining to controlled substances.
    b. Providing treatment and counseling of persons who abuse controlled substances.
    c. Regulating the legitimate handling of controlled substances.

13. How could Alaska's PDMP be more effective?

Alaska's PDMP was created to improve patient care and reduce misuse, abuse, and diversion of controlled substances. Alaska PDMP effectiveness is limited by:

1. Registering with the Alaska PDMP is voluntary. Only 13.5% of prescribers and 40% of dispensers have registered with the PDMP.
2. Prescribers and dispensers are not permitted to delegate PDMP access to an employee.
3. The Alaska PDMP is not permitted to notify prescribers or dispensers regarding specific patients who may be at high risk of controlled substance prescription misuse, addiction, or diversion (i.e., unsolicited notification).
4. The Alaska PDMP database is not updated in real time. Database updates may be delayed for up to one month.
5. The director of the State of Alaska Medicaid Pharmacy Program is not permitted access the PDMP database.
6. The State of Alaska Medicaid Drug Utilization Review Committee is not permitted access to the PDMP database.
7. The State of Alaska Medical Examiner is not permitted access to the PDMP database.

8. No State of Alaska public health agency is permitted access to the PDMP database.

The CSAC believes increasing PDMP utilization will increase PDMP effectiveness.

Greater PDMP utilization has reduced prescription opiate misuse, addiction, overdose, and death in states with higher PDMP utilization.

Research shows that there is a direct correlation between heroin use and prescription opiate addiction. The CSAC believes increasing PDMP utilization will reduce prescription opiate addiction and will reduce the number of people switching from prescription opiate use to heroin use.

14. The CSAC recommends the following modifications to Alaska's PDMP:

1. Require all prescribers and all pharmacists to register with the Alaska PDMP.
2. Require prescribers and pharmacists to review the PDMP database when prescribing or dispensing a controlled substance to a patient.
3. Authorize prescribers and pharmacists to delegate database access to supervised employees or clinical staff.
4. Authorize the Board of Pharmacy to forward unsolicited notifications to prescribers and dispensers database information about patients who may be obtaining controlled substances inconsistent with generally recognized standards of care.
5. Collect dispensing data and updating the PDMP database weekly.
6. Authorize PDMP database access to the State of Alaska Medicaid Pharmacy Program.
7. Authorize PDMP database access to the State of Alaska Medicaid Drug Utilization Review Committee.
8. Authorize PDMP database access to the State of Alaska Medical Examiner.
9. Authorize de-identified PDMP data access to the State of Alaska Department of Health and Social Services (Alaska DHSS) Division of Public Health.

The American Medical Association Task Force to Reduce Opioid Abuse urges states and providers to utilize prescription drug monitoring programs to reduce prescription drug misuse, overdose, and death.[12]

A partial list of Task Force members includes:

- American Academy of Family Physicians
- American Academy of Hospice and Palliative Medicine
- American Academy of Orthopaedic Surgeons
- American Academy of Pain Medicine
- American Academy of Pediatrics
- American College of Emergency Physicians
- American Dental Association
- American Medical Association
- American Osteopathic Association
- American Psychiatric Association
- American Society of Addiction Medicine

- American Society of Anesthesiologists

Each modification requires a statutory change to AS 17.30.200.

15. Require all prescribers and all dispensers register with the Alaska PDMP
The Alaska PDMP cannot meet its mandate or reach its full potential if underutilized.

Forty-nine (49) states have operational PDMPs.[3] When prescriber and dispenser registration is voluntary, less than fifty percent (50%) of possible prescribers and dispensers register.[13]

As of June 2014, all prescribers are required to register for their state PDMP in twenty (20) states.[13]

Registering for Alaska's PDMP is voluntary. 13.5% of Alaska prescribers and 40% of Alaska dispensers have registered with the PDMP. Requiring PDMP registration will increase registration to one hundred percent (100%).

Registering for Alaska's PDMP may be done on line. Linking PDMP registration with state professional licensing application or renewal would facilitate PDMP registration.

Some prescribers may oppose mandatory PDMP registration believing it an intrusion into clinical practice, workflow, and threaten patient privacy and confidentiality. Evidence supports the benefits of a state PDMP with high utilization. Reaching out to the medical community and other stakeholders will increase awareness and support for PDMP utilization.

16. Require prescribers and dispensers review the PDMP database[13]
Twenty-two (22) states require PDMP database review by prescribers and sometimes dispensers.[13]

Nevada requires prescribers review the PDMP database when "the practitioner has a reasonable belief that the patient may be seeking the controlled substance, in whole or in part, for any reason other than the treatment of an existing medical condition."

Oklahoma requires prescribers and dispensers review the PDMP database when prescribing, administering, or dispensing methadone.

Kentucky requires prescribers review the PDMP database before prescribing any Federal Schedule II drug and any Federal Schedule III drug containing hydrocodone and then every three months before prescribing refills. Between 2012 and 2013 prescriptions for controlled substances (medications) decreased more than eight percent (8.5%).

Tennessee requires prescribers review the PDMP database when first prescribing opiates and benzodiazepines for more than seven days and at least annually thereafter if prescribing

continues. Between 2012 and 2013 there was a thirty-six percent (36%) decrease in patients going to multiple prescribers and seeking the same prescription medications.

Some prescribers may oppose requiring PDMP database review believing that it as an intrusion into clinical practice and workflow. Permitting prescribers to delegate PDMP access to supervised employees may reduce concerns about the impact on clinical practice and workflow.

The CSAC believes communicating and coordinating with the medical community and other stakeholders before implementing any change is recommended. PDMP education, negotiation, and consensus building will improve Alaska PDMP awareness, utilization, and effectiveness.

The CSAC believes this will reduce controlled substance misuse, addiction, and diversion. The CSAC believes this will reduce opiate overdose deaths and the incidence of patients switching from prescription opiate use to heroin use.

17. Authorize PDMP database access to supervised employees (delegates)
Prescribers and dispensers may be concerned that reviewing the PDMP database will negatively impact clinical practice and workflow. Accessing and reviewing PDMP data may be perceived as time consuming.

Thirty-six (36) states authorize prescribers and dispensers to delegate PDMP database access to employees.[14] Employees (delegated users) input patient names to download PDMP data for prescribers and dispensers. Prescribers and dispensers are responsible for their employees' (the delegated users) use of PDMP information.

"Delegate accounts, properly supervised and maintained..., are a secure and effective means to increase PDMP utilization."[14]

At some point in the future, the PDMP database will likely be automatically incorporated into electronic health records.

18. Authorize the PDMP to forward unsolicited reports to prescribers and dispensers
A solicited report is a report initiated by a query from a prescriber or dispenser registered with the PDMP. The registered prescriber or dispenser is seeking PDMP database information about a specific patient. Solicited reports are most commonly on-line queries. The specific patient's PDMP information is most commonly provided instantaneously on-line.

An unsolicited report is a report initiated by the PDMP in response to specific patient prescription and dispensing patterns, specific prescriber patterns, and specific dispenser patterns. Possible end users of unsolicited reports include prescribers, dispensers, licensing boards, law enforcement, and public health agencies.

Thirty-eight (38) states authorize PDMPs to forward unsolicited notifications to one or more end users.[15]

Beginning in 2005, the Maine PDMP began sending prescribers written quarterly reports via the U.S. Postal Service.[15] The Maine PDMP reports are sent to prescribers who are prescribing for specific patients when the patient:

- Receives multiple prescriptions from multiple prescribers and uses multiple dispensing pharmacies.
- Is prescribed an unusually high average daily dose of an opiate.
- Is prescribed buprenorphine concurrent with another opiate.

The Maine PDMP report lists all providers, all pharmacies, and the details of all prescriptions during the prior three-month period.

In a 2009 survey[15] of Maine prescribers, a "substantial proportion" of those who had received a PDMP report took action because of the notification. The action taken was one or more of the following:

- Checking the PDMP database regarding that patient's prescription history.
- Calling other prescribers who had prescribed for the patient.
- Talking to the patient.
- Conducting a substance abuse screen and providing a brief intervention.

Between 2011 and 2012, the number of suspected "doctor shoppers" in Maine declined thirty-two percent (32%).[15]

19. Real Time Data Collection

The Alaska PDMP currently requires all dispensers (primarily pharmacies) to monthly report controlled substances dispensed. This means that the Alaska PDMP database may be up to four weeks out of date.

Most state PDMPs receive dispenser (primarily pharmacy) updates every 1-2 weeks.[16] Real time data collection and database updating may need to wait until health information technology facilitates this process. The CSAC recommends updating the PDMP database weekly.

20. Permit database access by the State of Alaska Medicaid Program

The State of Alaska Medicaid program currently has a Pharmacist Director and one supporting staff Pharmacist. The Medicaid Pharmacist Director:

1. Coordinates the Pharmacy & Therapeutics Committee.
2. Assists in coordinating the Drug Utilization Review Committee.
3. Supervises the prior authorization process.

Granting access to the PDMP for the State of Alaska Medicaid Pharmacy program would:

- Improve awareness of prescribing patterns and dispensing by prescribers and dispensers for patients in Alaska Medicaid.

- Increase awareness of those paying cash (not using their Medicaid benefits) for acquiring controlled substances.

National data indicate that people on Medicaid are prescribed opiates at twice the rate of non-Medicaid patients and are at six times the risk of prescription opiate overdose.[1]

21. Permit database access by the State of Alaska Medicaid Drug Utilization Review Committee

The Alaska Medicaid Drug Utilization Review Committee (Medicaid DUR) was created in 1990. The Medicaid DUR Committee conducts prospective and retrospective analyses to address safety, fraud, waste, abuse, misuse, and medically unnecessary care. The Medicaid DUR Committee is limited to prescribing and dispensing activities paid by Alaska Medicaid.

PDMP database access by the Medicaid DUR Committee would improve the ability to identify:

- Medicaid beneficiaries paying cash for controlled substances (medications).
- Medicaid beneficiaries obtaining possibly unnecessary medical care paid by Medicaid to obtain possibly unnecessary prescriptions for controlled substances paid by cash.

22. Permit database access by the State of Alaska Medical Examiner

The Alaska Medical Examiner investigates unexplained and/or unexpected deaths, and currently, the Medical Examiner (and/or staff) must obtain a search warrant, subpoena, or court order prior to receiving Alaska PDMP data.

Alaska's death rate from opiates and heroin is increasing. Between 2008 and 2013, there were more deaths in Alaska by prescription opioid and heroin overdoses than by motor vehicle accident.[7] Permitting access to the PDMP database is consistent with the Alaska Medical Examiner's role in investigating unexplained and/or unexpected deaths.

23. Permit database access by the State of Alaska Department of Health and Social Services Division of Public Health

The Alaska Department of Health and Social Services (DHSS) Division of Public Health does not have access to the Alaska PDMP database.

State PDMPs differ on their use of PDMP data to meet public health objectives. Common public heath objectives regarding controlled substances (prescription medications) include:

- Epidemiological surveillance to measure and track the incidence and prevalence of nonmedical use of prescription medications.
- Education about prescribing trends and raising awareness regarding the misuse of prescription medications.
- Early recognition and intervention of the possible misuse of prescription medications.
- Prevention of circumstances that increase the risk of prescription medication misuse, addiction, and overdose.
- Coordinate with federal and multistate efforts to prevent and reduce prescription medication misuse, addiction, and overdose.

The Division of Public Health could use de-identified data to meet public health objectives regarding controlled substances including prescription opiates. De-identified data could be similar to Medicaid DUR Committee data in that it is not identifiable data (de-identified regarding patient identity, prescriber identity, dispenser identity, and dispenser location).

24. Summary and Suggestions

PDMPs are increasingly utilized by states to improve clinical care and outcomes and to reduce controlled substances misuse, addiction, and overdose fatalities. Alaska has had a PDMP since 2008. But, only 13.5% of prescribers and only 40% of dispensers have registered with the Alaska PDMP. The Alaska PDMP permits access and review of the PDMP database only to providers who are registered with the Alaska PDMP. Providers who have registered with the Alaska PDMP must then query the system about specific patients.

The Alaska PDMP will be more useful and effective if database utilization is higher by:

- ✓ Requiring prescribers and dispensers to register for the PDMP.
- ✓ Requiring prescribers and dispensers to access and review the PDMP database.
- ✓ Permitting prescribers and dispensers to delegate PDMP database access by employees.
- ✓ Permitting the PDMP to alert providers of patients who may be at risk of misusing controlled substances (prescription medications).
- ✓ Updating the PDMP database weekly.
- ✓ Permitting PDMP database access by the Alaska Medicaid Pharmacists.
- ✓ Permitting PDMP database access by the Alaska Medicaid Drug Utilization Review Committee.
- ✓ Permitting PDMP database access by the Alaska Medical Examiner.
- ✓ Permitting access to de-identified PDMP data by the Alaska Department of Health and Social Services Division of Public Health.

The CSAC does not have recommendations regarding negative consequences for prescribers, dispensers, or pharmacies not adhering to the recommended PDMP changes should they be enacted.

Finally, Alaska's PDMP does not replace the necessity of evaluating and treating substance use disorders and does not replace controlled substances law enforcement.

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DRUG SCHEDULING

Drug Schedules

Drugs, substances, and certain chemicals used to make drugs are classified into five (5) distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs are considered the most dangerous class of drugs with a high potential for abuse and potentially severe psychological and/or physical dependence. As the drug schedule changes-- Schedule II, Schedule III, etc., so does the abuse potential-- Schedule V drugs represents the least potential for abuse. A Listing of drugs and their schedule are located at Controlled Substance Act (CSA) Scheduling or CSA Scheduling by Alphabetical Order. These lists describes the basic or parent chemical and do not necessarily describe the salts, isomers and salts of isomers, esters, ethers and derivatives which may also be classified as controlled substances. These lists are intended as general references and are not comprehensive listings of all controlled substances.

Please note that a substance need not be listed as a controlled substance to be treated as a Schedule I substance for criminal prosecution. A controlled substance analogue is a substance which is intended for human consumption and is structurally or pharmacologically substantially similar to or is represented as being similar to a Schedule I or Schedule II substance and is not an approved medication in the United States. (See 21 U.S.C. §802(32)(A) for the definition of a controlled substance analogue and 21 U.S.C. §813 for the schedule.)

Schedule I

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence. Some examples of Schedule I drugs are:

heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote

Schedule II

Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are:

Combination products with less than 15 milligrams of hydrocodone per dosage unit (Vicodin), cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin

Schedule III

Schedule III drugs, substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV. Some examples of Schedule III drugs are:

Products containing less than 90 milligrams of codeine per dosage unit (Tylenol with codeine), ketamine, anabolic steroids, testosterone

Schedule IV

Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence. Some examples of Schedule IV drugs are:

Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien, Tramadol

Schedule V

Schedule V drugs, substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes. Some examples of Schedule V drugs are:

cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin

>> Alphabetical listing of Controlled Substances