ASPE
ISSUE BRIEF

Opioid Abuse in the U.S. and HHS Actions to Address Opioid-Drug Related Overdoses and Deaths

March 26, 2015

Introduction

The abuse of and addiction to opioids is a serious and challenging public health problem. Deaths from drug overdose have risen steadily over the past two decades and have become the leading cause of injury death in the United States.[1] Prescription drugs, especially opioid analgesics—a class of prescription drugs such as hydrocodone, oxycodone, morphine, and methadone used to treat both acute and chronic pain— have increasingly been implicated in drug overdose deaths over the last decade.[2,3] From 1999 to 2013, the rate for drug poisoning deaths involving opioid analgesics nearly quadrupled.[4] Deaths related to heroin have also increased sharply since 2010, with a 39 percent increase between 2012 and 2013.[5] Given these alarming trends, it is time for a smart and sustainable response to prevent opioid abuse and overdose and treat people with opioid use disorder.

The U.S. Department of Health and Human Services (HHS) has made addressing the opioid abuse problem a high priority and is committed to accelerating its work towards two broad goals: 1) decreasing opioid overdoses and overall overdose mortality and 2) decreasing the prevalence of opioid use disorder. Priority areas for action were identified through a Department wide effort that tapped all the scientific, analytical and programmatic expertise contained in HHS agencies. The development effort also relied on discussions with states and other stakeholder organizations.

The Secretary's initiative targets three priority areas to combat opioid abuse:

- **Opioid prescribing practices** to reduce opioid use disorders and overdose
- Expanded use and distribution of **naloxone**
- Expansion of **Medication-assisted Treatment (MAT)** to reduce opioid use disorders and overdose

A wide variety of possible interventions exists; however, Secretary Burwell directed officials and staff leading the initiative's development to identify a small but targeted set of actions that have

the highest likelihood of producing clinically meaningful outcomes – intermediate and long-term. Specifically, the actions and strategies in the initiative are grounded in the best research and clinical science available. This means reliance on:

- The best available evidence
- The availability to HHS of policy levers to deliver measurable impact
- Policies targeted to high-risk populations
- Each proposed element of the strategy has a reasonable expectation of delivering a measurable impact within two years

These priorities—prescribing practices, naloxone, and MAT—will guide the Department's targeted efforts to take steps that will reduce opioid-related morbidity and mortality.

Epidemiology

Mortality data show that there was a 6 percent increase in drug overdose deaths between 2012 and 2013 (see Table 1). Approximately 37 percent (16,235) of overdose deaths involved prescription opioids, a number essentially unchanged from 2012. However, the mortality rate from heroin overdose increased each year from 2010 to 2013. Deaths from heroin overdoses increased by 39 percent from 2012 to 2013 alone and were approximately 19 percent (8,257) of all drug overdose deaths in 2013.

Prescription Opioids

Prescription opioids are available as immediate-release (IR) or extended release/long-acting (ER/LA) formulations. While improper use of any opioid can result in serious side effects, including overdose and death, that risk significantly increases with ER/LA formulations.[6] Prescription opioids also taken in combination with other misused or abused prescription drugs such as benzodiazepines (e.g. sedatives like Xanax) and antidepressants are commonly linked to overdose deaths.[7]

Existing evidence shows that individuals at greatest risk for prescription opioid overdose include:

- White and American Indian/Alaska Native people
- Men (although overdose among women is on the rise)
- People living in rural areas (clusters in the Southeast—especially in the Appalachian region)
- Adults aged 45-54 years
- People who obtain multiple controlled substance prescriptions (especially the combination of opioid analgesics and benzodiazepines) from multiple providers
- People who take high daily dosages of opioid pain relievers

In addition to mortality, other types of adverse health events tied to prescription opioid abuse have increased over the last decade. Rates of emergency department (ED) visits associated with

pharmaceutical misuse or abuse increased 114 percent between 2004 and 2011.[8] In 2011, more than 1.4 million ED visits annually were due to the misuse or abuse of pharmaceuticals, with 420,000 involving prescription opioids and 425,000 involving benzodiazepines. In addition, the admission rate for substance abuse treatment for prescription opioid abuse in 2009 was almost six times the rate in 1999.[2] Prescription opioid abuse can also result in other health consequences such as neonatal abstinence syndrome, [9] increased risk of transmission of HIV and Hepatitis C (associated with injection)[10, 11], and fractures in older adults (due to falls).[12,13]

Underlying prescription opioid-related morbidity and mortality is the large number of people who report nonmedical use of prescription drugs—use without a prescription or use for the feeling or experience the drug caused. Nonmedical use of psychotherapeutic drugs in the past year among people 12 years and older has ranged from 5.7 to 6.7 percent during 2002-2013, according to the National Survey on Drug Use and Health (NSDUH). For prescription pain relievers, the percentage has ranged from 4.2 percent to 5.1 percent during this time period.[14] However, these relatively flat rates of nonmedical use mask a sharp increase in nonmedical use of prescription pain relievers by a relatively small number of "heavy users." Chronic nonmedical use – nonmedical use of 200 days or more in the past year – had increased by roughly 75 percent between 2002-2003 and 2009-2010.[15]

Among persons aged 12 or older in 2012-2013 who used prescription pain relievers nonmedically in the past year, 53 percent received them from a friend or relative for free and approximately 15 percent bought or took them from a friend or relative.[16] However, recent research indicates that the source for nonmedical users varies significantly depending on the frequency of nonmedical use. While occasional nonmedical users (those who use the drugs nonmedically less than 30 days a year) are most likely to obtain their drugs from a friend or relative for free, the highest-use, highest-risk nonmedical users (i.e. those who reported nonmedical use 200 or more days a year) were more likely to obtain their drugs directly from a doctor's prescription than from any other source.[17]

Heroin

As noted earlier, heroin use has sharply increased in recent years. In 2013, the number of past year heroin users was 681,000, which was similar to the numbers in 2009 to 2012 (ranging from 582,000 to 669,000), but markedly higher compared to numbers in 2002-2005, and 2007-2008 (ranging from 314,000 to 455,000).[16] States and cities have reported significant increases in heroin deaths since 2010,[18] and recent analysis shows that the rate for deaths involving heroin has almost tripled since 2010.[5] A CDC analysis of 28 states from 2010-2012 show heroin overdose death rates in 2012 highest among:

- Adults aged 25-34 years old
- White, non-Hispanic people
- Men
- People living in the Northeast and Midwest

Between 2002–2004 and 2008–2010, past year heroin use increased among people reporting nonmedical use of prescription opioids within the past year, but not among those reporting no past year nonmedical use.[19] A retrospective analysis of heroin use in the United States over the last 50 years showed that among people who initiated abuse of opioids in the 1960s, 80 percent reported they initiated with heroin.[20] In contrast, among those who began abusing opioids in the 2000s, 75 percent of individuals indicated they initiated their abuse with prescription opioids. In terms of determining factors for this shift to heroin use, study results indicate that heroin has become more accessible and significantly cheaper, is easier to inhale/inject, and the potency is much greater than prescription opioids.[20]

Although available literature indicates that abuse of prescription opioids is a risk factor for future heroin use, only a small fraction, roughly 4 percent of opioid abusers, transition to heroin use within five years of initiating opioid abuse.[21] The assertion that a crackdown on the supply of opioid pain relievers is the driver of the recent increases in heroin use and deaths does not appear to be supported by the currently available data.

HHS continues to collect data to monitor the relationship between heroin and prescription opioids. These data underscore the importance of effective interventions to prevent opioid abuse and overdose and treat opioid use disorders.

What Works

There is a limited but growing body of research that supports the effectiveness of several interventions to address opioid abuse. Continued monitoring and evaluation are essential to further strengthen the evidence base and inform program and policy decision making.

Prescription Drug Monitoring Programs

Prescription drug monitoring programs (PDMPs) are state-run electronic databases of prescriptions for controlled substances and are among the most promising clinical tools to curb prescription opioid abuse. PDMPs can provide a prescriber or pharmacist with important information regarding a patient's prescription history, allowing prescribers to identify patients who are potentially abusing medications. The organization and operation of PDMPs varies among states (e.g. which state agencies houses the PDMP, which controlled substances must be reported, how often data are collected and reported, who can access the PDMP, etc.). Currently, 49 states, the District of Columbia, and one U.S. territory (Guam) have legislation authorizing the creation and operation of a PDMP and all but the DC program are operational.[22]

Existing evidence, though limited, indicates the potential of PDMPs to identify high-risk patients and impact key prescribing behaviors.[23] PDMP evaluations have detected positive changes in prescribing patterns, decreased use of multiple providers and pharmacies, and decreased substance abuse treatment admissions.[24,25,26,27,28] For example, a preliminary analysis of the impact of laws mandating use of PDMPs by prescribers in Kentucky, Tennessee, and New York showed reductions in multiple provider episodes (e.g., approximately 75 percent decline in New

York).[29] Controlled substance prescribing also declined (e.g., in Kentucky doses dispensed declined for hydrocodone by approximately 10 percent, oxycodone by 12 percent, and oxymorphone by 35 percent).[29] Clinical decision support tools and health IT systems incorporating PDMP and other clinical data also show promise for improving prescribing behaviors and reducing adverse events.[30,31,32,33] As states work to adopt more evidence-based PDMP practices such as collecting data for all controlled substances, proactive reporting to physicians and pharmacists, interstate data sharing, and integration with other health IT systems to improve provider use, their effectiveness is likely to increase.[34]

Guidelines

There is a clear correlation between opioid prescribing rates and overdose death rates in the United States. From 1999 to 2010, opioid prescribing quadrupled in parallel to increasing opioid overdose death rates.[2] These data underscore the importance of prescribing guidelines that encourage the use of opioids when benefits outweigh risks and that promote safe use when opioids are needed. There is limited research available to assess the impact of prescribing guidelines, and additional study is needed to better understand how to optimally operationalize them. However, a recent study of workers compensation patients in Washington State found that after the introduction of voluntary opioid guidelines in 2007, there was a 27 percent decline in the mean dose for long-acting opioids, a 35 percent decline in the percentage of patients receiving 120 morphine milligram equivalents per day or more, and a 50 percent reduction in opioid-related overdose deaths among injured workers.[35] If followed and universally implemented, integrating guidelines into electronic health records or clinical decision support platforms may help to reduce inappropriate prescribing of drugs commonly involved in overdose deaths.

Naloxone

Naloxone is an effective drug to reverse overdose from both prescription opioids and heroin.[36,37,38,39,40] As an opioid antagonist, naloxone binds to opioid receptors and can reverse the effects of other opioids. It can quickly restore normal respiration to a person whose breathing has slowed or stopped as a result of heroin or prescription opioid overdose. Several overdose education and naloxone distribution programs have been developed to issue naloxone and provide instructions on its use to opioid users, their friends and loved ones, and other potential bystanders. An article in *Morbidity and Mortality Weekly Report* reported that as of 2010, programs that distribute naloxone to nonmedical personnel had reported more than 10,000 overdose reversals nationwide since 1996.[41] As of November 2014, 23 states have statutes that allow for "third-party" prescriptions of naloxone (i.e. the prescription can be written to friend, relative or person in a position to assist a person at risk of experiencing an opioid overdose).[42] An evaluation of Massachusetts' overdose education and nasal naloxone distribution program found that opioid overdose death rates declined in communities where programs were implemented.[38] Given the effectiveness of naloxone in overdose reversal, the Food and Drug Administration (FDA) has encouraged innovations in more user-friendly naloxone delivery systems such as auto-injectors, made particularly for lay use outside of health care settings. FDA approved such an auto-injector in 2014.

Medication-assisted Treatment (MAT)

MAT is the use of medications (i.e. buprenorphine, methadone, extended-release injectable naltrexone), in combination with counseling and behavioral therapies, to provide a whole-patient approach to the treatment of substance use disorders, including opioid use disorders. MAT is a safe and effective strategy for decreasing the frequency and quantity of opioid use and reducing the risk of overdose and death.[43,44] Studies have shown that the most effective treatments for opioid use disorders are those that include a set of comprehensive medical, social, psychological and rehabilitation services that address all the needs of the individual. Furthermore, recently published research indicates that the most prevalent forms of MAT, buprenorphine and methadone, are similar in terms of effectiveness.[45] Although MAT has significant evidence to support it as an effective treatment, it remains highly underutilized, being used by an estimated 1 million of the 2.5 million Americans who might benefit from receiving it.[46]

Translating Evidence into Action

HHS is already taking steps to implement the Secretary's new initiative. President Obama's FY 2016 Budget includes an increase of $99 million above FY 2015 for targeted efforts to reduce opioid-related morbidity and mortality and the prevalence and impact of opioid use disorders.

Opioid Prescribing Practices (prescription opioids)

While actions to address prescription opioid abuse must target both prescribers and high-risk patients, prescribers are the gatekeepers for preventing inappropriate access. Interventions to improve safe and appropriate prescribing must balance the use of these drugs for legitimate purposes with the need to curb dangerous practices. Within this priority area are three objectives:

- Improve clinical decision-making to reduce inappropriate prescribing
- Enhance prescription monitoring and health information technology (health IT) to support appropriate pain management
- Support data sharing by providers to facilitate appropriate prescribing

Some key actions include:

Increased investments in evidence-based state prevention interventions, including PDMPs
Building off the infrastructure of the Prevention Boost and Core Violence and Injury Prevention programs, CDC received $20 million in FY 2015 and will launch the Prescription Drug Overdose Prevention for States program, which will target states with high burdens of prescription drug overdose morbidity and mortality. This funding will expand state-level interventions that focus on improving prescribing to prevent overdose, including enhancements to PDMPs. Another $65 million is proposed in the FY 2016 President's Budget to expand the program to all 50 states and Washington, DC. The PDMP component of this program is designed to advance broad adoption of universal, real-time, actively managed PDMPs. Also in

FY 2015, CDC is initiating a rigorous evaluation of this new program that will inform program improvements to ensure the highest public health impact as the program expands.

Establishing opioid prescribing guidelines for chronic pain and working to ensure effective implementation of guidelines
To improve clinical decision making to reduce inappropriate opioid prescribing, CDC is developing guidelines for opioid prescribing for chronic pain outside the setting of end-of-life care. To ensure effective implementation of guidelines, the Office of the National Coordinator for Health Information Technology (ONC) will build upon this work by exploring opportunities to convert guidelines into standardized, sharable, health IT-enabled clinical decision support interventions.

Naloxone (prescription opioids and heroin)

To support the important role of naloxone in overdose prevention, the initiative focuses on three objectives:

- Expand utilization of naloxone
- Accelerate the development and availability of new naloxone formulations and user friendly products
- Identify and disseminate best practice naloxone delivery models and strategies

Some key actions include:

Research trials on implementation and dissemination of overdose prevention programs
The National Institute on Drug Abuse (NIDA) within the National Institutes of Health (NIH) is supporting a number of research trials exploring the efficacy of prescribing take-home naloxone for individuals at high risk of prescription opioid or heroin overdose or at high risk of witnessing an overdose. FDA is also supporting the development of new opioid overdose treatments by using its expedited review programs.

Expanding utilization of naloxone through grants program to states
States are now permitted to use some of their substance abuse block grant funds to purchase naloxone and the necessary materials to assemble and disseminate overdose kits and increase education/training on the use of naloxone. The FY 2016 President's Budget proposes that Substance Abuse and Mental Health Services Administration (SAMHSA) issue $12 million in grants to states to purchase naloxone, equip first responders in high-risk communities, and provide education and the necessary materials to assemble overdose kits, as well as cover expenses incurred from dissemination efforts.

Medication-assisted Treatment (prescription opioids and heroin)

Given expanded coverage of substance abuse treatment services in recent years through the Affordable Care Act (ACA) and mental health parity, there is a greater need to address barriers that hinder access to treatment including policy and regulation that limit eligible providers or the

required training for delivering certain MAT services. Within the MAT priority area are two objectives:

- Support research that informs effective use and dissemination of MAT and accelerates development of new addiction treatment medications
- Increase access to clinically effective MAT strategies

Some key actions include:

Research to support effective MAT strategies
NIDA is currently supporting research on the effects of the ACA on MAT implementation and the efficacy of implementation strategies for MAT in medical and criminal justice settings, among other study topic areas. In addition, FDA is also promoting the development of medications for the treatment of opioid use disorders by using its expedited review programs.

Investments in MAT services
In FY 2015, SAMHSA will provide $12 million through a demonstration grant program to expand treatment services for opioid dependence. Grants will provide accessible, effective, comprehensive, coordinated, and evidence based MAT and recovery support services including the use of FDA-approved agonist medications (e.g., methadone, buprenorphine products including buprenorphine/naloxone combination formulations and buprenorphine mono-product formulations) for the maintenance treatment of opioid use disorder and opioid antagonist medication (e.g., naltrexone products including extended-release and oral formulations) to prevent relapse to opioid use education. The FY 2016 President's Budget proposed an additional $13 million expansion of this program to increase the number of states that would receive targeted funding to address prescription drug misuse and heroin use through expanded MAT services. HHS is also exploring policy changes that would increase access to providers certified to deliver MAT.

Many activities that fall within the three priority areas of the Secretary's initiative are currently or soon to be underway and represent significant additional investments in opioid-drug related activities proposed as part of the President's FY 2016 Budget. The President's FY 2016 Budget proposes an increase of $99 million above FY 2015 for targeted efforts to reduce opioid-related morbidity and mortality and the prevalence and impact of opioid use disorders, which includes both prescription opioids and heroin.

Next Steps

HHS continues to coordinate with agencies across the Department to ensure effective implementation of the initiative's programs and policies. HHS has also prioritized the development of an evaluation strategy to identify the most effective strategies and inform future policymaking that will have the greatest public health impact. Evaluation is a critical component of the initiative to identify what works and how the most effective interventions can be taken to scale.

HHS leadership has joined together to aggressively implement the new initiative and monitor progress. Many activities are already underway, and the Department continues to seek opportunities to work with its partners on this critical issue. The challenges are significant, and thus the Department looks to all stakeholders – at all levels of government, industry and providers – to help address this crisis.

Table 1. Number of Drug Poisoning Deaths by Category, United States, 2011-2013

	2011	2012	2013	% change from 2012-2013	% change from 2011-2013
Total drug-poisoning deaths (drug overdose deaths)	41,340	41,502	43,982	6.00%	6.40%
Heroin deaths	4,397	5,925	8,257	39.40%	87.80%
Opioid analgesics deaths	16,917	16,007	16,235	1.40%	-4.00%

Sources: Centers for Disease Control and Prevention. Wide Ranging Online Data for Epidemiologic Research (CDC WONDER). Available at: http://wonder.cdc.gov/.

Sources:

1. Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS) [online]. 2014. Retrieved from: http://www.cdc.gov/injury/wisqars/fatal.html.
2. Paulozzi L, Jones C, Mack K, Rudd R; Centers for Disease Control and Prevention (CDC). Vital signs: overdoses of prescription opioid analgesics—United States, 1999-2008. MMWR Morb Mortal Wkly Rep. 2011;60(43):1487- 1492.
3. Centers for Disease Control and Prevention/National Center for Health Statistics, National Vital Statistics System, Mortality File. Retrieved from: http://www.cdc.gov/nchs/data/hestat/drug_poisoning/drug_poisoning.htm.
4. Centers for Disease Control and Prevention. QuickStats: Rates of Deaths from Drug Poisoning and Drug Poisoning Involving Opioid Analgesics — United States, 1999–2013. MMWR Weekly. Retrieved from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6401a10.htm
5. Hedegaard H, Chen LH, Warner M.; National Center for Health Statistics (NCHS). Drug-poisoning deaths involving heroin: States, 2000–2013. NCHS data brief, no190. Retrieved from: http://www.cdc.gov/nchs/data/databriefs/db190.pdf .
6. Food and Drug Administration. Risk Assessment and Risk Mitigation Reviews. Retrieved from: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205777Orig1s000RiskR.pdf.
7. Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA. 2013 Feb 20;309(7):657-9
8. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality.The DAWN Report: Highlights of the 2011 Drug Abuse Warning Network (DAWN) Findings on Drug-Related Emergency Department Visits. Retrieved from : http://www.samhsa.gov/data/sites/default/files/DAWN127/DAWN127/sr127-DAWN-highlights.htm
9. Creanga AA, Sabel JC, Ko JY, Wasserman CR, Shapiro-Medoza CK, Taylor P, Barfield W, et al. Maternal drug use and its effect on neonates:a population-based study in Washington State. Obstet Gynecol. 2012;199(5):924-933.
10. Zibbell JE, Hart-Malloy R, Barry J, Fan L, Flanigan C. Risk factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. Am J Public Health. 2014 Nov;104(11):2226-32. doi: 10.2105/AJPH.2014.302142. Epub 2014 Sep 11.
11. Mateu-Gelabert P1, Guarino H2, Jessell L2, Teper A2. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. J Subst Abuse Treat. 2015 Jan;48(1):13-20. doi: 10.1016/j.jsat.2014.07.002. Epub 2014 Jul 11.
12. Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. J Am Geriatr Soc. 2013;61(3):335-340.
13. Miller M, Sturmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. J Am Geriatr Soc. 2011;59(3):430-438.
14. Substance Abuse and Mental Health Services Administration. Center for Behavioral Health Statistics and Quality. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. Detailed Tables, 7.2B. Retrieved from: http://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2013/NSDUH-DetTabs2013.htm#tab7.2b .
15. Jones CM. Frequency of prescription pain reliever nonmedical use: 2002-2003 and 2009-2010. Arch Intern Med. 2012;172(16):1265-1267
16. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. Retrieved from: http://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.htm
17. Jones CM, Paulozzi LJ, Mack KA. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use United States, 2008-2011. JAMA Intern Med. 2014 May;174(5):802-3.
18. Rudd RA, Paulozzi LJ, Bauer MJ, Burleson RW, Carlson RE, Dao D, Davis JW, Dudek J, Eichler BA, Fernandes JC, Fondario A, Gabella B, Hume B, Huntamer T, Kariisa M, Largo TW, Miles J, Newmyer A, Nitcheva D, Perez BE, Proescholdbell SK, Sabel JC, Skiba J, Slavova S, Stone K, Tharp JM, Wendling T,

Wright D, Zehner AM; Centers for Disease Control and Prevention (CDC). Increases in heroin overdose deaths - 28 States, 2010 to 2012. MMWR 2014 Oct 3;63(39):849-54. Retrieved from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6339a1.htm

19. Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers—United States, 2002–2004 and 2008–2010. Drug Alcohol Depend 2013;132:95–100.
20. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry 2014;71:821–6.
21. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. August 2013. Retrieved from: http://www.samhsa.gov/data/2k13/DataReview /DR006/nonmedical-pain-reliever-use-2013.pdf
22. PDMP Training and Technical Assistance Center. PDMP Frequently Asked Questions. Retrieved from: http://www.pdmpassist.org/content/prescription-drug-monitoring-frequently-asked-questions-faq
23. PDMP Center of Excellence at Brandeis University. Briefing on PDMP Effectiveness: Updated September 2014. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Briefing%20on%20PDMP%20Effectiveness%203rd%20revision.pdf
24. Curtis LH, Stoddard J, Radeva JI, Hutchison S, Dans PE, Wright A, et al. Geographic variation in the prescription of schedule II opioid analgesics among outpatients in the United States. Health Serv Res. 2006 2006;41:837-55.
25. Reifler L, Droz D, Bailey J, Schnoll S, Fant R, Dart R, et al. Do prescription monitoring programs impact state trends in opioid abuse/misuse? Pain Medicine. 2012;13(3):355-6.
26. Reisman RM, Shenoy PJ, Atherly AJ, Flowers CR. Prescription opioid usage and abuse relationships: an evaluation of state prescription drug monitoring program efficacy. Substance Abuse: Research and Treatment. 2009;3(SART-3-Shenoy-et-al):41.
27. Worley, J. Prescription drug monitoring programs, a response to doctor shopping: purpose, effectiveness, and directions for future research. Issues in Mental Health Nursing, 2012, 33:319-328.
28. Simeone R, Holland L. Washington, D.C.: U.S. Dept. of Justice, Office of Justice Programs 2006. Retrieved from: http://www.simeoneassociates.com/simeone3.pdf
29. PDMP Center of Excellence at Brandeis University. COE Briefing—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
30. Charles K, Cannon M, Hall R, Coustasse A. Can Utilizing a Computerized Provider Order Entry (CPOE) System Prevent Hospital Medical Errors and Adverse Drug Events? Perspect Health Inf Manag. 2014 Oct 1;11:1b. eCollection 2014.
31. Department of Health and Human Services. Connecting Prescribers and Dispensers to PDMPs through Health IT; 2013. Retrieved from: http://www.healthit.gov/sites/default/files/pdmp_pilot_studies_summary.pdf
32. Wolfstadt JI, Gurwitz JH, Field TS, Lee M, Kalkar S, Wu W, Rochon PA The effect of computerized physician order entry with clinical decision support on the rates of adverse drug events: a systematic review.J Gen Intern Med. 2008 Apr;23(4):451-8. doi: 10.1007/s11606-008-0504-5.
33. Mishuris RG, Linder JA, Bates DW, Bitton A Using electronic health record clinical decision support is associated with improved quality of care. Am J Manag Care. 2014 Oct 1;20(10):e445-52.
34. PDMP Center of Excellence at Brandeis University. Prescription Drug Monitoring Programs: An Assessment of the Evidence for Best Practices, September 2012. Retrieved from: http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_PDMP_Report.pdf
35. Franklin GM, Mai J, Turner J, Sullivan M, Wickizer T, Fulton-Kehoe D. Bending the prescription opioid dosing and mortality curves: impactof the Washington State opioid dosing guideline. Am J Ind Med. 2012;55(4):325-31.
36. Boyer EW. Management of opioid analgesic overdose. N Engl J Med. 2012;367(2):145-155.
37. Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. Ann Intern Med.2013;158(1):1-9
38. Walley AY, Xuan Z, Hackman HH, Quinn E, Doe-Simkins M, Sorensen-Alawad A, Ruiz S, Ozonoff A. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013 Jan 30;346:f174. doi: 10.1136/bmj.f174.

39. Haegerich TM, Paulozzi LJ, Manns BJ, Jones CM. What we know, and don't know, about the impact of state policy and systems-level interventions on prescription drug overdose. Drug Alcohol Depend. 2014 Dec 1;145:34-47.
40. Clark AK, Wilder CM, Winstanley EL. A systematic review of community opioid overdose prevention and naloxone distribution programs. J Addict Med. 2014 May-Jun;8(3):153-63.
41. Centers for Disease Control and Prevention. Community-based opioid overdose prevention programs providing naloxone—United States, 2010. MMWR. 2012;61(6):101–105. Retrieved from: http://www.cdc.gov/mmwr/pdf/wk/mm6106.pdf
42. White House Office of National Drug Control Policy. Infographic Update: Overdose Prevention, State by State. Retrieved from: http://www.whitehouse.gov/blog/2014/12/17/updated-infographic-overdose-prevention-state-state
43. Kresina TF, Lubran RL. Improving public health through access to and utilization of medication assisted treatment. Int J Environ Res Public Health. 2011;8:4102-4117
44. National Institutes on Drug Abuse. Cost effectiveness of drug treatment. Retrieved from: http://www.drugabuse.gov/publications/teaching-packets/understanding-drug-abuse-addiction/sectioniv/6-costeffectiveness-drug-treatment
45. Potter, J.S.; Marino, E.N.; Hillhouse, M.P., et al. Buprenorphine/naloxone and methadone maintenance treatment outcomes for opioid analgesic, heroin, and combined users: findings from Starting Treatment with Agonist Replacement Therapies (START). Journal of Studies on Alcohol and Drugs 74(4):605-613, 2013.
46. Volkow ND1, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies--tackling the opioid-overdose epidemic. N Engl J Med. 2014 May 29;370(22):2063-6. doi: 10.1056/NEJMp1402780. Epub 2014 Apr 23.