Executive Summary: Health Impact Review of SB 6150

Concerning Opioid Use Disorder Treatment, Prevention, and Related Services
(2017-2018 Legislative Session)

Evidence indicates that SB 6150 has the potential to decrease health complications and deaths from opioid use and decrease health disparities by race/ethnicity.

BILL INFORMATION

Sponsors: Cleveland, Rivers, Carlyle, Kuderer, Fain, Hasegawa, Mullet, Saldaña, Conway, Van De Wege, Chase, Keiser, Liias

By Request: Governor Inslee

Companion Bill: HB 2489

Summary of Bill:
Full details about the provisions of this bill can be found in the bill text linked above. Given the length of the bill and the large number of provisions, the summary below only highlights particularly relevant sections.

- Eliminates barriers and promotes access to evidence-based opioid use disorder treatment services and opioid overdose reversal medication such as naloxone.
- Promotes coordination of services and strengthens partnerships between opioid use disorder treatment providers, the recovery support system, and their allied community partners.
- Establishes a mechanism for the Secretary of Health, or their designee, to issue a standing order for prescribing opioid overdose reversal medications such as naloxone to any person at risk of experiencing or witnessing an overdose.
- Expands the use of Washington State's Prescription Drug Monitoring Program (PDMP) by requiring electronic health record (EHR) vendors to ensure their federal certified systems can integrate with PDMP data.

HEALTH IMPACT REVIEW

Summary of Findings:
This Health Impact Review found the following evidence regarding the provisions in SB 6150:

- Strong evidence that promoting access to and use of opioid overdose reversal medication will likely result in opioid overdose reversal medication being more frequently distributed and administered.
- Very strong evidence that increasing distribution and administration of opioid overdose reversal medication will likely decrease health complications and deaths from opioid use.
- Very strong evidence that promoting access to medication-assisted therapies for opioid dependence will likely decrease health complications and deaths from opioid use.
- Strong evidence that expanding the use of the state PDMP will likely improve clinical decision-making and reduce "doctor shopping" and diversion of prescription opioids.
- Strong evidence that improving clinical decision-making and reducing "doctor shopping" and diversion of prescription opioids will likely decrease health complications and deaths from opioid use.
- Strong evidence that decreasing health complications and deaths from opioid use will likely decrease health disparities.

For more information contact:
(360)-236-4106 | hir@sboh.wa.gov
or go to sboh.wa.gov

WASHINGTON STATE BOARD OF HEALTH
Working for a safer and healthier Washington since 1889

HEALTH EQUITY
Governor's Interagency Council on Health Disparities

Health Impact Review of SB 6150

Concerning Opioid Use Disorder Treatment, Prevention, and Related Services (2017-2018 Legislative Session)

January 18, 2018

Staff Contact: Alexandra Montaño

Contents

Introduction and Methods

A Health Impact Review is an analysis of how a proposed legislative or budgetary change will likely impact health and health disparities in Washington State (RCW 43.20.285). For the purpose of this review 'health disparities' have been defined as the differences in disease, death, and other adverse health conditions that exist between populations (RCW 43.20.270). This document provides summaries of the evidence analyzed by State Board of Health staff during the Health Impact Review of Senate Bill 6150 (SB 6150) from the 2017-2018 legislative session.

Staff analyzed the content of SB 6150 and created a logic model depicting possible pathways leading from the provisions of the bill to health outcomes. We consulted with experts and stakeholders to better understand the potential impacts of this bill. State Board of Health staff can be contacted for more information on which stakeholders were consulted on this review. Staff conducted objective reviews of the literature for each pathway using databases including PubMed and Google Scholar.

The following pages provide a detailed analysis of the bill including the logic model, summaries of evidence, and annotated references. The logic model is presented both in text and through a flowchart (Figure 1). The logic model includes information on the strength of the evidence for each relationship. The strength-of-evidence has been defined using the following criteria:

- **Not well researched:** the literature review yielded few if any studies or only yielded studies that were poorly designed or executed or had high risk of bias.
- **A fair amount of evidence:** the literature review yielded several studies supporting the association, but a large body of evidence was not established; or the review yielded a large body of evidence but findings were inconsistent with only a slightly larger percent of the studies supporting the association; or the research did not incorporate the most robust study designs or execution or had a higher than average risk of bias.
- **Strong evidence:** the literature review yielded a large body of evidence on the relationship (a vast majority of which supported the association) but the body of evidence did contain some contradictory findings or studies that did not incorporate the most robust study designs or execution or had a higher than average risk of bias; or there were too few studies to reach the rigor of 'very strong evidence'; or some combination of these.
- **Very strong evidence:** the literature review yielded a very large body of robust evidence supporting the association with few if any contradictory findings. The evidence indicates that the scientific community largely accepts the existence of the association.

This review was subject to time constraints, which influenced the scope of work. The annotated references are only a representation of the evidence and provide examples of current research. In some cases only a few review articles or meta-analyses are referenced. One article may cite or provide analysis of dozens of other articles. Therefore the number of references included in the bibliography does not necessarily reflect the strength-of-evidence.

Analysis of SB 6150 and the Scientific Evidence

Summary of SB 6150

Full details about the provisions of this bill can be found in the bill text linked above. Given the length of the bill and the large number of provisions, the summary below only highlights particularly relevant sections.

- Eliminates barriers and promotes access to evidence-based opioid use disorder treatment services and opioid overdose reversal medication such as naloxone.
- Promotes coordination of services and strengthens partnerships between opioid use disorder treatment providers, the recovery support system, and their allied community partners.
- Establishes a mechanism for the Secretary of Health, or their designee, to issue a standing order for prescribing opioid overdose reversal medications such as naloxone to any person at risk of experiencing or witnessing an overdose.
- Expands the use of Washington State's Prescription Drug Monitoring Program (PDMP) by requiring electronic health record (EHR) vendors to ensure their federal certified systems can integrate with PDMP data.

Health impact of SB 6150

Evidence indicates that SB 6150 has the potential to decrease health complications and deaths from opioid use and decrease health disparities by race/ethnicity.

Scope of this Health Impact Review

This Health Impact Review was subject to time constraints and due to the length of the bill and the large number of provisions, the scope of the literature search needed to be narrowed. Staff focused on provisions in the bill that fell into three broad pathways to health instead of each individual provision. These pathways include promoting access to and use of opioid overdose reversal medication, promoting access to medication-assisted therapies for opioid dependence, and expanding the use of the state PDMP. It is important to note that there are a number of provisions that fell outside of this scope and therefore SB 6150 may have impacts on health and health disparities that were not explored in this review.

Pathways to health impacts

The potential pathways leading from the provisions of SB 6150 to decreased health disparities are depicted in Figure 1. There is strong evidence that promoting access to and use of opioid overdose reversal medication such as naloxone will likely result in opioid overdose reversal medication being more frequently distributed and administered.[1-8] There is very strong evidence that increasing distribution and administration of opioid overdose reversal medication will likely decrease health complications and deaths from opioid use.[1-6,9-11] There is very strong evidence that promoting access to medication-assisted therapies for opioid dependence, such as methadone and buprenorphine, will likely decrease health complications and deaths from opioid use.[12,13] There is strong evidence that expanding the use of the state PDMP will likely improve clinical decision-making and reduce "doctor shopping" and diversion of prescription opioids,[14-20] and that these actions will likely decrease health complications and deaths from opioid use.[18,19] Finally, there is strong evidence that decreasing health complications and deaths from opioid use will likely decrease health disparities.[21-27]

Magnitude of impact

Data indicate that there are high rates of fatal opioid overdoses in Washington State, with an average of 608 opioid related overdose deaths each year between 2010 and 2015. However, these data only capture fatal overdose deaths and do not consider the large number of individuals who are likely victims of non-fatal opioid overdoses each year in Washington, but who may experience serious negative health effects resulting from extended drug-induced central nervous system and respiratory depression.[9-11] Therefore, SB 6150 has potential to save a large number of lives and to prevent other serious adverse health outcomes.

Logic Model

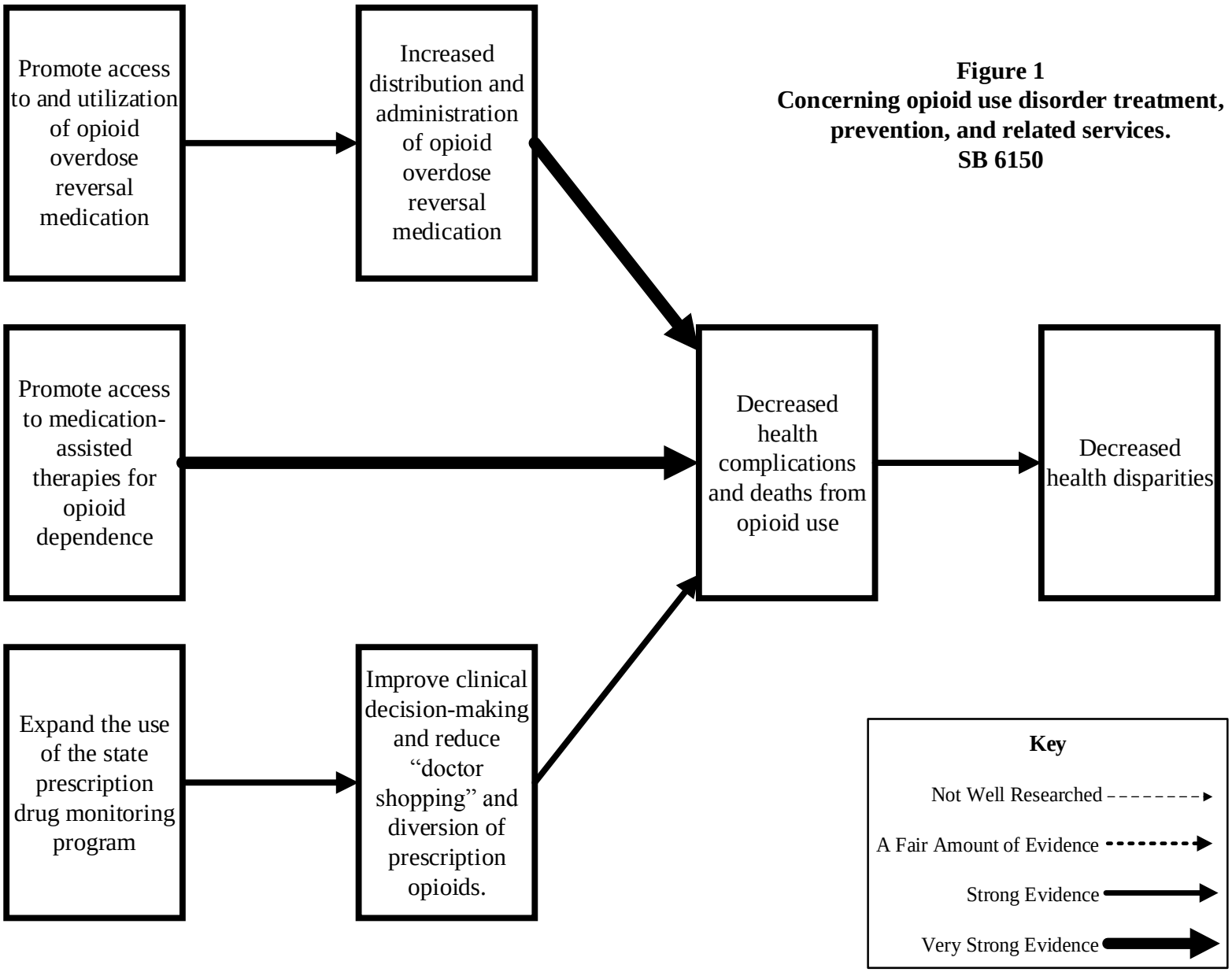

Figure 1
Concerning opioid use disorder treatment, prevention, and related services.
SB 6150

Summaries of Findings

Will promoting access to and use of opioid overdose reversal medication result in opioid overdose reversal medication being more frequently distributed and administered?
There is strong evidence that promoting access to and use of opioid overdose reversal medication will likely result in opioid overdose reversal medication being more frequently distributed and administered.[3-5] Evidence indicates that at least one barrier to distributing naloxone is the need for practitioners to individually prescribe each naloxone kit.[3] SB 6150 includes provisions that allow for the Secretary of Health, or their designee, to issue a standing order for prescribing opioid overdose reversal medications such as naloxone to any person at risk of experiencing or witnessing an overdose. This authority and the accompanying provisions that allow physicians to dispense and individuals to possess these medications in accordance with the standing order will likely help minimize this current barrier. The American Medical Association has issued policies and public statements endorsing legislation to increase the availability of naloxone to patients, first responders, and bystanders indicating widespread access to opioid overdose reversal medications saves tens of thousands of lives.[1]

Evidence also indicates that non-medical witnesses to drug overdoses have demonstrated a willingness to administer naloxone.[4,6-8] This is further supported by the large number of bystanders who seek naloxone refills and report that they administered naloxone in response to an opioid overdose.[3-5,7,8] One study based out of harm reduction-based health care centers found that 70% of the naloxone refills received during the study were used on an overdose and overdose reversals were successful in 96% of reported events.[7] Individuals that use drugs and their friends and family, emergency medical personnel, and police officers frequently witness opioid overdoses.[1-4] This indicates that increasing access to opioid antagonists for these individuals and the providers that serve them has great potential to ensure that these bystanders can respond to overdoses.

Will increasing distribution and administration of opioid overdose reversal medication decrease health complications and deaths from opioid use?
There is very strong evidence that naloxone effectively reverses opioid drug overdoses. This has been demonstrated in animal trials, human clinical trials, and field experience.[3,4,9,10] For example, there is evidence that opioid overdose reversal medication, such as naloxone, is highly effective and has been shown to reverse between 72% and 100% of opioid overdoses when administered.[3,4,9,10] This indicates that opioid antagonists are effective both in decreasing deaths from overdoses and minimizing other adverse health effects associated with overdose. Adverse health effects of nonfatal opioid overdoses are extensive and include: build-up of fluid in the lungs (edema), pneumonia, heart issues (arrhythmia, acute cardiomyopathy, hemoglobinemia), dissolution of muscle cells, kidney failure, inadequate oxygen to the brain, and cognitive impairment.[11]

In addition evidence indicates that naloxone can be administered safely and effectively by overdose witnesses such as EMTs, police officers, friends, family, and other bystanders.[2-6] One study found that nonmedical individuals likely to witness an overdose who were given a brief training (15-120 minutes) in a variety of settings including in private homes, on the street, and in needle exchange programs were as skilled as medical experts trained in overdose recognition and

treatment both in recognizing hypothetical overdose scenarios and instances when naloxone should be administered.[6] A retrospective study of actual responses in the field found that formally trained bystanders and untrained individuals were just as likely to properly administer naloxone. The authors indicate that "untrained individuals" received the kits from their social networks and that they often also received training on how to use the kits from these same individuals.[4] Further, CDC data indicate that from 1996 through June 2014 in the United States, layperson administration of naloxone saved the lives of more than 26,000 people.[1]

Will promoting access to medication-assisted therapies for opioid dependence decrease health complications and deaths from opioid use?

There is very strong evidence that promoting access to medication-assisted therapies for opioid dependence will likely decrease health complications and deaths from opioid use.[12,13] A systematic review by Garcia-Portilla et al. summarizes the existing scientific literature (N= 25 studies) on the long term outcomes of different pharmacological treatment options for opioid dependence. Treatment with methadone, buprenorphine, and buprenorphine/naloxone have demonstrated safety and effectiveness in different practice settings such as physicians' offices and specialized clinics.[12] In addition, Garcia-Portilla et al. describe that, "…in 2009, the World Health Organization Guidelines recommended methadone and buprenorphine as first line agents for agonist maintenance treatment."[12] Furthermore, literature about methadone maintenance treatment demonstrates a high retention rate in treatment, significant reduction in drug use (as identified by self-report and/or urine drug screens) and HIV risk behaviors, a significant decline in overdoses from baseline reports, and improved functioning and quality of life.[12] Similar outcomes were reported among studies examining the long term outcomes of buprenorphine and buprenorphine/naloxone treatments.[12] Another systematic review of randomized control trials (N=31) found that very few included studies reported any adverse events associated with treatment and among those that did, all but one found no statistically significant difference in adverse events between treatment options (buprenorphine versus methadone).[13] The authors discussed that although these treatments demonstrate advantages over one another in particular settings, both methadone and buprenorphine are effective at suppressing opioid use.[13]

Will expanding the use of Washington State's Prescription Drug Monitoring Program (PDMP) improve clinical decision-making and reduce "doctor shopping" and diversion of prescription opioids?

There is strong evidence that expanding the use of the state PDMP will likely improve clinical decision-making and reduce "doctor shopping" and diversion of prescription opioids. Data indicate that implementation and use of PDMPs is associated with improved clinical decision-making and a reduction in overall opioid prescribing.[14-20] In one study, the opioid prescribing rate decreased from 12.4% to 10.2% after implementation of a PDMP.[20] This number continued to decline 0.46% (95% CI, -.38% to -.53%) in the percentage of patients discharged with an opioid prescription per month through the end of the study.[20] Another study found that after providers reviewed data in the PDMP they, "…changed the clinical management in 41% (N=74) of cases. In cases of altered management, the majority (61%; N= 45) resulted in fewer or no opioid medications prescribed than originally planned…"[15] Overall, the body of literature demonstrates reductions in total opioids prescribed, total opioid volume, and mean morphine milligram equivalent per transaction following PDMP implementation as well as a reduction in opioid shipments to states with PDMPs compared to non-PDMP states.[18] Law enforcement

agencies also reported that rates of drug diversion (i.e., channeling of prescription drugs to illicit markets) declined in Florida following statewide policy changes regarding opioid prescribing.[19] Finally, it has also been described that PDMP use results in a significant decrease in "doctor shopping." A study from Virginia found after implementation of a PDMP there was a, "... 73 percent decline in the number of patients identified as seeking simultaneous care from numerous physicians through multiple pharmacies to obtain Schedule II – IV medications."[14]

Will improving clinical decision-making and reducing "doctor shopping" and diversion of prescription opioids decrease health complications and deaths from opioid use?

There is strong evidence that that improving clinical decision-making and reducing "doctor shopping" and diversion of prescription opioids will likely decrease health complications and deaths from opioid use. A systematic review of 11 studies found health outcomes associated with PDMPs that included mitigating opioid misuse, decreasing opioid treatment admissions (presumably due to less misuse), smaller increases in drug abuse over time, and a decline in opioid-specific mortality.[18] For example, one study reported that after implementation of statewide policy changes around opioids (including use of the PDMP), overdose death rates for opioid analgesics overall declined 27.0% and overdose death rates for benzodiazepines declined 28.4%.[19]

Will decreasing health complications and deaths from opioid use decrease health disparities?

There is a strong amount of evidence that decreasing adverse effects from opioid overdose would decrease health disparities by race/ethnicity.[23-26] Washington state data from 2012-2016 indicate that American Indian/Alaska Native (AI/AN) populations have the highest drug overdose death rates in the state.[22] Data further indicate that this association remains true for overdoses specifically related to opioids in Washington. Vital statistics data from 2011-2013 show that AI/AN populations are significantly more likely to be victims of fatal opioid overdose than any other racial/ethnic group.[27] This is true for both prescription and non-prescription opioids. Finally, data show that AI/ANs have significantly higher death rates than most other subpopulations.[26] Therefore, decreasing the disproportionate negative impact of opioid overdoses could help decrease racial/ethnic disparities both for opioid overdose fatalities and for death rates in general.

Nationally researchers have found that populations that face health disparities, such as individuals who are unstably housed, are at greater risk of death from opioid overdose and are more likely to access naloxone through distribution programs.[24] Due to time limitations and a lack of readily available data for Washington State we did not evaluate the potential impacts that this bill could have on disparities by, for example, housing status, educational attainment, mental health co-morbidities, or income. We also did not have time to consider disparities that may exist if access to treatment and medication such as naloxone is not being accessed equitably.

Other Considerations

Due to time constraints, we were unable to evaluate the evidence about potential unintended consequences of decreasing the availability of prescription opioids such as an increase in heroin use. However, in a presentation before the Federal Senate Judiciary Committee in 2016, Dr. Nora Volkow, Director of the National Institute on Drug Abuse, shared the following:

> There is some concern that the increase in heroin-related overdoses may be an unintended consequence of reducing the availability of prescription opioids. Research has shown that prescription opioid misuse is a risk factor for heroin use. The incidence of heroin initiation is 19 times higher among those who report prior non‑medical pain-reliever use than among those who do not (0.39 percent vs. 0.02 percent). Indeed, eighty percent of new heroin users started by abusing prescription opioids. However, there are many more prescription opioid users than heroin users, and, overall, heroin use is rare among individuals who misuse prescription opioids.[a]

Data also indicate that the majority of individuals that report using nonmedical prescription pain relievers, only 3.6% initiate heroin use within a 5-year period.[b] Therefore, although there is the potential for unintended consequences with any shift in policy, Dr. Volkow concluded by stating that a critical component of preventing heroin use in the first place is to prevent the initiation of prescription opioid misuse.

[a] What Science tells us About Opioid Abuse and Addiction. 2016; https://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2016/what-science-tells-us-about-opioid-abuse-addiction, 2018.
[b] Muhuri Pradip, Gfroerer Joseph, Davies Christine. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality Data Review;2013.

Annotated References

1. **American Medical Association. Help save lives: Increase access to naloxone. 2015; https://www.aafp.org/dam/AAFP/documents/news/opioid-naloxone-ama.pdf, 2018.**

The American Medical Association has issued policies and public statements endorsing legislation to increase the availability of naloxone to patients, first responders, and bystanders.

2. **Banta-Green C. J., Beletsky L., Schoeppe J. A., et al. Police officers' and paramedics' experiences with overdose and their knowledge and opinions of Washington State's drug overdose-naloxone-Good Samaritan law. *Journal of urban health : bulletin of the New York Academy of Medicine.* 2013;90(6):1102-1111.**

Banta-Green et al. surveyed police officers (n=251) and paramedics (n=28) in Seattle, Washington following the passage of 2010 state legislation (RCW 69.50.315) that increased availability of naloxone and provided immunity from drug possession charges for overdose victims and bystanders who seek medical aid. Researchers conducted self-administered written surveys with officers in the fall of 2011 in-person at staff meetings ("roll calls"). The researchers attended each shift time once in each of the five precincts in Seattle to conduct the surveys. There was a 97% response rate among officers present at roll calls and respondents represented 50% of the patrol officers in Seattle. During the same time the authors surveyed paramedics at a single staff meeting. Half of the paramedics in Seattle were surveyed. Ninety-three percent of surveyed officers had been at an opioid overdose in their careers and 64% had attended one in the past year. All of the surveyed paramedics had been at an opioid overdose in their career and 89% had been at an opioid overdose in the previous year. Only 16% of officers and 7% of paramedics were aware of the 2010 law—but only a very small percent of overdoes victims (1%) or bystanders (1%) had been arrested at the officers' most recent overdose encounter.

3. **Centers for Disease Control and Prevention. *Morbidity and Mortality Weekly Report February 17, 2013: Community-Based Opioid Overdose Prevention Programs Providing Naloxone — United States, 2010.* 2012.**

This Morbidity and Mortality Weekly report indicates that in 2010 the Harm Reduction Coalition surveyed 50 programs in the United States known to distribute naloxone. Forty-eight programs representing 188 local programs completed the survey (96% response rate). The first opioid overdose program began distributing naloxone in 1996—since this date the respondent programs reported training and delivering naloxone to a cumulative 53,032 people (average per program 1,104.8) and receiving reports of a cumulative 10,171 overdose reversals from naloxone (average per program 211.9). In the previous 12 months the programs reported distributing 38,860 naloxone vials (average per program 809.6). Depending on the indicator, between 22 and 29 of these programs were able to use program data to supply these numbers while the other programs provided estimates. The authors cite evidence that drug users frequently witness drug overdoses. Over 40% of the programs reported problems obtaining naloxone in the months leading up to the survey. Cited barriers include the cost of naloxone and the inability of suppliers to fill orders for reasons such as not having a medical provider to either order naloxone from suppliers or prescribe naloxone to users.

4. **Clark A. K., Wilder C. M., Winstanley E. L. A systematic review of community opioid overdose prevention and naloxone distribution programs. *Journal of addiction medicine.* May-Jun 2014;8(3):153-163.**

Clark et al. conducted a systematic review of the literature on the state and effectiveness of opioid overdose prevention programs (OOPP). The authors indicate that naloxone is a Food and Drug Administration approved medication with "well established efficacy and safety" and cite four studies to support this assertion. Nineteen peer-reviewed articles met their inclusion criteria. A majority of the program participants across all studies which reported each demographic were white (61/4%) and male (68.3%). One program reported serving primarily African American participants. Nearly 80% of all participants reported witnessing an overdose during their lifetime. The OOPPs curriculum usually included several components including how to recognize an overdose and how to administer naloxone. These trainings varied in length from 10 to 60 minutes. The authors found that naloxone was used successfully by participants in 18 of the 19 studies for a total of 1,949 naloxone administrations across 18 programs. These studies reported a survival rate following administration from 83-100% with eleven studies reporting 100% survival rate. The studies which found the lowest rates of survival had the greatest number of unknown overdose outcomes. Authors of one study found that naloxone was not used in any of the witnessed overdoses for which they had data. Nine studies reported adverse outcomes following administration of naloxone including vomiting, problems with the naloxone syringe, and rarely seizures (4 total cases reported). Five studies compared the rate of EMS notification pre-and post-training and the results were mixed with two studies finding an increase in notification, two finding a decrease, and one finding no change. The authors cite evidence indicating that EMS is rarely contacted following an overdose even without the availability of bystander-administered naloxone. The authors rated the quality of the studies and found that the published studies were of "fair" quality because the quantitative studies used self-report and did not use randomization. They do note that the well-established efficacy of naloxone may make randomized studies unethical. The study quality scores ranged from 4 to 7 (average 6.1) out of a possible 8. The authors gave seven of these studies a quality rating of 7 out of 8 with a point being deducted for lack of randomization.

5. **Davis C. S., Ruiz S., Glynn P., et al. Expanded access to naloxone among firefighters, police officers, and emergency medical technicians in Massachusetts. *American journal of public health.* Aug 2014;104(8):e7-9.**

Davis et al. indicate that in 2012 the Massachusetts Office of Emergency Medical Services began allowing EMS medical directors to write standing order to EMTs to administer intranasal naloxone without a waiver. In 2013 Boston EMS service responded to 1207 overdose calls and EMTs administered naloxone in 458 cases. They found that serious adverse reactions were uncommon. In 2010 firefighters in Revere, Massachusetts were trained and permitted to administer naloxone. Between 2010 and 2013 these firefighters administered naloxone 114 times. Police officers in Quincy, Massachusetts were trained and given authority to administer naloxone. In three years these police officers administer naloxone 201 times.

6. **Green T. C., Heimer R., Grau L. E. Distinguishing signs of opioid overdose and indication for naloxone: an evaluation of six overdose training and naloxone distribution programs in the United States. *Addiction (Abingdon, England).* Jun 2008;103(6):979-989.**

Green et al. assessed the knowledge of current and former opioid users who were either trained or untrained in overdose response by six naloxone distribution programs across the United States as well as the knowledge of medical experts. Three of the training programs were new while three were well established. Trainings were brief (ranging from 15 to 120 minutes) and took place in a number of settings including syringe exchange programs, private homes, and on the street. Each site recruited five participants who the program had trained and five who the program had not trained but that were using their other programs (e.g. syringe exchange, drop-in site). Trained participants had, on average, received their training 8 months (range 1-80 months) prior to the evaluation. Participants were provided with 16 scenarios and asked if each was an opioid overdose and if naloxone should be administered. The authors found that, after controlling for demographic and overdose experience factors, potential bystanders who had received training were significantly more likely than untrained bystanders to recognize opioid overdose scenarios accurately and to accurately identify scenarios when naloxone should be used. Trained individuals on average correctly indicated if naloxone should be administered in 13.5 of 16 scenarios while untrained individuals identified this correctly in 11.1 scenarios. The authors note the relatively high opioid overdose symptom knowledge even among untrained participants. Trained bystanders were as skilled as medical experts trained in overdose recognition and treatment both in recognizing overdose scenarios and instances when naloxone should be administered.

7. **Madah-Amiri D., Clausen T., Lobmaier P. Rapid widespread distribution of intranasal naloxone for overdose prevention. *Drug Alcohol Depend.* Apr 1 2017;173:17-23.**

In this article by Madah-Amiri et al. the authors aimed to describe a multi-site naloxone distribution program in Norway and present findings from the program. Between June 2014 and December 2015, participants were recruited from harm reduction-based health care centers, known as low-threshold facilities, to take part in naloxone training sessions. Of note, the authors indicate that, "[a] key component for accessibility for this project included the approval to distribute intranasal naloxone without need for individual prescription. This was achieved by involvement of a community physician appointed to the project, who could order naloxone in bulk from contracted pharmacies for the facilities involved. This allowed for distribution to occur without a physician present, given that the appropriate rescue training was accompanied." Participants filled out a questionnaire upon enrollment and again when returning to the site for naloxone replenishment. Questions included topics such as drug use, overdose risk factors, actions they would take during an overdose, if they have ever witnessed an overdose, and use and dosage of naloxone (on replenishment questionnaire). During the study period, 2,056 naloxone nasal sprays were distributed from 20 participating facilities. Response rates for questionnaires during the initial training and refill visits were 32.8% and 54.6% respectively. Results indicate that 70% of the naloxone refills received during the study were used on an overdose and overdose reversals were successful in 96% of reported events. The authors conclude that the data support the feasibility of "take home" naloxone programs, particularly among those in an at-risk population.

8. **Siegler A., Huxley-Reicher Z., Maldjian L., et al. Naloxone use among overdose prevention trainees in New York City: A longitudinal cohort study. *Drug Alcohol Depend.* Oct 1 2017;179:124-130.**

In this prospective observational study, Siegler et al. aimed to identify the impact of a naloxone distribution program in New York City (NYC). Participants were recruited to participate in overdose prevention training (OPT) from six of the largest overdose prevention programs in NYC between June and September 2013. Immediately following OPT and at three, six, and 12 months after training, participants were given closed-ended questionnaires that asked, among other questions, if they had witnessed or experienced any drug overdoses since the last data collection point. If a participant witnessed an overdose they were asked about naloxone administration. Of the 675 participants that completed OPT only 270 completed the 12 month questionnaire. During the study period, 312 overdose events were witnessed and naloxone was administered in 77% of these cases with 60% of those administrations done by study participants. The authors indicate that these outcomes demonstrate that, "[t]raining individuals at high risk for witnessing overdoses may reduce opioid overdose mortality at a population level if sufficient numbers of potential responders are equipped with naloxone."

9. **Dahan A., Aarts L., Smith T. W. Incidence, Reversal, and Prevention of Opioid-induced Respiratory Depression.** ***Anesthesiology.*** **2010;112(1):226-238.**

Dahan et al. provide a review of the evidence on naloxone efficacy and dosage. The authors cite a large number of studies indicating that naloxone has been shown to effectively and rapidly reverse respiratory depression induced by opioids. This relationship has been found in human and animal trials. They note that the extent and the duration of the reversal are dependent on many factors such as the opioid used, the opioid dose, and mode of administration. The evidence provided by Dahan et al. indicate that naloxone is more effective for some opioid overdoses than for others and that opioids with high receptor affinity require greater naloxone concentrations or a continuous infusion of naloxone in order to be fully effective compared with an opioid with lower receptor affinity.

10. **Robinson A., Wermeling D. P. Intranasal naloxone administration for treatment of opioid overdose.** ***American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists.*** **2014;71(24):2129-2135.**

Robinson et al. provide a review of the literary evidence on the efficacy of intranasal naloxone. The authors summarize two studies which found low adverse events associated with naloxone administration (both intramuscular and intranasal) following an overdose although minor adverse effects such as agitation, sweating, vomiting, headaches, and tremor were observed. The authors highlight evidence that naloxone is generally well tolerated and severe negative responses that have been observed, such as cardiac arrhythmias, heart attacks, and seizures generally result from underlying medical problems. Naloxone can also cause abstinence syndrome (withdrawals) in opioid-dependent individuals. The authors indicate that naloxone does not produce physical dependence and thus does not have an abuse potential. They summarize two studies that randomized overdose victims to receive either intramuscular naloxone or intranasal naloxone and found that while intramuscular injections were more effective than nasal applications, both methods of administration were safe and reversed the effects of the opioid overdose in over 72% of the cases. One author of this review is the Chief Executive Officer of a company funded to develop and commercialize a ready-to-use naloxone nasal spray which could introduce a conflict of interest.

11. **Warner-Smith M., Darke S., Lynskey M., et al. Heroin overdose: causes and consequences.** ***Addiction (Abingdon, England).*** **2001;96(8):1113-1125.**

Warner-Smith et al. provide a review of the literature on heroin overdose including publications on the complications following nonfatal overdose. The negative health effects associated with heroin overdose include: build-up of fluid in the lungs (oedema), pneumonia, heart issues (arrhythmia, acute cardiomyopathy, haemoglobinaemia), dissolution of muscle cells, kidney failure, inadequate oxygen to the brain, and cognitive impairment.

12. **Garcia-Portilla M. P., Bobes-Bascaran M. T., Bascaran M. T., et al. Long term outcomes of pharmacological treatments for opioid dependence: does methadone still lead the pack?** ***British Journal of Clinical Pharmacology.*** **Feb 2014;77(2):272-284.**

In this systematic review by Garcia-Portilla et al., the authors aimed to update and summarize existing scientific literature on the long term outcomes of different pharmacological treatment options for opioid dependence. The authors identified 140 articles of which 25 met their inclusion criteria. Literature was described based on the treatment option of interest such as methadone, buprenorphine, buprenorphine/naloxone, heroin-assisted treatment, and levo-alpha-acetyl-methadol. The paper describes that, "[w]ith regard to methadone, research has shown that it is useful in increasing retention in treatment, physical and mental health levels, functioning and quality of life, and in decreasing the use of illicit drugs and HIV risk behaviours. In fact, in 2009, the World Health Organization Guidelines recommended methadone and buprenorphine as first line agents for agonist maintenance treatment. Methadone has demonstrated its effectiveness in different practice settings (physician offices, specialized clinics) and...There is copious evidence of the efficacy and safety of buprenorphine and buprenorphine/naloxone." Additionally, literature about methadone maintenance treatment demonstrates a high retention rate in treatment, significant reduction in drug use as identified by self-report and/or urine drug screens, and a significant decline in overdoses from baseline reports. Similar outcomes were reported among studies examining the long term outcomes of buprenorphine and buprenorphine/naloxone treatments. Studies about heroin-assisted treatment indicate that it is a feasible treatment for patients with heroin abuse and dependence who lack response to at least two trials of methadone. The authors conclude with recommendations about best options for treatment and future areas for research.

13. **Mattick R. P., Breen C., Kimber J., et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence.** ***Cochrane Database Systematic Review.*** **Feb 6 2014(2):CD002207.**

Mattick et al. conducted a systematic review of the literature to evaluate buprenorphine maintenance treatment compared to methadone maintenance and placebo in the management of opioid dependence. The authors only included randomized controlled trials(N=31 studies) and rated the quality of evidence of these studies as high to moderate quality. Key results of included studies indicates that, "...buprenorphine at high doses (16 mg) can reduce illicit opioid use effectively compared with placebo, and buprenorphine at any dose studied retains people in treatment better than placebo. Buprenorphine appears to be less effective than methadone in retaining people in treatment, if prescribed in a flexible dose regimen or at a fixed and low dose (2 - 6 mg per day). Buprenorphine prescribed at fixed doses (above 7 mg per day) was not different from methadone prescribed at fixed doses (40 mg or more per day) in retaining people

in treatment or in suppression of illicit opioid use." Few studies reported any adverse events and among those that did, all but one found no statistically significant difference in adverse events between treatment options. The authors discuss that although these treatments demonstrate advantages over one another in particular settings, both methadone and buprenorphine are effective at suppressing opioid use.

14. **Doctor Shopping in Virginia for Illicit Use of Pain Mediciation is on the Decline-Virginia Department of Health Professions' Prescription Monitoring Program Releases 2013 Data [press release]. 2014.**

This press release highlights data from the Prescription Monitoring Program (PMP) in Virginia collected between 2012 and 2013. Data indicate that during this time period the number of PMP requests increased while the overall number of prescriptions being dispensed was decreasing. Further, authors describe a significant decrease in "doctor shopping" as the data show, "... there has been a 73 percent decline in the number of patients identified as seeking simultaneous care from numerous physicians through multiple pharmacies to obtain Schedule II – IV medications." The authors promote the use of the PMP as a real-time risk management tool.

15. **Baehren D. F., Marco C. A., Droz D. E., et al. A statewide prescription monitoring program affects emergency department prescribing behaviors. *Ann Emerg Med.* Jul 2010;56(1):19-23 e11-13.**

In this prospective quasiexperimental study by Baehren et al., the authors aimed to identify the impacts of a statewide prescription monitoring program (PMP) on clinical management of emergency department patients reporting pain. In 2006, Ohio implemented a statewide PMP know as the Ohio Automated Rx Reporting System (OARRS) that collects data on more than 18 million prescriptions from about 2,800 prescribers annually. For this study, researchers enrolled patients age 18 or older with a chief complaint of pain that visited the University of Toledo Medical Center Emergency Department between June and July 2008 (N=179). Providers answered a series of questions about anticipated pain prescriptions for a patient at two time points: after clinical evaluation and again after presentation of OARRS data. Results indicate that, "[f]our providers treated 63% (N=114) of the patients in the study. After review of the OARRS data, providers changed the clinical management in 41% (N=74) of cases. In cases of altered management, the majority (61%; N= 45) resulted in fewer or no opioid medications prescribed than originally planned, whereas 39% (N=29) resulted in more opioid medication than previously planned." Prescribers discussed a number of reasons that their management decision changed including number of previous prescriptions filled, number of addresses listed, number of physicians writing prescriptions, provider assessment of pain, truthfulness of patient statements compared to OARRS data, and patient demeanor.

16. **Bao Y., Pan Y., Taylor A., et al. Prescription drug monitoring programs are associated with sustained reductions in opioid prescribing by physicians. *Health Affairs.* Jun 1 2016;35(6):1045-1051.**

Using data from the National Ambulatory Medical Care Survey (NAMCS) Bao et al. assessed the impact of state implementation of prescription drug monitoring programs (PDMPs) on the prescribing of opioids in ambulatory care settings. NAMCS is a nationally representative annual survey of ambulatory visits by the National Center for Health Statistics that collects information

about patients, visits, and clinicians or practices. The study population included patients over the age of 18 that reported pain as one of the reasons for the visit. The analysis was restricted to 24 states that had implemented PDMPs during the study period (2001-2010). Outcome measures of interest included, "...having at least one Schedule II opioid analgesic and having at least one opioid of any kind prescribed or continued at a pain-related ambulatory care visit." During the study period there were 26,275 ambulatory care office visits for pain and of these visits, 5% resulted in the prescription of at least one Schedule II opioid, 15% in at least one opioid analgesic, and 41% in any pain medication. However, the authors also found that, "...implementation of a PDMP was associated with more than a 30 percent reduction in the rate of prescribing of Schedule II opioids."

17. **Deyo R. A., Hallvik S. E., Hildebran C., et al. Association of prescription drug monitoring program use with opioid prescribing and health outcomes: A comparison of program users and nonusers. *Journal of Pain.* Oct 18 2017.**

Deyo et al. conducted a retrospective cohort study from October 2011 through October 2014 to determine of prescriber use of Oregon's prescription drug monitoring program (PDMP) led to fewer high-risk opioid prescriptions or overdose events. The authors describe that the primary analysis included, "...'early registrants' who registered for the PDMP in December 2011 through February 2012, the “registration interval.” This provided 2 months (October and November 2011) of PDMP data before registration for all clinicians (the “baseline interval”). Non-registrants were clinicians who had not registered for the PDMP as of October 2014." Outcome measures included four metrics that are associated with increased risk of opioid overdose including high doses, overlapping opioid and benzodiazepine prescriptions, opioid prescriptions from multiple prescribers, and inappropriate prescriptions. Results demonstrated a decline in per capita opioid prescribing statewide following the implementation of the PDMP however PDMP registrants did not have significantly better outcomes in the four metrics than nonregistrants. The authors discuss a potential "observer effect" (i.e. clinicians perceived that prescribing was being more closely scrutinized) as a reason for the overall decline in prescribing.

18. **Finley E. P., Garcia A., Rosen K., et al. Evaluating the impact of prescription drug monitoring program implementation: a scoping review. *BMC Health Service Research.* Jun 20 2017;17(1):420.**

In this systematic review by Finley et al., the authors primary goal was to describe available evidence regarding the impact of prescription drug monitoring programs (PDMPs) in the United States. Using the Arksey and O'Malley scoping systematic review protocol, the authors identified 11 studies published between January 2000 and May 31, 2016 that met their inclusion criteria. The authors did not describe in detail specifics about the included studies (such as country of origin, demographics reported, etc.) but instead focused solely on a thematic analysis and a summary of research findings. The authors categorized the literature into four domains (each article can fall into more than one domain) including opioid prescribing behavior, opioid diversion and supply, opioid misuse, and opioid-related morbidity and mortality. The included studies demonstrated mixed evidence about the impact of PMDPs, however the majority of the body of literature supports a positive association between PDMP use and outcomes in the four domains. Studies from New York and Florida demonstrate reductions in total opioids prescribed, total opioid volume, and mean morphine milligram equivalent per transaction following PDMP

implementation. Further, two studies discussed a reduction in opioid shipments to states with PDMPs compared to non-PDMP states. When looking specifically at health outcomes associated with PDMPs, evidence demonstrates positive outcomes such as mitigating opioid misuse, decrease in opioid treatment admissions (presumably due to less misuse), smaller increases in drug abuse over time, and a decline in opioid-specific mortality. The authors discuss that the variation in study outcomes may be due to a number of factors such as study design and methods, characteristics of individual state PDMPs, state level policies about PDMP use, and variations in PDMP data availability and timeliness.

19. **Johnson Hal, Paulozzi Leonard, Porucznik Christina, et al. *Decline in Drug Overdose Deaths After State Policy Changes- Florida, 2010-2012.* Morbidity and Mortality Weekly Report;2014.**

In this case study for the Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report, Johnson et. al describe policy changes around opioid prescribing in Florida between 2010 and 2012 and outcomes that followed these changes. Policy changes implemented by Florida's legislature during this time included laws that regulated pain clinics, regulation of physician dispensing of schedule II or II drugs from their offices, mandatory dispenser reporting to the prescription drug monitoring program, and further regulation of wholesale drug distributors. Analysis of data from the Florida Medical Examiners Commission from 2003-2012 demonstrate a decline in the prescribing of drugs following legislation. The authors further describe that, "...overdose death rates for opioid analgesics declined 27.0%, from 13.6 to 9.9 per 100,000 persons, and overdose death rates for benzodiazepines declined 28.4%, from 6.9 to 5.0 per 100,000 persons. ... Law enforcement agencies in Florida also reported that rates of drug diversion (i.e., channeling of prescription drugs to illicit markets) declined during 2010–2012."

20. **Suffoletto B., Lynch M., Pacella C. B., et al. The effect of a statewide mandatory prescription drug monitoring program on opioid prescribing by emergency medicine providers across 15 hospitals in a single health system. *Journal of Pain.* Dec 11 2017.**

Suffoletto et al. conducted a retrospective interrupted time series analysis of electronic medical records to evaluate the effect of a state-mandated prescription drug monitoring program (PDMP) on opioid prescribing by emergency medicine providers. Researchers collected electronic medical record data from all patients over the age of 18 that were discharged with a prescription for an opioid from any of the 15 emergency departments in the University of Pittsburgh Medical Center system from July 2015 to March 2017. The primary outcome measure of interest was percentage of discharged patients prescribed an opioid. Secondary outcomes included percentage of opioid prescriptions for greater than 12 tablets and the number of prescriptions written per month. The final sample included de-identified patient data from 122,732 patients (57% female) with a mean age of 44.6 years. "From August (pre-PDMP) to September, 2016 (post-PDMP), the opioid prescribing rate decreased from 12.4% (95% confidence interval [CI], 10.8%-14.1%) to 10.2% (95% CI, 8.8%-11.8%). For each month from September 2016 to March 2017, there was a mean decline of .46% (95% CI, -.38% to -.53%) in the percentage of patients discharged with an opioid prescription." There was also a reduction in prescriptions greater than 12 tablets, which the authors believe is due more to accumulating evidence and awareness about high-volume opioid prescriptions than the PDMP itself.

21. **What Science tells us About Opioid Abuse and Addiction. 2016; https://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2016/what-science-tells-us-about-opioid-abuse-addiction, 2018.**

22. ***Washington State Health Assessment.*** **Washington State Department of Health;2018.**

In this draft of the 2018 State Health Assessment, death certificate data from 2012-2016 indicate that American Indian/Alaska Natives(AI/AN) had the highest drug overdose death rate followed by Blacks and whites. The authors discuss that, "In 2016, there were 4.5 times as many hospitalizations and nearly 11 times the number of visits to emergency departments for drug overdose compared to the number of deaths. In addition, many nonfatal overdoses are not treated at a hospital and, therefore, are not counted in currently available data."

23. **Centers for Disease Control and Prevention.** ***Morbidity and Mortality Weekly Report November 1, 2011. Vital Signs: Overdoses of Prescription Opioid Pain Relievers--United States, 1999-2008.*** **2011.**

The Centers for Disease Control and Prevention analyzed 2008 National Vital Statistics data and found that AI/AN populations had the highest age-adjusted rates of overdose deaths from opioid pain relievers with rates for non-Hispanic white populations being nearly as high. These rates were nearly three times higher than those for black and Hispanic white populations. The authors cite two studies which indicate that these death rates mirror the non-medical and medical use of opioid pain relievers by subpopulations. Vital statistic data is subject to limitations such as misclassification of race/ethnicity and cause of death on death certificates.

24. **Enteen L., Bauer J., McLean R., et al. Overdose prevention and naloxone prescription for opioid users in San Francisco.** ***Journal of Urban Health.*** **Dec 2010;87(6):931-941.**

Enteen et al. cite three studies which indicate that EMS is called in fewer than half of overdose events. The authors also highlight evidence that intravenous drug users often make attempts to revive overdose victims without calling EMS and demonstrate a willingness to administer naloxone during an overdose if it was made available. Programs that administer naloxone typically provide overdose response education and training on how to administer naloxone. The authors also cite findings from four studies in the United States of programs that distribute and train individuals to administer naloxone. The findings indicate that nearly half of the individuals provided with naloxone indicated having used the reversal drug in the previous 3 to 6 months with 74-100% of these individuals reporting reversal. One additional study with a longer-term follow-up in Chicago found that 9% of individuals provided with naloxone had administered the opioid antagonist while a long-term study in Massachusetts found that 19% of individuals provided with naloxone administered the opioid antagonist. Enteen et al. evaluated the Drug Overdose Prevention and Education (DOPE) Project run by the San Francisco Department of Public Health to train and distribute naloxone to populations at high risk for overdose. Trainings typically last between 10 and 30 minutes. Participants in the program were asked to complete a brief questionnaire following training and all participants who received naloxone refills were asked to complete an additional questionnaire. Between 2003 and 2009 the DOPE Project prescribed naloxone to 1,942 individuals with the number of new individuals increasing steadily

each year. Seventy-five percent of participants reported their race/ethnicity (61% Caucasian, 15% African American, 7% Latino, 2% Asian/Pacific Islander, 2% Native American, 3% more than one race/ethnicity, 3% other). The authors do not indicate if this is reflective of the at-risk population or the service area population in general. Eighty-eight percent of participants reported their housing status with 59% reporting being homeless or unstably housed. Previous studies in San Francisco have found unstably housed individuals to be at increased risk of opioid overdose death. The program provided 1,020 refills, 399 (40%) of which were provided after participants reported using naloxone to respond to an overdose. Participants reported that 89% of overdose events were reversed with an additional 3% of overdose outcomes being unknown to the administrator. Four victim deaths were reported, and in three of these cases the victim had been unconscious for an indeterminate amount of time. Adverse effects following naloxone use were rarely reported and included vomiting, discomfort, anger, and seizures (3 cases). The authors note the limitations of this study include reliance on self-report, a lack of ability to know how many of the participants administered naloxone since the evaluation only captured those who returned for a refill, and that those with positive experiences may have been more likely to return for a refill.

25. **Northwest Portland Area Indian Health Board.** ***American Indian/Alaska Native Community Health Profiles: Washington Substance Abuse.*** **2014.**

The Northwest Portland Area Indian Health Board analyzed Washington state death certificate data for 2006-2010 and corrected for misclassification of AI/AN individuals using the Improving Data & Enhancing Access – Northwest Project. These data indicate that prescription opioid pain relievers contributed to 2.9% of deaths among AI/AN populations and 1.1% of deaths among non-Hispanic white populations. This report does not indicate if these differences are statistically significant.

26. **Poel Amy.** ***Health of Washington State Report - Mortality and Life Expectancy.*** **2015.**

Age-adjusted death rates from 2012-2014 Washington state death certificate data indicate that AI/ANs have significantly higher death rates than black, white, Hispanic and Asian populations. This report indicates that death certificates often misclassify race/ethnicity and highlights that death data may underreport for American Indians and Alaska Natives.

27. **Washington State Department of Health.** ***Vital Statistics Data.*** **2011-2013.**

Vital statistics data indicate that between 2011 and 2013 in Washington state, 1,176 individuals died of prescription opioid overdose and 658 individuals died of non-prescription opioid overdose. American Indian/Alaska Natives (AI/AN) were significantly more likely than any other racial/ethnic group to be victims of fatal overdoses from both prescription and non-prescription opioids. The AI/AN population had an age-adjusted rate almost three times higher than that for the overall population. The numbers for the Native Hawaiian and Other Pacific Islander population were too low to calculate the rates for both prescription and non-prescription as were the numbers for the Asian population for non-prescription. Rates were calculated per 100,000, age-adjusted for the United States 2000 population. The data also show a steady increase in the number of opioid overdose deaths for all populations between 1995 and 2013 with a larger increase among prescription-related overdose deaths. The rate increased from an age-adjusted death rate for all opioids of 3.3/100,000 (95% CI 2.9-3.8/100,000) in 1995 to

8.6/100,000 (7.9-9.3/100,000) in 2013. It is important to note the potential limitations of death certificate data such as possible misclassification of both race/ethnicity and cause of death. The age-adjusted rates for 2011-2013 were as follows for opioid overdose deaths:

Category	Race	Count	Age-adjusted Rate	Lower CI	Upper CI
Prescription	Total	1176	5.00	4.71	5.30
Prescription	White	1025	6.37	5.97	6.79
Prescription	African American	37	4.98	3.49	7.00
Prescription	AI/AN	44	16.20	11.72	21.92
Prescription	Asian	12	0.77	0.39	1.34
Prescription	NHOPI	2			
Prescription	Multi-race	21	3.71	2.24	5.83
Prescription	Hispanic	34	0.84	0.56	1.21
Prescription	Unknown	1			
Non-Prescription	Total	658	2.85	2.63	3.08
Non-Prescription	White	558	3.79	3.48	4.13
Non-Prescription	African American	27	3.47	2.28	5.19
Non-Prescription	AI/AN	30	10.92	7.33	15.75
Non-Prescription	Asian	3			
Non-Prescription	NHOPI	3			
Non-Prescription	Multi-race	12	1.83	0.91	3.40
Non-Prescription	Hispanic	25	0.68	0.43	1.04
Non-Prescription	Unknown	0			

AI/AN: American Indian/Alaska Native

NHOPI: Native Hawaiian and Other Pacific Islander

Rate per 100,000 age-adjusted to U.S. 2000 population; Rates not calculated when counts are fewer than 5. Residents who died outside of Washington excluded.

Only included deaths with underlying cause of death: ICD-10 X40-X49 or where a term to indicate acute was reported and the manner of death was not undetermined.

Morphine and hydromorphone were excluded from prescription category unless it was specifically reported as pharmaceutical or it was the only drug reported and medication use was also reported.

Center for Health Statistics, Washington State Department of Health, February 2, 2015.