

MassCALL2 Opioid Overdose Annotated Bibliography

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**Developed by Center for the Application of Prevention Technologies/
Northeast Resource Team**

INTERVENING VARIABLES

The following list of intervening variables, risk factors, and high-risk populations has been updated from the original MassCALL2 guidance document titled Revised 2008. The following are updates to the literature from 2008 MassCALL2 guidance documents and contains articles from 2007 to October 2012. The original citations from the 2008 MassCALL2 guidance document are omitted from the current version, although the categorization/groupings have been retained so that the original citations might be added back in to represent a broader picture of the supporting literature base.

Actively injecting drug users with HIV/AIDS or Hepatitis C Virus (HCV) (Bohnert et al. 2012)

Barriers (failures or delay) to contacting emergency medical services out of fear for police involvement (no new articles for 2012 update).

Co-morbid substance abuse and mental health (e.g., anxiety, depression) issues (Havens et al. 2012).

Concomitant use of alcohol, benzodiazepines, and other drugs (e.g., cocaine) with opioids (Havens et al. 2012; Jenkins et al. 2011).

Drug users who drop out of treatment especially during the first 12 months following dropout (no new articles for 2012 update)

Fluctuations in heroin purity levels (no new articles for 2012 update)

Individuals who use opioids alone (no new articles for 2012 update)

Intravenous drug users presenting in the Emergency Department with soft tissue infections (no new articles for 2012 update).

Intravenous drug users with impaired hepatic or pulmonary function (no new articles with 2012 update)

History of intravenous drug use (Bohnert et al. 2012; Havens et al. 2012; Silva et al. 2012)

Loss of tolerance due to abstinence, incarceration in prison or jail, detoxification, treatment and other periods of non-use of opioids (Hickman et al. 2006; Jenkins et al. 2011)

Opioid users who are homeless or marginally housed (Bohnert et al. 2012; Jenkins et al. 2011)

New with 2012 update

Opioid users who had prior history of non-fatal overdose (Bohnert et al. 2012)

Opioid users who had witnessed overdose (Bohnert et al. 2012; Havens et al. 2011; Silva et al. 2012)

Active methadone prescription (Hickman et al. 2006)

Overdose Prevention – Strategies for Opioid Users/Bystanders

Provide information/training to opioid users and bystanders (friends, family, co-users) on overdose risk factors Phillips, P., C. Glover, et al. (2009);

Provide information/training to opioid users and bystanders (friends, family, co-users) on overdose prevention strategies including use of including intramuscular, subcutaneous and intranasal naloxone

(narcan) (Phillips, P., C. Glover, et al. (2009); Dope Project; Enteen, L., J. Bauer, et al.(2010); Kerr et al. (2008); Strang et al. (2008).

Overdose Prevention – Strategies for Healthcare Providers

Identification of individuals at-risk for overdose through screening conducted by emergency department (ED) staff, emergency medical technicians (EMT), and/or hospital staff (No new articles for 2012 update).

Identification of individuals at-risk for overdose through targeting intravenous drug users with soft tissue infections seeking care in the Emergency Department, hospital, or primary care physician (No new articles for 2012 update).

EMTs and first responders distribute information about causes and consequences of overdose to victims and bystanders – especially those refusing transport to the hospital (no new articles for 2012 update).

Deliver overdose risk and response training (including intramuscular, subcutaneous and intranasal naloxone(narcan)) to clients recruited from needle exchange sites (Bennett, A. S., A. Bell, et al. (2011); Doe-Simkins et al. (2008); Piper, T. M., S. Stancliff, et al. (2008); Sherman et al. (2008); Sporer and Kral 2007; Wheeler, E., P. J. Davidson, et al. (2010).

Overdose Prevention – Strategies for Opioid Users in Treatment

Provide information on how to reduce overdose risk for opioid users admitted to treatment– including:

- o Information on loss of drug tolerance after completion or withdrawal from treatment (Walley et al. 2012);
- o Increased risk of overdose for clients in the first few weeks of initiating methadone substitution therapy (Walley et al. 2012).
- o Increased risk of overdose using heroin or other opiates while on methadone or other replacement/maintenance therapy (Walley et al. 2012)
- o Incorporate information on opioid overdose prevention into relapse management trainings – how to avoid overdose if relapse occurs (no new articles with 2012 update)
- o (New 2012) Use of “cascade method” training model for clinicians on recognition of opioid overdose risk factors, signs of opioid overdose and administration of naloxone so that they can train other clinicians and clients in overdose prevention and reversal strategies (Mayet et. al. 2011).

Identification of individuals at-risk for overdose through screening detoxification patients for mental health issues (depressive symptoms) and other risk factors for overdose – particularly history of prior overdose (Bohnert et al. 2012).

Provide education and support for individuals completing detoxification particularly information on loss of tolerance after detoxification (Walley et al. 2012).

Overdose Prevention – Strategies for Criminal Justice System Personnel

Provide incarcerates with a history of opioid use with overdose prevention information upon release from prison or jail (no new articles with 2012 update);

Provide incarcerates with a history of opioid use with overdose prevention information PRIOR to release from prison or jail including information about risks of re-initiation of use after release (Wakeman et al. 2009; Thurman and Bowman 2007)

Utilize parole/probation officers to provide former incarcerates that have a history of opioid use with overdose prevention information during re-entry into the community (no new articles with 2012 update)

ANNOTATED BIBLIOGRAPHY – UPDATES 2007 - 2012

Bennett, A. S., A. Bell, et al. (2011). "Characteristics of an overdose prevention, response, and naloxone distribution program in Pittsburgh and Allegheny County, Pennsylvania." *Journal Of Urban Health: Bulletin Of The New York Academy Of Medicine* 88(6): 1020-1030. *In 2002 Prevention Point Pittsburgh (PPP), a public health advocacy organization that operates Allegheny County's only needle exchange program, implemented an Overdose Prevention Program (OPP) in response to an increase in heroin-related and opioid-related overdose fatalities in the region. In 2005, the OPP augmented overdose prevention and response trainings to include naloxone training and prescription. The trainings included information on identifying overdoses and overdose risk factors, performing rescue breathing, and safely administering naloxone. 426 individuals participated in the OPP between July 1, 2005, and December 31, 2008 and of these, 89 individuals reported administering naloxone in response to an overdose in a total of 249 separate overdose episodes. Of these 249 overdose episodes in which naloxone was administered, participants reported 96% were reversed. Participants who used naloxone reported very few problems, and only two fatalities were recorded. 61% of study participants also reported performing rescue breathing in an overdose situation indicates that the general knowledge and skills conveyed during trainings were being translated into action.*

Doe-Simkins, M., A. Y. Walley, et al. (2009). "Saved by the Nose: Bystander-Administered Intranasal Naloxone Hydrochloride for Opioid Overdose." *American Journal of Public Health* 99(5): 788-791. *The Boston Public Health Commission passed a regulation in 2006 authorizing distribution of intranasal naloxone by trained nonmedical public health workers as part of efforts to reduce fatalities from opioid overdose. This intervention specifically targeted bystanders who could be trained to recognize symptoms of overdose and administer intranasal naloxone to reverse overdose. The 15 minute bystander training covered overdose prevention techniques and included distribution of the naloxone with an atomizer for intranasal administration. The program provided training and intranasal naloxone to 385 participants who reported 74 successful overdose reversals during a 15 month period.*

Enteen, L., J. Bauer, et al. (2010). "Overdose Prevention and Naloxone Prescription for Opioid Users in San Francisco." *Journal of Urban Health* 87(6): 931-941. *Presents findings from the Drug Overdose Prevention and Education (DOPE) Project which was the first naloxone prescription program (NPP) established in partnership with a county health department (San Francisco Department of Public Health), and is one of the longest running NPPs in the USA. From September 2003 to December 2009, 1,942 individuals were trained and prescribed naloxone through the DOPE Project, of whom 24% returned to receive a naloxone refill and 11% reported using naloxone during an overdose event. Of 399 overdose events where naloxone was used, participants reported that 89% were reversed. In addition, 83% of participants who reported overdose reversal attributed the reversal to their administration of naloxone, and less than 1% reported serious adverse effects. Side effects included several instances of seizures and negative effects included vomiting and "anger" or discomfort expressed by victim upon waking. Victim death was reported by participants in four (1%) events where naloxone was used, but in three of these cases participants reported that the victim had been unconscious for an undetermined amount of time before they were found.*

Hickman, M., S. Carrivick, et al. (2007). "London audit of drug-related overdose deaths: characteristics and typology, and implications for prevention and monitoring." *Addiction* 102(2): 317-323 *The authors, one an expert in toxicology and the other in emergency medicine and poisons conducted an audit of 148 drug overdose deaths (involving heroin, methadone, dihydrocodeine, cocaine, amphetamine or MDMA) investigated by coroners in London, England during 2003. Information on toxicology, pathology and circumstances were used to identify drug(s) implicated in the death. Poly- or multiple drug use was detected in the overwhelming majority of deaths (90% of the fatalities). A witness was present and the death was not instantaneous in 92 (61%) cases, although evidence in the coronial file suggested that in the majority of cases the overdose went unnoticed until too late to intervene. In all, 15 (one in 10) of the deceased were released from prison within 3 months of death; and 37 (one in four) were reported as in receipt of a methadone prescription.*

Jenkins, L. M., C. J. Banta-Green, et al. "Risk factors for nonfatal overdose at Seattle-area syringe exchanges." *Journal Of Urban Health: Bulletin Of The New York Academy Of Medicine* **88**(1): 118-128. *In a survey of 443 participants at syringe exchanges in Seattle, Washington, 16% had overdosed in the last year. Only recent incarceration and sharing of injection materials were significantly associated with overdose in a multivariate logic regression analysis.*

Havens, J. R., C. B. Oser, et al. "Individual and network factors associated with non-fatal overdose among rural Appalachian drug users." *Drug And Alcohol Dependence* **115**(1-2): 107-112. *The authors examined correlates of non-fatal overdose and witnessed overdose among rural Appalachian drug users participating in a longitudinal study of social networks and HIV transmission. Factors independently associated with a greater number of overdoses included having ever been in drug treatment, past 30-day injection of prescription opioids, meeting the criteria for post-traumatic stress disorder and/or antisocial personality disorder and having more members in one's support network. The authors described the findings related to the number of members in one's support network as counterintuitive, but theorized that this may be due to a higher proportion of network members abusing substances and thus providing more access or support for substance use. Rural drug users with history of overdose were more likely to have injected with prescription opioids--which is different from urban heroin users. The authors suggested that current overdose prevention strategies employed in urban settings may be effective in preventing fatal overdose in this population.*

Kerr, D., P. Dietze, et al. (2008). "Attitudes of Australian heroin users to peer distribution of naloxone for heroin overdose: perspectives on intranasal administration." *Journal Of Urban Health: Bulletin Of The New York Academy Of Medicine* **85**(3): 352-360. *This study explored attitudes of 99 Australian IDUs to administration of naloxone to others after heroin overdose, and preferences for method of administration. The majority of the sample reported positive attitudes toward naloxone distribution (good to very good idea: 89%) and 92% said they were willing to participate in a related training program. Some participants raised concerns about peer administration including the competence of IDUs to administer naloxone in an emergency, victim response on wakening and legal implications. Most (74%) preferred intranasal administration in comparison to other administration methods (21%).*

Mayet, S., V. Manning, et al. "Impact of training for healthcare professionals on how to manage an opioid overdose with naloxone: Effective, but dissemination is challenging." *International Journal of Drug Policy* **22**(1): 9-15. *Clinicians from addiction services across England received training about overdose risk signs and overdose management and prevention strategies including administration of naloxone. Clinicians were supposed to train other clinicians (train the trainer) and the cadres of trained clinicians would in turn train patients in overdose prevention strategies ("cascade method"). Participants self-completed pre and post-tests consisting of a structured questionnaire recording overdose knowledge, confidence and barriers to implementation. One hundred clinicians were trained initially, who trained a further 119 clinicians (n =219) and thereafter trained 239 drug users. The clinicians demonstrated statistically significant improvements in knowledge opioid overdose risk signs and actions and willingness to use naloxone in an opioid overdose after training. Barriers to implementing training were clinician time and confidence, service resources, client willingness and naloxone formulation. The authors concluded that the training clinicians how to manage an opioid overdose and administer naloxone was effective but that that "cascade method" was only modestly successful for disseminating training to a large clinician workforce.*

"Naloxone distribution saves more than 400 lives in SF overdose project." *DATA: The Brown University Digest of Addiction Theory & Application* 29(12): 4-5. *Overview of San Francisco's Drug Overdose Prevention and Education (DOPE) Project, the first naloxone prescription program supported by a county department of public health. It is modeled on underground community-based programs that conduct outreach to street-level drug users via needle exchange programs. County medical providers conducted training and distributed prefilled syringes to syringe exchange programs, methadone maintenance and buprenorphine treatment programs, and single-room occupancy hotels about 8 times a month throughout San Francisco. The project changed from dispensing intramuscular syringes to intranasal administration in the spring of 2010 because of preconceptions around giving a drug user a medication that's injected*

and researcher Joshua Bamberger, M.D. then noticed a large uptick in dispensation of the intranasal naloxone. There were 399 Participant-reported responses and outcomes of opioid overdose events where naloxone was administered, among participants receiving a naloxone refill from the DOPE Project from 2004-2009. 36% used naloxone on a companion (e.g. friend, spouse), 15% on a stranger, and 21% used it on themselves. In 75% of the cases the participant reported using another strategy in addition to using naloxone including Sternum rub, awakening the victim, and rescue breathing. 83% of the reported situations were reversed due to participant administering naloxone.

Horyniak, D., P. Higgs, et al. "An evaluation of a heroin overdose prevention and education campaign." *Drug and Alcohol Review* **29**(1): 5-11. Provides an overview of a Victoria Department of Human Services (Australia) campaign targeted at injecting drug users' (IDU) and details the campaign's evaluation. The campaign was aimed at increasing injecting drug users' (IDU) awareness of overdose risks and prevention strategies as well as encouraging them to access treatment. Stickers, wallet cards, and posters featuring five key messages were distributed via needle and syringe programs (NSP) and other drug and alcohol services between November 2005 and April 2006. An evaluation of the campaign was conducted in late 2006. The evaluation included survey questions and follow-up interviews with IDU who were NSP clients during the campaign period and interviews with 9 NSP staff and other key stakeholders. While key experts felt that the campaign messages had lasting impact for at least some IDU, these positive impressions did not show up in NSP client data, with less than one quarter of all campaign messages being mentioned by a significantly higher proportion of clients during the post-campaign period compared with baseline. Key experts perceived the greatest weakness of the campaign to be the delay between issue identification and the introduction of campaign materials. Article not used due to very small n and lack of reliability/generalizability.

Phillips Phillips, P., C. Glover, et al. (2009). "Using a Group Approach to Preventing Heroin Overdose in North London." *Drugs: Education, Prevention & Policy* **16**(4): 328-342. Outlines a group psycho-education intervention used to assist injecting heroin users in preventing, and responding to overdose. An 'OD Prevention' group was advertised in a London prescribing service and associated primary care unit. The intervention took place in a small group over one afternoon (3.5 hours), and trained participants, who were all injecting heroin users, in recognizing, and responding to heroin overdoses (defining overdose, discussing known risk factors and on-site instruction in cardio-pulmonary resuscitation (CPR). Participants completed pre- and post-group questionnaires. Of the 107 people who attended the group, 42% had witnessed others' overdose and 29% had witnessed one or more deaths as a result of overdose. Following the group intervention more participants reported feeling 'quite or very confident' in managing an OD situation, confident in undertaking CPR with someone who had overdosed, and were less likely to pursue 'folklore' remedies to overdose.

Bohnert, A. S. B., M. Tracy, et al. "Characteristics of drug users who witness many overdoses: implications for overdose prevention." *Drug And Alcohol Dependence* **120**(1-3): 168-173. A cross-sectional study of 1184 New York City residents aged 18 and older with heroin and/or cocaine use in the past two months revealed a number of factors predicting risk for witnessing overdose. The participants were part of a larger study focused on determinants of HIV and concurrent were administered structured interviews exploring various probing overdose response, drug use behavior, treatment history and demographic information. Factors predictive of witnessing overdose included being male, history of homelessness, prior non-fatal overdose, and history of heroin and injection drug use. Respondents who reported witnessing a greater number of overdoses also reported using ineffective actions to prevent or reverse overdose. The implications of the study are that witnessing overdose. The authors proposed that individuals who have witnessed many overdoses are likely key targets of overdose response training.

Piper, T. M., S. Stancliff, et al. (2008). "Evaluation of a naloxone distribution and administration program in New York City." *Substance Use & Misuse* **43**(7): 858-870. This report summarizes the first systematic evaluation of large-scale naloxone distribution among injection drug users (IDUs) in the United States. In 2005 an evaluation was conducted of a comprehensive overdose prevention and naloxone administration training program in New York City. One hundred twenty-two IDUs at syringe exchange programs (SEPs) were trained in Skills and Knowledge on Overdose Prevention (SKOOP), and all were given a prescription for naloxone by a physician. Participants in SKOOP were over the age of 18, current

participants of SEPs, and current or former drug users. Participants completed a questionnaire that assessed overdose experience and naloxone use. Naloxone was administered 82 times; 68 (83.0%) persons who had naloxone administered to them lived, and the outcome of 14 (17.1%) overdoses were unknown. Ninety-seven of 118 participants (82.2%) said they felt comfortable to very comfortable using naloxone if indicated; 94 of 109 (86.2%) said they would want naloxone administered if overdosing. In addition to administering the naloxone, responses to overdose included trying to cause pain, administering a shower or bath, and/or applying ice (41, 82%) and calling an ambulance (37, 74%). The valuation supports Naloxone administration by IDUs as a feasible as part of a comprehensive overdose prevention.

Sherman, S. G., D. S. Gann, et al. (2008). "A qualitative study of overdose responses among Chicago IDUs." *Harm Reduction Journal* 5: 2-2. *The current study is based upon qualitative interviews (N = 31) with injection drug using clients of the Chicago Recovery Alliance needle exchange program who had witnessed an overdose in the past six months to determine the effectiveness of use of naloxone to reverse overdose. The interviews explored participants' drug use history, personal overdose experiences, and details concerning their last witnessed overdose. Verbatim transcripts were coded and analyzed thematically to address major study questions. Participants were 81% were male, their median age was 38. They reported having a median of a 10 year history of injection drug use and witnessing a median of six overdoses in their lifetime. All described overdoses were recognized and responded to quickly. None of the overdoses resulted in a fatality and naloxone was successfully administered in 58% of the last witnessed overdoses. Emergency medical personnel were called in 10 of the 31 described overdoses, including four in which participants administered naloxone. The overwhelming majority of experiences with police and paramedics were positive. The authors reported that overdose prevention efforts build on extensive knowledge possessed by IDUs including use of naloxone are an effective risk reduction strategy for overdose.*

Silva, K., S. M. Schrage, et al. (2012). "Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs." *Drug and Alcohol Dependence*. *This article contains the results of a cross sectional study of 16-25 year old non-medical users of prescription opioids and tranquilizers and examined the prevalence and correlates of lifetime non-fatal overdose (OD) in New York, NY and Los Angeles, CA (n=596). Lifetime prevalence of non-fatal overdose involving prescription opioids and/or tranquilizers was 23.6%. Factors associated with increased risk of non-fatal overdose included lower social class while growing, having ever received care at a psychiatric hospital, ever witnessing a family member OD on drugs, being prescribed tranquilizers, ever snorting or sniffing opioids, injecting tranquilizers and past 90-day injection drug use. Participants who reported past 90-day stimulant misuse had lower odds of reporting OD compared to those who were not recent stimulant users.*

Sporer, K. A. and A. H. Kral (2007). "Prescription naloxone: a novel approach to heroin overdose prevention." *Annals Of Emergency Medicine* 49(2): 172-177. *This article reviews the use of naloxone education programs and their effectiveness in reducing overdose. Key findings include greater efficacy of educational curricula accompanying naloxone administration offered in shorter sessions offered at needle exchange programs as well as intramuscular or subcutaneous administration of naloxone over intranasal administration.*

Strang, J., V. Manning, et al. (2008). "Family carers and the prevention of heroin overdose deaths: Unmet training need and overlooked intervention opportunity of resuscitation training and supply of naloxone." *Drugs: Education, Prevention & Policy* 15(2): 211-218. *Carers attending local support groups for friends and families of drug users were surveyed to assess experience of witnessing overdose, interest in receiving training on overdose management and their training needs (n=147). The sample was drawn from local support groups for families and friends of drug users throughout England. Carers were usually parents (80%); 89% were currently caring for a heroin user of whom 49% had already had an overdose (93% involving opiates). One third had witnessed heroin being used, and 31 had witnessed an overdose. Respondents reported a lack of knowledge of how to effectively manage an overdose. Only a quarter had received advice on overdose management (26%) and only one third knew of the opiate antagonist naloxone (33%). The majority (88%) wanted training in overdose management, especially in emergency naloxone administration (88%). Authors recommended targeting carers for bystander training on*

management of opioid overdose.

Wakeman, S. E., S. E. Bowman, et al. (2009). "Preventing death among the recently incarcerated: an argument for naloxone prescription before release." *Journal of Addictive Diseases* **28**(2): 124-129. *This study assessed overdose experience and response among long-term opiate users involved in the criminal justice system. One hundred thirty-seven subjects from a project linking opiate-dependent individuals being released from prison with methadone maintenance programs were asked 73 questions regarding overdose. Most had experienced (53%) and witnessed multiple overdoses (80%); 911 was often not called. The majority of personal overdoses occurred within 1 month of having been institutionalized. Nearly all participants expressed an interest in being trained in overdose prevention with Naloxone. The authors advocated for use of pre-release program of overdose prevention education, including Naloxone prescription, for inmates with a history of opiate addiction to prevent overdose deaths.*

Walley, A. Y., M. Doe-Simkins, et al. (2012). "Opioid overdose prevention with intranasal naloxone among people who take methadone." *Journal of Substance Abuse Treatment*. *This study describes the implementation of overdose education and naloxone distribution (OEND) among people taking methadone in the previous 30 days in various settings in Massachusetts. OEND programs are public health interventions that address overdose risk among people who take methadone and their social networks. From 2008 to 2010, 1553 participants received OEND who had taken methadone in the past 30 days. Settings included inpatient detoxification (47%), HIV prevention programs (25%), methadone maintenance treatment programs (MMTP) (17%), and other settings (11%). Previous overdose, recent inpatient detoxification and incarceration, and polysubstance use were overdose risks factors common among all groups. Participants reported 92 overdose rescues.*

Wheeler, E., P. J. Davidson, et al. "Community-Based Opioid Overdose Prevention Programs Providing Naloxone- United States, 2010." *JAMA: Journal of the American Medical Association* 307(13): 1357-1364. *This report summarizes the findings for the 48 of the 50 programs known to distribute naloxone in the United States that completed an online survey the Harm Reduction Coalition e-mailed in October of 2012. The 48 responding programs (including health departments) were located in 15 states and the District of Columbia and provided information for 188 local programs that distributed naloxone. Since the first opioid overdose prevention program began distributing naloxone in 1996, the respondent programs reported training and distributing naloxone to 53,032 persons and receiving reports of 10,171 overdose reversals. During a recent 12-month period, respondents had distributed an estimated 38,860 naloxone vials. Twenty-one (43.7%) responding programs reported problems obtaining naloxone in the "past few months" before the survey. The most frequently reported reasons for difficulties obtaining naloxone were the cost of naloxone relative to available funding and the inability of suppliers to fill orders. In this analysis, the majority (76.0%) of the 25 states with 2008 age-adjusted drug overdose death rates higher than the median did not have a community based opioid overdose prevention program that distributed naloxone. The findings in this report suggest that distribution of naloxone and training in its administration might have prevented numerous deaths from opioid overdoses.*