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Effects of Naloxone Prescription Programs on Opioid Overdoses in Three Months

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ABSTRACT

Background: Fatal opioid overdose is a growing concern in the United States (U.S.). The medical community was assured by pharmaceutical companies that opioid pain relievers were not addictive. As a result, providers prescribed them at a significantly higher rate, which led to more extensive use of authorized and unauthorized opioid before it was realized that they can be highly habit forming (The U.S. Department of Health and Human Services [HHS], 2019). A growing body of evidence supports Naloxone Prescription Programs (NPP) for the prevention of fatal overdoses (Enteen et al., 2010).

Objective: To describe evidence found to answer the following clinical question: In rural communities, do naloxone prescription programs affect opioid overdoses within three months? *Method:* An intensive search of Cochrane, Joanna Briggs, CINAHL, PubMed and Scopus databases, which yielded a total of 64 possible articles of which 10 were summarized and used for the paper. *Result:* NPP decreases the rate of fatal opioid overdoses. *Conclusion:* Educating laypersons through community naloxone prescription programs, and distribution of take-home naloxone kits can decrease the occurrences of fatal opioid overdoses.

Effects of Naloxone Prescription Programs on Opioid Overdoses in Three Months

The prevalence of fatal drug overdose continues to increase in the U.S., as more than 700,000 Americans have died due to overdose on drugs between 1999 and 2017 (Centers for Disease Control and Prevention [CDC], 2019). Approximately 68% of the over 70,200 fatal drug overdoses in 2017 contained an opioid. The daily death toll of Americans from opioid overdose averages 130 (CDC, 2019). The medical community was assured by pharmaceutical companies that opioid pain relievers were not addictive. As a result, providers prescribed them at a significantly higher rate, which led to more extensive use of authorized and unauthorized opioids before it was realized that they can be highly habit forming (HHS, 2019). As a result of the effects on breathing, high doses of opioids can suppress the drive to breathe and can be fatal (World Health Organization [WHO], 2019).

Naloxone is an inexpensive, nonscheduled opiate antagonist that can readily reverse the respiratory depression and sedation caused by opioids (Sproler & Karl, 2007). The purpose of this paper is to describe evidence found to answer the following clinical question: In a rural community, does naloxone prescription program, compared to no program, decrease opioid overdoses over three months?

Search Method

The student carried out an intensive search of Cochrane, Joanna Briggs, CINAHL, PubMed and Scopus databases, which yielded several articles. The student used main topic and search terms such as “naloxone prescription program and opioid overdoses,” “naloxone effectiveness,” “opioid overdoses,” “opioid overdose and naloxone prescription program,” “naloxone take home kits and opioid overdoses,” “naloxone take home kits,” and “naloxone take home kit and peer administration.” Inclusion criteria of research articles in the U.S., ranging from 2015-2020. A total of 64 possible articles were yielded, of which 8 were chosen for this assignment. The remaining two articles were chosen from similar article search option in CINAHL search. The systematic review articles were selected since they are the highest

level of evidence based on the hierarchy of evidence. Longitudinal cohort study, retrospective study, and a literature review were chosen as they were related to the topic and higher on research evidence hierarchy, compared to some unrelated studies, case studies and expert opinions found. The articles were appraised using the Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal Tool.

Review of Literature

Chimbar & Moleta (2018) in their high-quality level II systemic review, aimed to explore the benefit of naloxone prescription program on decreasing opioid overdose deaths among users. Several major scholarly search engines were used to explore studies that supported the aim, which initially yielded 118 studies. A total of nine studies met the inclusion criteria, from which information was extracted. Overall, the finding suggests take-home naloxone kits (THK) reduce the rate of mortality from opioid overdose. One study revealed a 98% rate of successful rescue attempts, and another revealed confidence interval (CI) of 95.5 upper estimates and 97.1 lower estimates of successful opioid survival.

Another study revealed 96% upper estimates and 83% lower estimates of reduction in mortality rate of opioid overdose. One limitation was due to underreported data from the studies. As a result, further studies were recommended to include improved data collection method, and specific follow up periods from 3- 12 months when determining patient outcomes from THK compared to communities that have no THK (Chimbar & Moleta, 2018).

McDonald & Strang (2016) in their level II high-quality systematic review aimed to reveal information about usefulness of THK, the effect of overdose deaths, and the safety of such programs. They performed a structured search of the literature using the “PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)” as a guide to extract information. They searched electronic databases to explore peer-reviewed studies issued January 1946 and third week in June 2015. Twenty

two articles met inclusion criteria. The articles were analyzed and found to meet the nine Bradford Hill original criteria, which included experimental and quasi-experimental evidence known to be strong (McDonald and Strang, 2016). They concluded that THN programs help to reduce fatal opioid overdoses, lower rate of adverse events, and very cost effective. In total 2249 of the 2336 THN administrations resulted in a successful overdose reversal (CI of 95.5 upper estimates and 97.1 lower estimates of successful opioid survivals). Bias in the selection process might have influenced the result, since 10 studies result depended on follow up to evaluate overdose events, only 22.9% of participants followed up (i.e., 1973 of 8602).

McAuley, Aucott, and Matheson (2015) in their level II high-quality systematic review aimed to determine the effects of THN programs on opioid overdoses. They explored studies conducted from 1992 to 2014. They searched major scholarly electronic databases and utilized specific search terms related to topic. Studies that detailed THN programs met the inclusion criteria and were selected or excluded if they failed to include information on the overall outcome of the total naloxone administrations by peers. They analyzed each study by utilizing the “proportion of use (PoU)” approach to calculate the amount of naloxone given by a peer, the number of candidates received training and supplies of naloxone. They focused mainly on persons who use drugs over three months period. McAuley et al. (2015) revealed that in the United States (U.S.) THN training could yield 35,000 to 88,000 uses every 3 months, which constitute to the greatest number of lives potentially saved. They also highlighted application of THN based on the effects of opioids dosage and the increase rate of enforcement that resulted in substantial reductions in overdoses mortality rates. McAuley et al. (2015) recommended exploration of the effects from the time participants received naloxone utilization training to naloxone use. Moreover, high-quality level of research must be a priority in future studies. They recommended PoU method to validate peers reports in future studies, having had success in one study (McAuley et al., 2015).

Hanson, Porter, Zold, & Terhorst-Miller (2020) in their level III good quality qualitative research, studied the effects of preventing opioid overdoses through implementation of NPP in rural Alaska. In 2017, Alaska Department of Health and Social Services (DHSS), and several other organizations in the community provided education on opioid overdose and distributed naloxone rescue kits to 18 laypersons. The participants were selected from two urban and two rural communities and interviewed for approximately 17 minutes regarding accessibility to naloxone, naloxone training, overall knowledge and prior use. The interviews were recorded and analyzed for correctness (Hanson et al., 2020). They found success in accessibility among participants, nature of naloxone to reverse overdoses, overdose education, and overall fatal overdoses (Hanson et al., 2020). However, rural participants transportation issues compared to urban participants limited the trustworthiness of the findings. Participants feared arrest, stigma, housing and custody issues if 911 was contacted, in addition to some not trusting the Alaska's Good Samaritan Law. Hence, further studies are warranted to explore differences in peers' experiences related to gender and rurality, to explore other groups, and not solely peers of opioid users, in receiving and giving naloxone (Hanson et al., 2020).

Siegler et al. (2017) conducted a longitudinal cohort that explored the effects of naloxone prescription program on decreasing fatal overdoses. Individuals who completed the training on preventing opioid overdose from June and September 2013 were selected. Participants were chosen from six of the largest overdose prevention programs in New York. Closed-ended questions were asked immediately after the training, then at 3 months interval for 6 months, followed by 12 months after the training. Data were analyzed using descriptive analysis, bivariate and multivariate synthesis to reveal possible link with observing an overdose and giving naloxone. Logistic regression was utilized to compute the odds ratio, which were analyzed using a 95% confidence interval (CI). A sensitivity analysis was done to determine if there were any statistically significant relationship between demography and differences in drug uses over 12 months period (Siegler et al., 2017). They found that of the 675

individuals who completed the overdose prevention training (OPT), 312 witnessed opioid overdoses, naloxone was administered in 241 events (77%) by 188 (60%) of the OPT study participants. Thus, there can be tremendous impact on decreasing fatal opioid overdoses if participants likely to observe and act on an overdose events are adequately trained (Siegler et al., 2017).

There were discrepancies in number fatal opioid overdoses and rates of naloxone administrations, loss of valuable information limiting follow ups and generalizability, all affected the reliability and trustworthiness of information. They concluded If naloxone distribution is prioritized and provided to a population likely to witness an event, the impact on opioid overdose mortality will be tremendous (Siegler et al., 2017). Population training is recommended to target adequate number of candidates likely to observe and act on an overdose event in order to decrease the number of fatal opioid overdoses (Siegler et al., 2017).

Mitchell & Higgins (2016) in their level III good quality literature review sought to identify the effects of public access to naloxone and the effects on fatal opioid overdose. The review included 38 articles. Several international countries and states in the U.S. recorded success in reversal rates using NPP. One study that had 152,283 candidates received THK after training on opioid overdose revealed 26,463 overdoses were reversed, while another revealed an 89% success rate in reversals. Some limitations were due to stigma associated with illicit users, which could affect trustworthiness of the result if participants fail to report findings or follow up. Moreover, prescribers were reluctant to prescribe due to fear of liability issues, also high price of naloxone forced users to more affordable forms or discouraged use. Well renown organizations including Office of National Drug Control Policy support NPP. They recommended intranasal naloxone due to its safety, protocol implementation for naloxone distribution, legislative reform, and holistic approach in preventing overdoses.

Wheeler, et al. (2015) level III good quality literature review on a survey conducted by the Harm Reduction Coalition (HRC) on 140 organizations in the United states that supply naloxone to laypersons.

HRC aimed to determine the effects of NPP on fatal opioid overdoses from 1996 through June 2014. The research results included 136 organizations responded to the survey and revealed that a total of 152,283 naloxone kits were given to laypersons of which 26,463 reported successful reversals in opioid overdoses. They concluded that if training for opioid overdose events and naloxone rescue kits are provided to candidates more likely to observe an opioid overdose, there can be a reduction of fatal opioid overdoses. Further studies are recommended to include laypersons likely to witness an overdose.

Ogeil et al. (2018) conducted a retrospective review to reveal the effects of THN on the effect of fatal opioid overdoses. It was appraised as a level III good quality evidence. They reviewed pharmaceutical overdose deaths records through periods of January 2011 and December 2013 from Coroners Court Victoria in South-Eastern Australia. There was a total of 125 participants, 69.6% males with age ranging from 16-65 years, and 30.4% female with age ranging from 22-63 years; descriptive statistic was used to analyze the results. They revealed that to reduce fatal opioid overdose, overdose education including naloxone administration to layperson including families must be implemented. A limitation is that there might have been cases where a witness was present at the initial stage of the overdose but was not questioned or included in the coroner report. Another is that witnesses might withhold information to avoid any law enforcement interaction. Altogether, with witnesses' absence or withholding information, the generalization and validity of the finding might be affected.

Furlan et al. (2018) carried out a level II high quality systematic review of peer-reviews and untraditional published literature that sought the correlation between approaches to monitor the proper use of opioids and reducing fatal opioid overdoses. A total of 65 studies were used to extract information. PRISMA checklist was utilized, qualitative systematic review including Cohen's d tests were done to analyze the result. Naloxone distribution was among the most common approach to decrease fatal opioid overdoses with large positive feedback. Some limitations were selection bias and problems with participant follow up as one study reported a 39% dropout rate. Another was lacking in description

of the formulation of the various groups in the studies. Further studies are recommended to include adequate description of the study groups, overall limiting risk for bias.

Mueller et al. (2015) in their level III good quality literature review sought to reveal the effects of community naloxone prescription program on opioid overdose. A total of 41 articles obtained from PubMed were used in the research. PRISMA was used to condense the studies. One study found that naloxone administration was effective with 86% reversal rate, another reported an 80% reversal rate. Some limitations were related to some witnesses were not comfortable administering naloxone, prescribers were not willing to prescribe naloxone, and underreported data due to possible legal implications associated with reporting to law enforcement.

Analysis

After reviewing the evidence of the ten research articles, naloxone prescription program is consistently believed to decrease opioid overdose mortality rates in five of the articles. The naloxone prescription program entails providing education to laypersons on identifying and managing opioid overdose and distributes naloxone rescue kits to the attendees. The other five articles revealed high chance of reduction in fatal opioid overdoses if training is provided on opioid overdose and THK are given to candidates attending the training, and who are more likely to observe and act on an overdose. Further research was recommended to collectively include improved data collection, follow up period from 3-12 months after participants received naloxone education, differences among peers' experiences to include gender and rurality. In addition to population training to target participants more likely will experience and act on an overdose event.

One of the main strengths contributing to the validity and reliability of the findings was consistent with the level of evidence found. They were mainly systematic reviews with one using meta-analysis to support the evidence. Systematic reviews are known to have the most rigorous approach to limit bias in condensing research (Melnyk & Fineout-Overholt, 2019, p. 171). A meta-

analysis uses statistical approach to generate new evidence from the available data. The studies were within the past 5 years, which add to relevancy and appropriateness when implementing the findings.

The inconsistencies were mainly with selection and analysis of data. Even though there were consistencies in the overall findings, each selection and or analysis method have their limitations that can impact the overall findings. Also, two of the ten studies revealed participants feared arrest, stigma, housing and custody issues if 911 was contacted. Another study done in Alaska revealed lack of trust in the Good Samaritan Law.

Discussion and Conclusion

Even though the studies highlighted several limitations, consensus on the major conclusion was Fifty-fifty. Five of the studies revealed NPP consistently proved to decrease opioid overdose mortality. The other five articles revealed high chance of reduction in fatal opioid overdoses if training is provided on opioid overdose and THK are given to candidates attending the training who are more likely to observe and act on an overdose based of place of residence or simply locations they frequent. With this result from such strong evidence, medical facilities in rural communities should utilize the concept of naloxone prescription program to help in decreasing fatal opioid overdose.

In addition, NPP should ensure implementation of opioid overdose education and training of persons in rural areas with higher chances of observing an opioid overdose event and act on it. Further studies are needed to yield more consistent information as Nurse Practitioners (NPs) depend on consistent and reliable evidence to advocate NPP in medical facilities. NPs should become familiar with NPPs considering the associated benefits to patient outcomes and become more engaged with policy proposals that target such program implementation. In addition, NPs should prescribe naloxone to patients who are at risk for opioid overdose to help decrease opioid overdose mortality rate. NPs should also be involved in teaching efforts on proper usage of naloxone, including signs and symptom of opioid overdose to ensure patients are adequately informed. Lastly, NPs should also work on limiting the

stigmas associated with opioid use disorder completing continue education courses on opioid use and misuse.

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