


RESEARCH ARTICLE

Assessment of knowledge and awareness regarding opioid overdose and toxicity among a sample of healthcare providers

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Abstract

Background: Knowledge and attitudes of healthcare providers regarding opioid toxicity are significant concerns. **Objective:** Investigate the knowledge, attitudes, awareness, and comfort level regarding overdosing among a sample of healthcare providers working at the Armed Forces Hospital Southern Region (AFHSR). **Methods:** Anonymous surveys were administered to AFHSR staff to assess attitude, knowledge, comfort level, and fear of consequences using a 5-point scale. Participants were AFHSR primary care physicians/internists, surgeons, physician assistants/advanced practice registered nurses, and pharmacists. **Results:** Healthcare providers demonstrated a lack of knowledge, awareness, and fear of the consequences associated with opioid use, overdose, and the indications and administration of naloxone. This study's findings indicate that healthcare providers are hesitant to engage in discussions with patients about preventative measures for opioid overdose, with the majority believing that doing so will make no difference in preventing opioid overdose incidence. Additionally, a distinct difference in knowledge and perceptions of opioid abuse and toxicity was found between nurses and physicians. Further, the findings indicate a difference in knowledge and awareness regarding opioid overdose and toxicity between nurses and pharmacists.

Introduction

For decades, opioid overdose deaths have risen by an unusual 200 per cent (Rudd *et al.*, 2016). From 2001 to 2012, 663,715 prescription opioids and heroin-related overdoses were expected to lead to hospitalisation. In 2014, 28,647 deaths occurred from an opioid overdose, including heroin, representing the most significant number of drug deaths per year to date in the Americas (Hsu *et al.*, 2017). Besides, heroin overdose death in 2015 was 12989, a massive rise from 2088 respective deaths in 2006. This alarming rise has put the United States in the face of an opioid epidemic caused by increased percentages of heroin and prescription drug overdoses (Rudd *et al.*, 2016). Opioids are the leading

cause of drug overdoses and deaths in the United States (Mattson *et al.*, 2017; Scholl *et al.*, 2019) and globally (Wermeling, 2013; Whiteford, 2013), highlighting the urgent need for successful opioid overdose prevention strategies.

Naloxone has a higher affinity than opioids and binds preferentially to mu receptors. In the presence of an opioid, naloxone displaces the opioid at the receptor, reversing its effects, particularly respiratory depression that leads to death. When administered intramuscularly, naloxone takes a few minutes to begin working and has a half-life of approximately an hour. The rationale for expanding access to naloxone, or 'take-home naloxone,' is that it is extremely safe, has

no abuse potential, and is highly effective at reversing the effects of opioids (McDonald & Strang, 2016). It has no clinical impact on healthy volunteers who have not been recently exposed to opioids (Foldes, 1964).

Federal and professional guidelines, such as the centres for disease control and prevention (CDC) guidelines, have endorsed the use of naloxone in patients at risk of opioid overdose abuse (Wheeler, 2015; Dowell *et al.*, 2016). Naloxone has also been distributed to individuals who use heroin and illicit opioids through community-based programmes (Darke & Hall, 1997). These programmes, which include education, are effective in preventing fatal overdoses (Walley *et al.*, 2013; Wheeler *et al.*, 2015; Giglio *et al.*, 2015; McDonald & Strang *et al.*, 2016; Strang, 2019). However, while prescription opioids are significant contributors to opioid overdose rates (Bohnert *et al.*, 2011; Coe & Walsh, 2015; Glanz *et al.*, 2018), programmes to distribute naloxone effectively to chronic pain patients who have been prescribed opioids are lacking (Binswanger *et al.*, 2015).

The barriers to prescribing naloxone in primary care settings include a lack of knowledge of patients, practitioners, and pharmacists about the availability of naloxone (Binswanger *et al.*, 2015; Behar *et al.*, 2018; Thakur *et al.*, 2020), negative attitudes toward naloxone distribution among providers and pharmacists (Coffin *et al.*, 2016; Haug *et al.*, 2016; Mueller *et al.*, 2017; Behar *et al.*, 2018; Haffajee & French, 2019; Bounthavong *et al.*, 2020), and patient perceptions of being at low risk of an overdose (Mueller *et al.*, 2017; Behar *et al.*, 2018).

Moreover, heroin, methadone, and other medications were reported as causative agents in 38.6 per cent of US veteran injury poisonings (Bohnert *et al.*, 2011). This elevated risk is attributable to the increased prevalence of mental illness among the veteran population, resulting in a heightened likelihood of dually diagnosed drug use disorder (Scholl *et al.*, 2019). Solving this crisis means increased access to naloxone to counteract opioid overdose effects rapidly. Therefore, the US under-secretary of health ordered, in May 2014, the introduction of OEND (Overdose Education and Naloxone Distribution) services to address the opioid epidemic across all Veterans Affairs (VA) facilities.

However, practitioners were often reluctant or uninterested in engaging in risk-reducing services linked to naloxone, with the reasoning behind these behaviours being somewhat variable (Bazazi *et al.*, 2010; Green *et al.*, 2013; Gatewood *et al.*, 2016; Winstanley *et al.*, 2016). Fear of adverse effects, such as increased drug use or decreased probability of seeking medical treatment and suspicion that nonmedical practitioners are not well prepared to cope

with a medical emergency like an overdose, are common reasons for opposition to OEND services. While any conceivable opposition to ambulatory naloxone distribution is difficult to understand, common patterns are known.

A study involving 56 medical practitioners identified a general lack of awareness, fear of consequences, and reduced comfort as significant obstacles to programme implementation (Binswanger *et al.*, 2015). It is uncertain which barrier is considered the greatest, but up to 52 per cent of emergency department practitioners report a lack of awareness. Past recognition of these obstacles in VA hospitals has enhanced targeted education to strengthen experience and opioid addiction behaviours and eventual implementation of the naloxone program (Dwyer *et al.*, 2013). Variable levels of knowledge, comfort and fear of consequences among healthcare practitioner specialities were reported (Peckham *et al.*, 2018).

Due to morbidities and deaths associated with opioids and the demonstrated positive impact on the community of harm reduction efforts, the focus on naloxone use and distribution has never been more critical. For more than 20 decades, naloxone has been identified as a safe agent to reverse the effects of opioid overdose (Sporer, 2003; Doyon *et al.*, 2014). In 2018, the United States surgeon general issued the decade's first public health advisory to encourage all Americans to carry and learn how to use naloxone (Yarlagadda *et al.*, 2020). With no known severe side effects, naloxone is distributed as part of a broader harm reduction plan to initial respondents (including law enforcement) and community members. Mortality rates from opioid overdoses decreased by up to 11% (Devries *et al.*, 2017).

When combined with education on overdose recognition and response, naloxone has been associated with significantly decreased community-level opioid overdose mortality rates in individuals with opioid disorders and their family members and friends (Walley *et al.*, 2013). Naloxone prescription regulations vary from one country to another. In 2015, a new law to facilitate naloxone distribution in Ohio enabled pharmacy professionals to supply naloxone with no prescription (Dixit *et al.*, 2016). Thus, pharmacies are now playing an increasing role in the direct education of patients/caregivers receiving naloxone.

Many doctors have described naloxone as a barrier to treating patients because they are concerned about using naloxone (Binswanger *et al.*, 2015). Clinicians also expressed doubts about whether these patients were correctly identified as at high risk of dependence (Green *et al.*, 2013). Medical training programmes have found that medical professionals report limited

knowledge and low confidence in naloxone overdose and discomfort in the patchwork of naloxone administration legislation and policies across the country (Monteiro *et al.*, 2017). Although many factors may contribute to low rates of naloxone prescription, the integration of knowledge, attitudes, and efficacy process begins in training programmes. In the efforts to introduce engaging platforms to support desired behaviours and skills, graduate medical education programmes were highly recommended with trained and experienced faculty, good didactic and experience courses, and clinical exposure to opioid-dependent patients (Kunins *et al.*, 2013).

Based on the aforementioned, this study has been developed to assess knowledge, attitude, and concern among healthcare providers of different specialities, including physicians, pharmacists, and nurses, exposed to opioid prescribing, administration, and dispensing. Awareness and attitude measure knowledge about overdose and the proper action to deal with such cases. A comfort level describes confidence about these decisions. Also, exploring fears when dealing with the antidote is a cornerstone to help establish suitable educational programs.

This study aimed to explore the attitudes, awareness, comfort level, and concerns of physicians, pharmacists, and nurses at the Armed Forces Hospital Southern Region (AFHSR) toward opioid overdosing, compare the three groups and determine the difference between overdose and toxicity. It also aimed to investigate the ethical concerns of healthcare providers.

Methods

This cross-sectional study conducted from February 2021 to April 2021 among healthcare providers used a questionnaire for data collection. It involved health professionals of the following specialities: primary care, internal medicine, surgery, orthopaedics, pharmacy, and nursing at AFHSR. The anonymity of participants was guaranteed during the data collection process.

Participants were informed about the study objective and were provided with the questionnaire after giving consent to participate. Data were collected during personal visits, as it was necessary to allow participants time to complete the questionnaire due to their tight schedules. The primary aim was to measure healthcare providers' knowledge, awareness, and concern regarding naloxone and opioid overdose. This study relied on the survey developed by Peckham and colleagues (2018) after getting permission to use the study materials. Knowledge of opioid overdose was measured with 24 items rated on a 5-point Likert scale,

ranging from 5 (strongly agree) to 1 (strongly disagree). The survey was distributed at department staff meetings and practice sites. It included questions about participant occupation and practice area in addition to items covering four fields related to opioid overdose, i.e., (1) attitudes toward opioid overdose preventive strategies; (2) comfort with practising opioid overdose prevention strategies; (3) knowledge of opioid overdose prevention strategies; and (4) fear of naloxone prescription-related consequences.

Results

The study sample included 188 participants, distributed as follows: 98 nurses, 23 pharmacists, and 67 physicians.

Nurses

Nurse attitudes on engaging patients in opioid overdose prevention

Nurses tended to have different beliefs compared to other specialities, especially about engaging patients in discussions about opioid overdose. Based on the results, over 70% of nurses believed that it is good practice to engage the patients in discussing measures that could be taken in overdose prevention. The findings show that 31% of the nurses agree that talking about opioid prevention does not make a difference, while 35% believe it does. This result indicates that most nurses are not sure whether conversations with opioid users have a greater likelihood of changing their behaviours. About 37% of the nurses believe that it is not their responsibility to talk about safe ways to use illegal opioids, 21% were neutral, and 29% thought it was their duty to speak to patients about safer ways to use a prescribing opioid. Moreover, 45% of the nurses agreed that abstinence is the only prevention strategy for illicit opioid users, while 22% disagreed (Figure 1).

Nurses knowledge on naloxone and awareness on preventing overdose

The results show that 53% of the nurses agreed about being uncomfortable educating patients (Figure 2). Also, 42% were not familiar with naloxone administration to discuss it, and only 31% reported being familiar. Thus, the knowledge regarding naloxone among nurses is still low, and there is a need for education if nurses are supposed to enhance the prescription of naloxone. However, attitudes regarding the administration of naloxone seem to be quite different. Indeed, 55% of the nurses demonstrated positive attitudes, especially about providing patients with the necessary training about naloxone. This

finding indicates that nurses have positive attitudes regarding the provision of naloxone to patients, and they believe it is their mandate to ensure the best for their patients. Nurses also tended to demonstrate positive attitudes on helping patients deal with opioid overdose. Figure 2 shows that 67% of the nurses

reported engaging with patients to prevent opioid overdose, while 63% were satisfied to engage patients using illicit opioids for pain management. These results show that most nurses within this healthcare setting are more willing and inclined towards the idea of conversing with their patients.

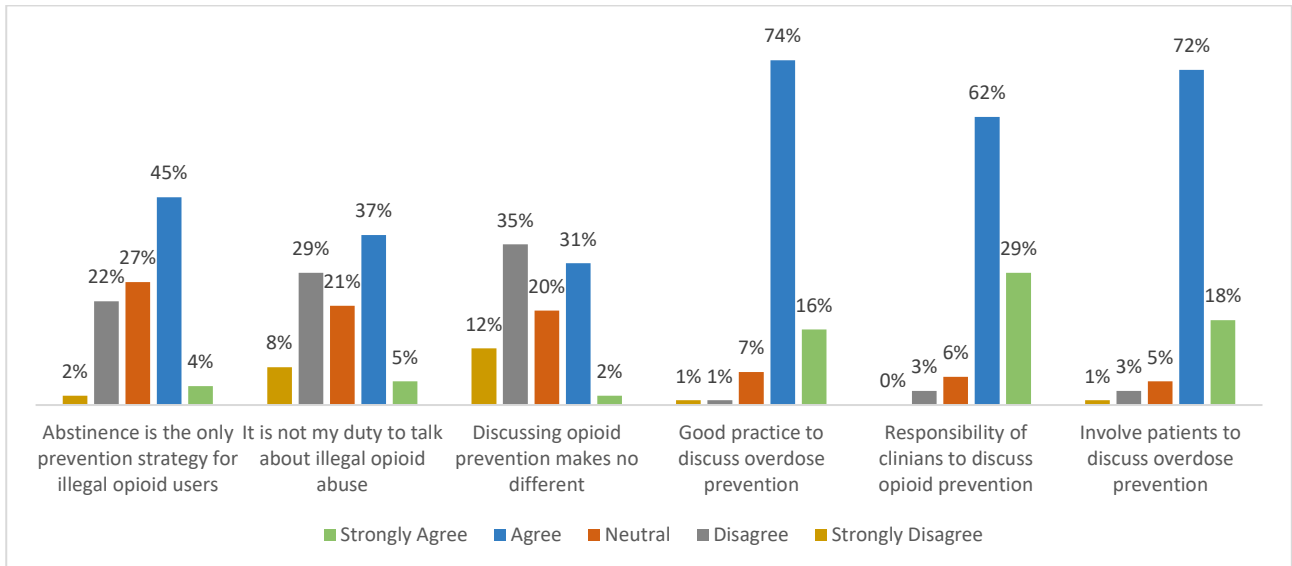


Figure 1: Nurse attitudes on engaging patients in opioid overdose prevention

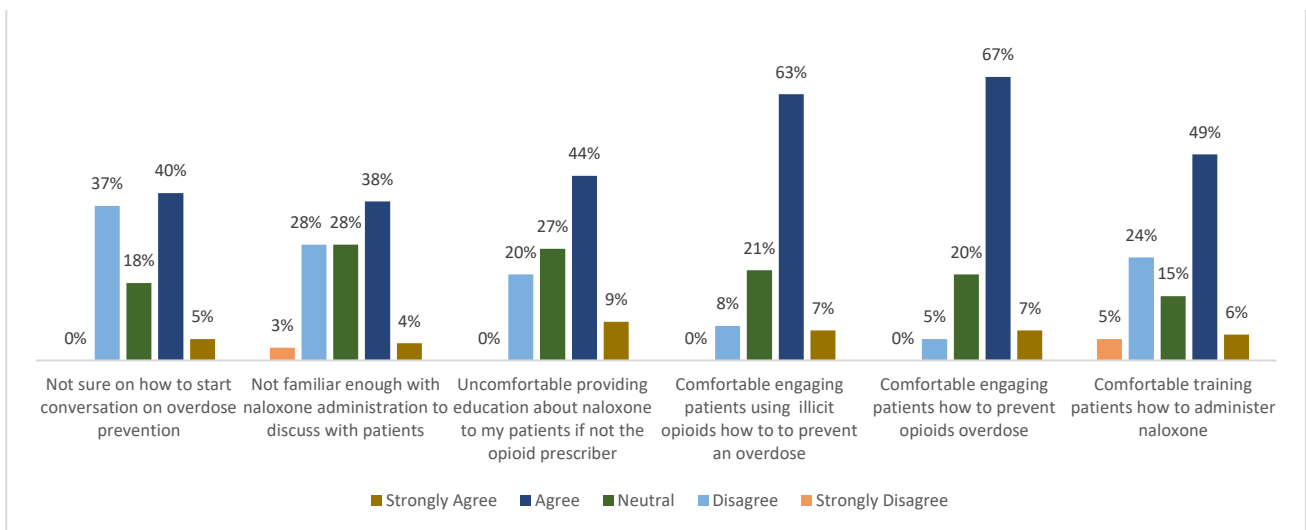


Figure 2: Nurses knowledge on naloxone and awareness on preventing overdose

Nurses concerns about naloxone

Figure 3 shows a myriad of concerns and worries that most nurses have regarding naloxone and how to handle issues related to opioids. For example, 79% of nurses are concerned about naloxone side effects, while only 6% of the respondents reported not being concerned. Furthermore, 66% of nurses reported that

providing access to naloxone would motivate them to focus on getting more opioids since they feel they have the remedy in case of an overdose. Finally, ethical concerns include co-prescribing opioids with naloxone, which might imply that the nurses tend to endorse opioids without control, as 56% agreed that it would send a wrong impression while only 14% of the respondents tended to disagree.

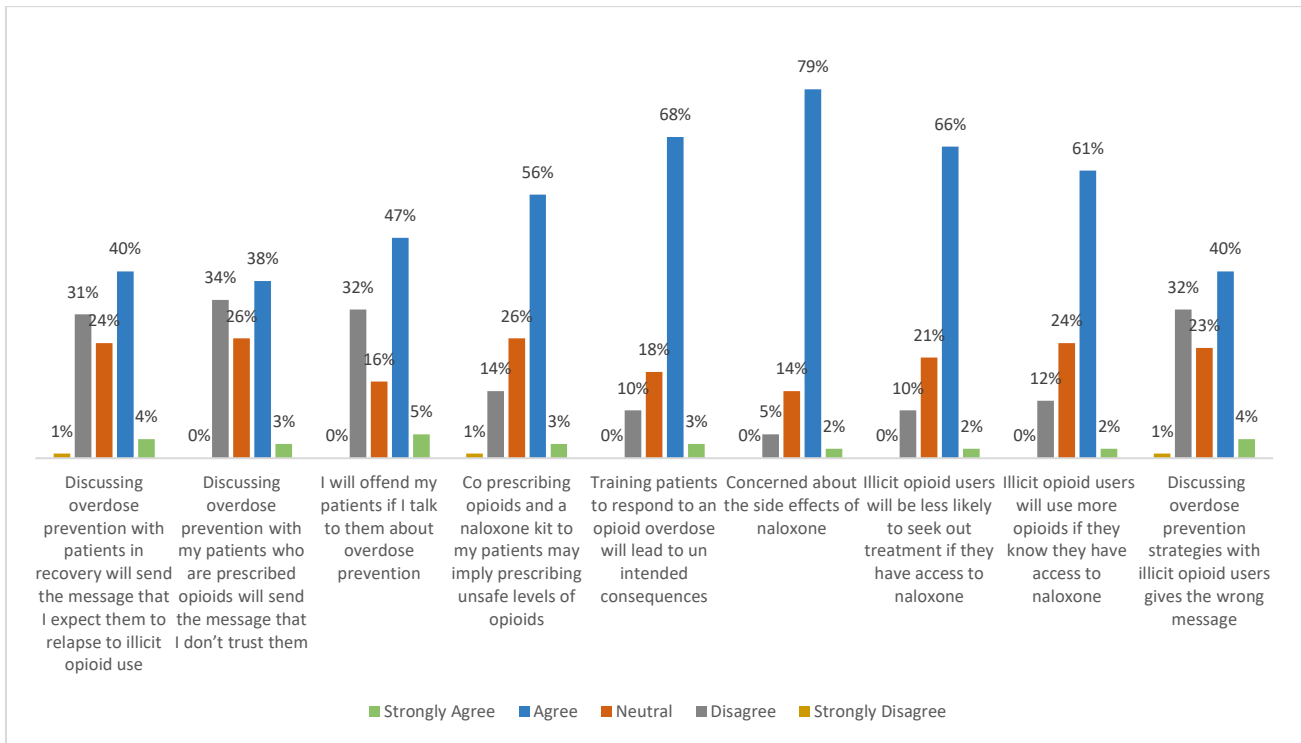


Figure 3: Nurses concerns about naloxone

Pharmacists

Pharmacist attitudes on engaging patients in opioid overdose prevention

The number of pharmacists included was 23. As seen in Figure 4, 55% of pharmacists are neutral, indicating they are undecided about involving patients and holding discussions about overdose prevention. Only 35% of pharmacists agreed it is a viable idea, meaning that most pharmacists from this healthcare institution still do not feel the importance of involving patients in discussing measures for stopping addiction. Additionally, 45% of pharmacists agreed, and 45%

strongly agreed that it is the responsibility of clinicians to discuss opioid prevention. In this case, pharmacists feel they are not obliged to discuss opioid prevention with patients, as their responsibility is limited mainly to preparing and dispensing prescriptions. Also, 35% strongly agreed, and 30% agreed that it is good practice to discuss overdose prevention. The data show that most pharmacists feel they do not have an obligation engaging patients to talk about opioid overdose prevention. Also, they tended to be divided mainly regarding how they think about the changes that discussing opioids with clinicians might make (Figure 4).

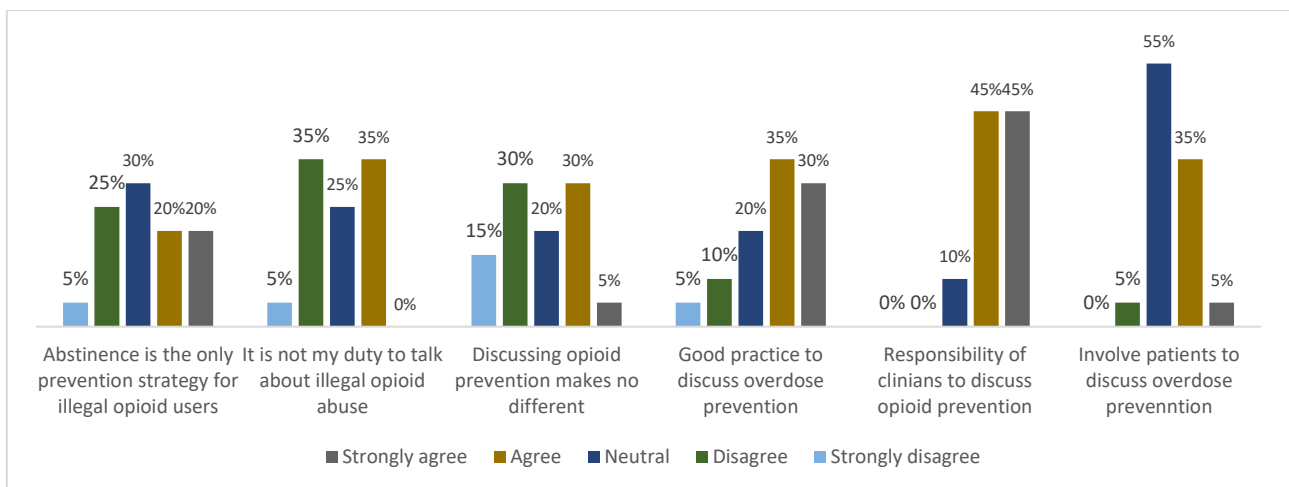


Figure 4: Pharmacist attitudes toward engaging patients in Opioid overdose prevention

Pharmacists awareness of engaging patients and knowledge of naloxone

From the data provided, the pharmacist tended to have high knowledge and awareness about the effectiveness of naloxone, as 60% of pharmacists reported being comfortable training patients to administer naloxone, and 75% were satisfied with engaging patients on how to prevent opioid overdose. Only 5% reported not being familiar with naloxone administration, and 55%

were undecided about being familiar with naloxone administration. It can be noted that pharmacists tended to know about naloxone and were also aware of strategies that can be used to prevent opioid overdose. However, from the data, it is also clear that pharmacists still lack the knowledge to engage in discussion with patients about opioid overdose, as 30% of the respondents reported not being sure they could initiate a conversation with patients regarding opioid overdose prevention (Figure 5).

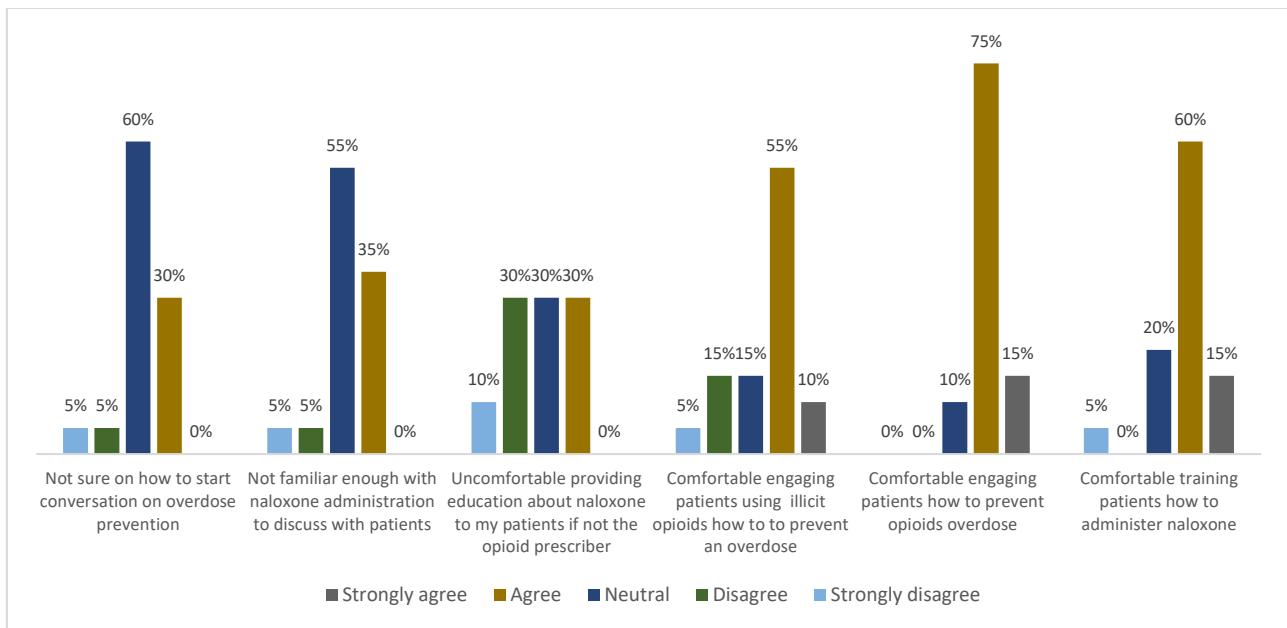


Figure 5: Pharmacists awareness of engaging patients and knowledge of naloxone

Pharmacist concerns about naloxone

Pharmacists were also concerned and worried about naloxone. Based on the reports, 65% of pharmacists agreed that illicit opioid users might abuse it, especially when they know they have access to opioids. Moreover, ethical concerns are also a big issue among pharmacists, which might impede efforts regarding illegal opioid use. Consequently, according to the data, 40% of respondents agreed that discussing overdose prevention strategies with illicit opioid users will convey the wrong message. It is worth noting that the main concern is because the discussions might imply that healthcare providers are allowing the users to use illicit opioids even if it is in low amounts. Finally, 45% of pharmacists also agreed that co-prescribing opioids and naloxone might mean that they are given unsafe levels of opioids because they believe they provide naloxone to contain the detrimental effects of an overdose (Figure 6).

Physicians

Physicians attitudes in involving patients about opioid overdose prevention

Of the 67 physicians participating in the study, 48% believed it is good to involve patients and discuss opioid overdose prevention. Additionally, 33% strongly agreed to engage patients in discussing opioid prevention. Another significant finding is that physicians feel it is the clinician’s responsibility to discuss opioid prevention with patients, with 43% strongly agreeing and 46% agreeing with this statement. Physicians think it is good to discuss opioid prevention measures with patients, as 52% agreed and 27% strongly agreed. Physicians also believed that discussing opioid prevention tends to make a difference, especially in opioid overdose prevention among patients. There were 46% of the physicians disagreed that discussing opioid prevention strategies did not make a difference in reducing the risk of opioid toxicity, while 26% strongly disagreed with the statement. Moreover, physicians also feel they should discuss illegal opioid abuse with their patients, as 34% disagreed with the idea that it is not their duty, while 22% strongly disagreed (Figure7).

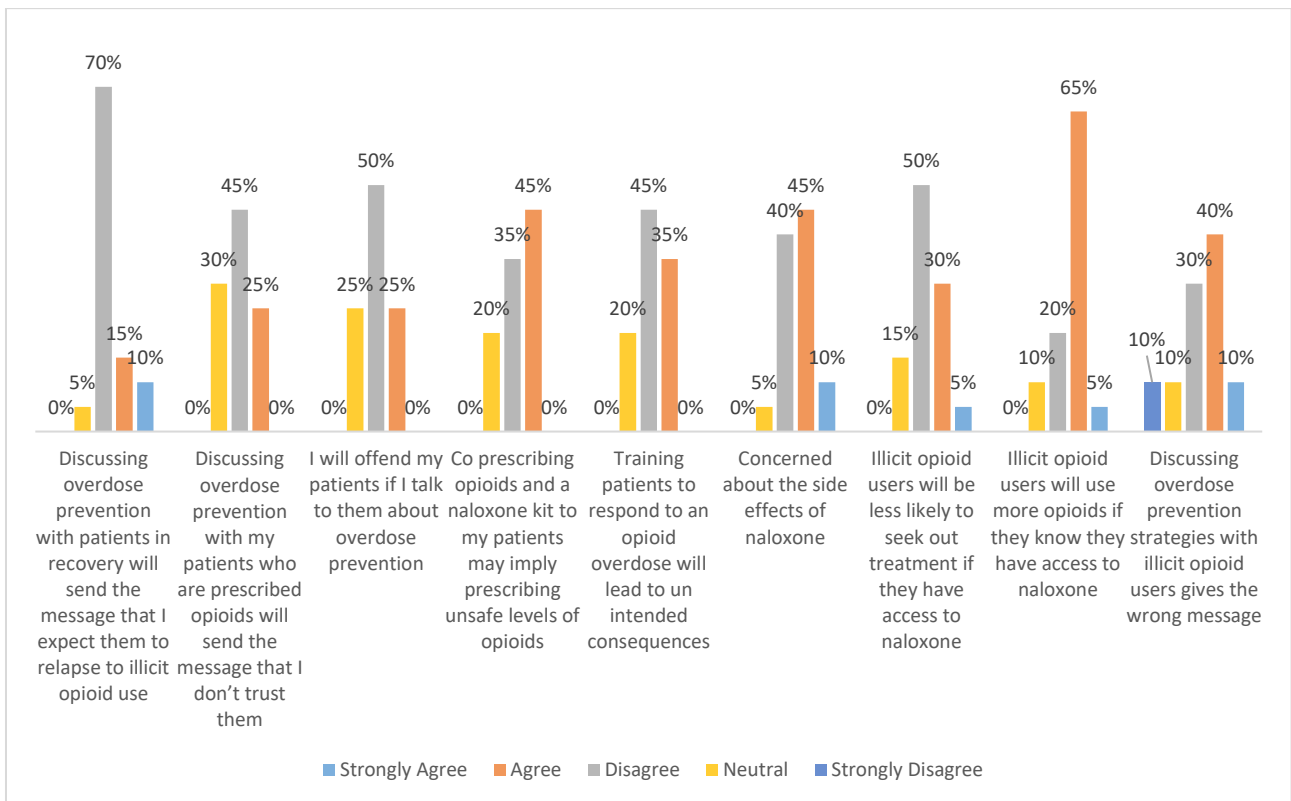


Figure 6: Pharmacist concerns about naloxone

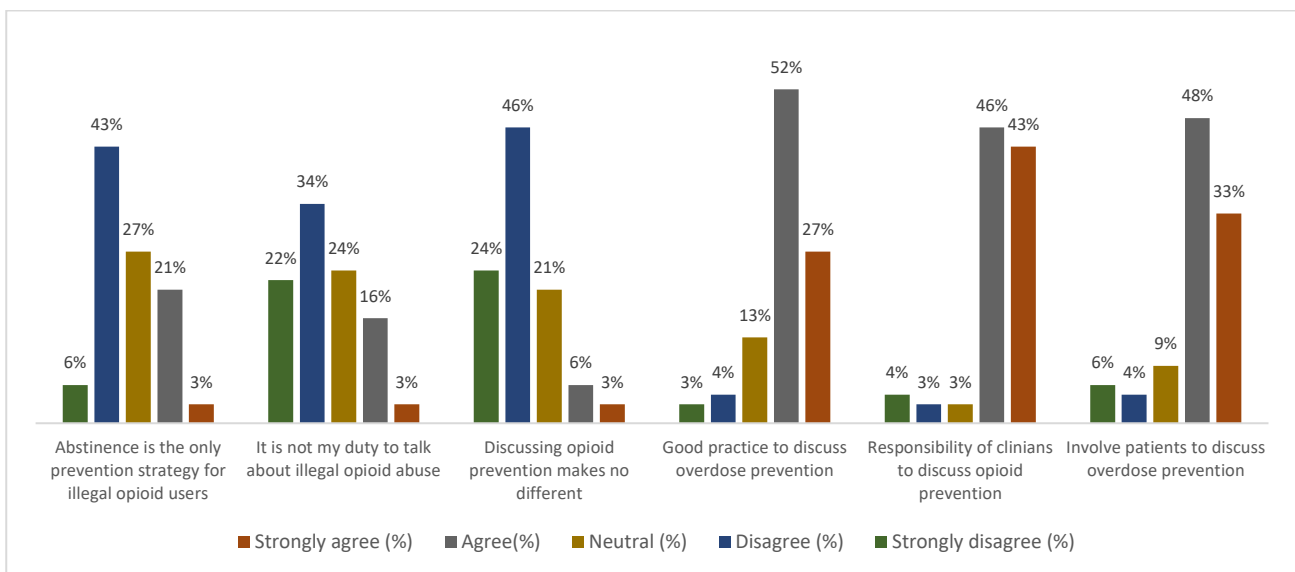


Figure 7. Physicians attitudes in involving patients in opioid overdose prevention

Physicians awareness of engaging patients and knowledge of naloxone

Physicians were aware of the significance of engaging patients, especially regarding opioid overdose prevention. Most physicians were comfortable engaging patients to prevent opioid overdose, with 57% agreeing, while 18% strongly agreeing with the

statement. Moreover, 51% of physicians were comfortable discussing the use of illicit opioids with patients and how to prevent an overdose, while 13% strongly agreed. However, knowledge about naloxone among physicians is still limited. Indeed, 33% of physicians reported not being familiar with naloxone, while only 21% reported being familiar with naloxone to discuss with patients (Figure 8).

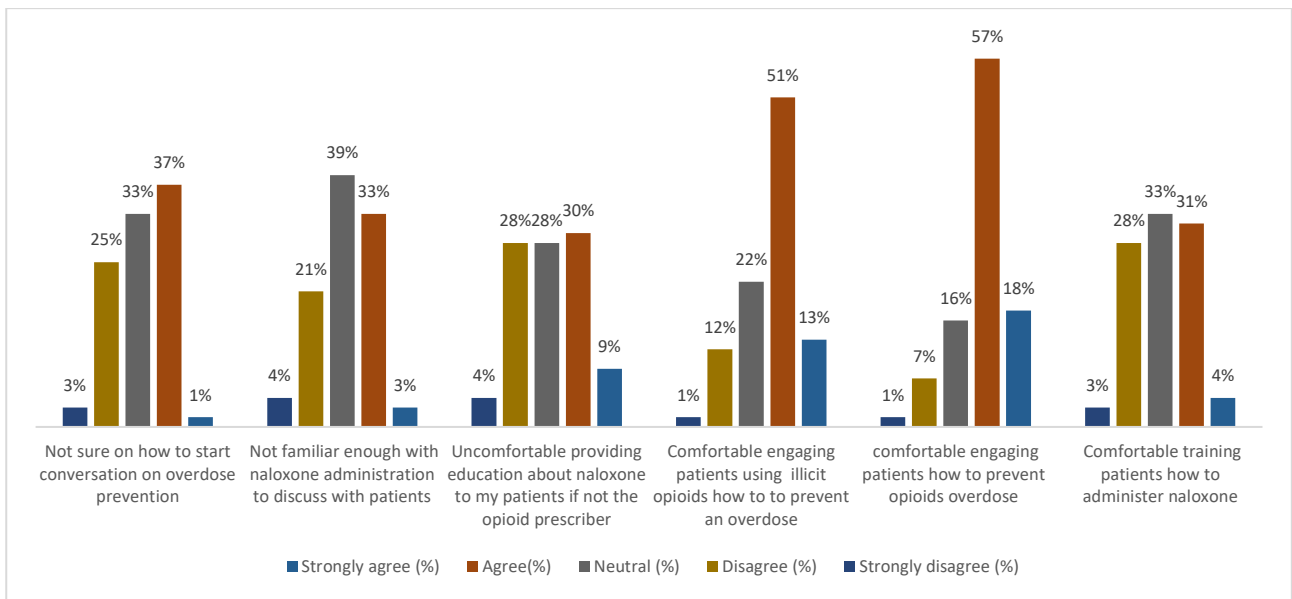


Figure 8: Physicians awareness on engaging patients and knowledge on naloxone

Physicians concerns about naloxone

From the data provided, it is evident that 57% of the physicians were concerned about the side effects of naloxone if it has been co-prescribed to the patients as an antidote in case of opioid toxicity. If the patients

have access to naloxone, Physicians are also concerned that the number of illicit opioid users will use more opioids. For example, 43% agreed that it would increase opioid overdose, while 4% of the physicians strongly agreed of this statement (Figure 9).

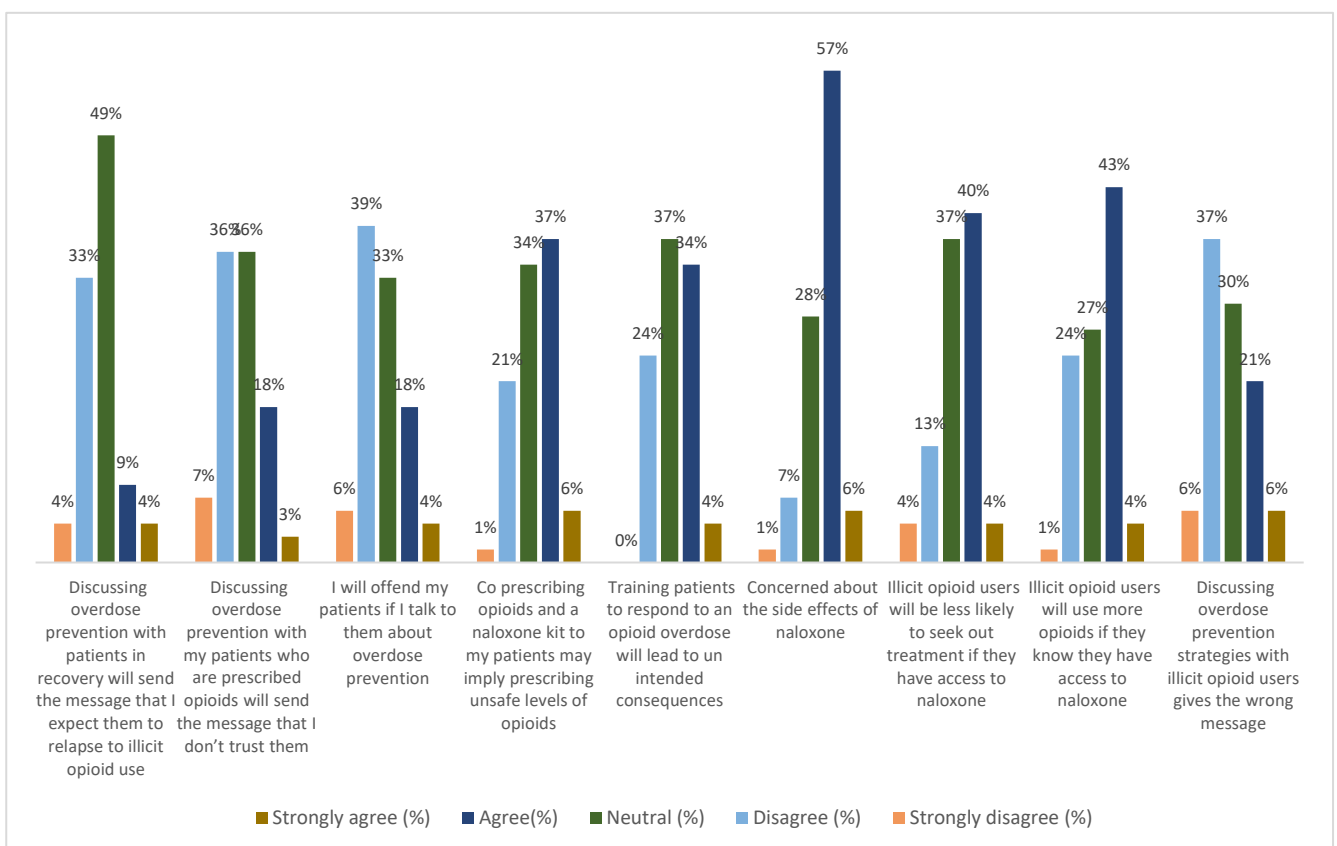


Figure 9: Physicians concerns about naloxone

Discussion

This study revealed that healthcare providers still have attitudes and concerns that might impede avoiding opioid overdose. Healthcare providers tended to be reluctant, especially in engaging patients in the strategies they should undertake to limit opioid overdose. Additionally, some healthcare providers believe that engaging the patients is good but will not change opioid overdose. However, most healthcare professionals are still unsure whether discussing opioid prevention impacts patient lives. Pharmacists tended to have different attitudes regarding engaging patients about matters related to opioid abuse. The results also showed that physicians welcomed the idea of discussing opioid abuse with patients and reaching a consensus about it. A previous study conducted by Peckham and collaborators (2018) reported different levels of knowledge, comfort, and fear of impact among healthcare practitioners, depending on the speciality. Furthermore, insufficient knowledge about naloxone is also an issue that might prevent prescription among healthcare providers.

Nurses' knowledge showed to be insufficient, especially about training patients on administering naloxone and general education about naloxone. Similarly, physicians had concerns about administering naloxone, finding it difficult to recommend and increase naloxone administration. However, pharmacists were comfortable engaging patients and training them on administering naloxone. According to Dwyer and colleagues, it is unclear which obstacle is considered the greatest. Up to 52% of emergency practitioners report a lack of awareness. Past acknowledgement of these barriers in VA hospitals has increased focused learning to reinforce the experience and behavioural opioid addiction and eventual implementation of the naloxone program (Dwyer *et al.*, 2013). Likewise, medical training programs found that health professionals report limited knowledge and trust issues in the patchwork of naloxone administration laws and policies throughout the country overdose and discomfort (Monteiro *et al.*, 2017).

This study also indicated that most nurses were worried about patient reactions, jeopardising healthy relationships and ethical conduct as practitioners. Pharmacists feared that prescribing naloxone to most patients might be an incentive for opioid overdose. Studies demonstrate that many physicians are uncomfortable training patients on how to administer naloxone and provide education about naloxone, as they are not familiar with naloxone administration. The general lack of awareness, fear of consequences, and reduced comfort of the 56 practitioners, were

significant obstacles to implementing the program, consistent with previous findings (Binswanger *et al.*, 2015).

There was a difference between nurses and physicians regarding knowledge, opioid abuse, and toxicity perceptions. Moreover, there tended to be a difference between nurses and pharmacists regarding knowledge and awareness of opioid overdose and toxicity. When comparing physicians and pharmacists, the test value was higher than the critical value. Therefore, the difference between pharmacists and physicians regarding perceptions and attitudes on opioid overdose and toxicity was acceptable. Several factors could contribute to low prescription rates of naloxone; integration into training programmes begins with knowledge, attitudes, and efficacy. Therefore, graduate medicine programmes were strongly recommended with trained and experienced teaching professionals, sufficient training and experiential courses, and clinical exposure of opioid-dependent patients to create engaging platforms to support desired behaviour and qualifications (Kunins *et al.*, 2013).

Nurses were more inclined towards agreeing about discussing overdose prevention, different from physicians who tended to be neutral. Moreover, the three groups tended to agree that it is the responsibility of clinicians to involve the nurses. However, both the physicians and pharmacists did not believe that discussing opioids might result in any differences, while nurses were neutral. Generally, nurses tended to have positive attitudes compared to physicians and pharmacists towards engaging patients in programmes to reduce opioid overdose.

Conclusion

Opioid overdose prevention is crucial to saving patient lives. Healthcare providers showed questionable knowledge, awareness, and fear of the consequences of opioid overdose and naloxone indications and administration. The findings also indicated that healthcare providers were hesitant toward engaging patients in programmes to prevent opioid overdose, with the majority believing that it would not make a significant difference. Besides, there was a clear distinction between nurses and physicians regarding knowledge, perceptions of opioid abuse, and toxicity. Furthermore, knowledge and awareness of opioid overdose and toxicity were different between nurses and pharmacists.

Implementing a programme to train healthcare practitioners and improve their knowledge about opioids would optimise their ability to manage opioid

overdose and administer naloxone appropriately and timely. Additional studies are necessary to identify the factors that affect prescribing, dispensing, and administering naloxone.

Conflict of interest

The authors declare no conflict of interest.

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References

- Bazazi, A. R., Zaller, N. D., Fu, J. J., & Rich, J. D. (2010). Preventing opiate overdose deaths: examining objections to take-home naloxone. *Journal of health care for the poor and underserved*, *21*(4), 1108
- Behar, E., Bagnulo, R., & Coffin, P. O. (2018). Acceptability and feasibility of naloxone prescribing in primary care settings: A systematic review. *Preventive medicine*, *114*, 79-87. <https://doi.org/10.1016/j.ypmed.2018.06.005>
- Binswanger, I. A., Koester, S., Mueller, S. R., Gardner, E. M., Goddard, K., & Glanz, J. M. (2015). Overdose education and naloxone for patients prescribed opioids in primary care: a qualitative study of primary care staff. *Journal of general internal medicine*, *30*(12), 1837-1844. <https://doi.org/10.1007/s11606-015-3394-3>
- Bohnert, A. S., Valenstein, M., Bair, M. J., Ganoczy, D., McCarthy, J. F., Ilgen, M. A., & Blow, F. C. (2011). Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*, *305*(13), 1315-1321. <https://doi.org/10.1001/jama.2011.370>
- Bounthavong, M., Suh, K., Christopher, M. L., Veenstra, D. L., Basu, A., & Devine, E. B. (2020). Providers' perceptions on barriers and facilitators to prescribing naloxone for patients at risk for opioid overdose after implementation of a national academic detailing program: A qualitative assessment. *Research in Social and Administrative Pharmacy*, *16*(8), 1033-1040. <https://doi.org/10.1016/j.sapharm.2019.10.015>
- Coe, M. A., & Walsh, S. L. (2015). Distribution of naloxone for overdose prevention to chronic pain patients. *Preventive medicine*, *80*, 41-43. <https://doi.org/10.1016/j.ypmed.2015.05.016>
- Coffin, P. O., Behar, E., Rowe, C., Santos, G. M., Coffa, D., Bald, M., & Vittinghoff, E. (2016). Nonrandomized intervention study of naloxone co-prescription for primary care patients receiving long-term opioid therapy for pain. *Annals of internal medicine*, *165*(4), 245-252. <https://doi.org/10.7326/M15-2771>
- Darke, S., & Hall, W. (1997). The distribution of naloxone to heroin users. *Addiction*, *92*(9), 1195-1200. <https://doi.org/10.1111/j.1360-0443.1997.tb03681.x>
- Devries, J., Rafie, S., & Polston, G. (2017). Implementing an overdose education and naloxone distribution program in a health system. *Journal of the American Pharmacists Association*, *57*(2), S154-S160. <https://doi.org/10.1016/j.japh.2017.01.002>
- Dixit, D., Endicott, J., Burry, L., Ramos, L., Yeung, S. Y. A., Devabhakthuni, S., ... & Bulloch, M. N. (2016). Management of acute alcohol withdrawal syndrome in critically ill patients. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *36*(7), 797-822. <https://doi.org/10.1002/phar.1770>
- Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC guideline for prescribing opioids for chronic pain—the United States, 2016. *JAMA*, *315*(15), 1624-1645. <https://doi.org/10.1001/jama.2016.1464>
- Doyon, S., Aks, S. E., & Schaeffer, S. (2014). Expanding access to naloxone in the United States. *Clinical Toxicology*, *52*(10), 989-992. <https://doi.org/10.3109/15563650.2014.968657>
- Dwyer, K. H., Samuels, L., Moore, R. L., Langlois, B. K., Mitchell, P. M., Grimsmann, J., & Bernstein, E. (2013). Physician attitudes and perceived barriers to prescribing nasal naloxone rescue kits in the emergency department. *Annals of Emergency Medicine*, *62*(4), S43. <https://doi.org/10.1016/j.annemergmed.2013.07.400>
- Foldes, F. F. (1964). The human pharmacology and clinical use of narcotic antagonists. *Medical Clinics of North America*, *48*(2), 421-443. [https://doi.org/10.1016/S0025-7125\(16\)33474-5](https://doi.org/10.1016/S0025-7125(16)33474-5)
- Gatewood, A. K., Van Wert, M. J., Andrada, A. P., & Surkan, P. J. (2016). Academic physicians' and medical students' perceived barriers toward bystander administered naloxone as an overdose prevention strategy. *Addictive behaviors*, *61*, 40-46. <https://doi.org/10.1016/j.addbeh.2016.05.013>
- Giglio, R. E., Li, G., & DiMaggio, C. J. (2015). Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. *Injury epidemiology*, *2*(1), 1-9. <https://doi.org/10.1186/s40621-015-0041-8>
- Glanz, J. M., Narwaney, K. J., Mueller, S. R., Gardner, E. M., Calcaterra, S. L., Xu, S., ... & Binswanger, I. A. (2018). Prediction model for two-year risk of opioid overdose among patients prescribed chronic opioid therapy. *Journal of general internal medicine*, *33*(10), 1646-1653. <https://doi.org/10.1007/s11606-017-4288-3>
- Green, T. C., Bowman, S. E., Zaller, N. D., Ray, M., Case, P., & Heimer, R. (2013). Barriers to medical provider support prescription naloxone as overdose antidote for lay responders. *Substance use & misuse*, *48*(7), 558-567. <https://doi.org/10.3109/10826084.2013.787099>
- Haffajee, R. L., & French, C. A. (2019). Provider perceptions of system-level opioid prescribing and addiction treatment policies. *Current opinion in psychology*, *30*, 65-73. <https://doi.org/10.1016/j.copsyc.2019.01.018>

- Haug, N. A., Bielenberg, J., Linder, S. H., & Lembke, A. (2016). Assessment of provider attitudes toward# naloxone on Twitter. *Substance abuse*, **37**(1), 35-41. <https://doi.org/10.1080/08897077.2015.1129390>
- Hsu, D. J., McCarthy, E. P., Stevens, J. P., & Mukamal, K. J. (2017). Hospitalizations, costs and outcomes associated with heroin and prescription opioid overdoses in the United States 2001–12. *Addiction*, **112**(9), 1558-1564. <https://doi.org/10.1111/add.13795>
- Kunins, H. V., Sohler, N. L., Giovanniello, A., Thompson, D., & Cunningham, C. O. (2013). A buprenorphine education and training program for primary care residents: implementation and evaluation. *Substance abuse*, **34**(3), 242-247. <https://doi.org/10.1080/08897077.2012.752777>
- Mattson, C. L., Schieber, L., Scholl, L., Rudd, R. A., Seth, P., Xu, L., ... & Paulozzi, L. J. (2017). Annual surveillance report of drug-related risks and outcomes—the United States, 2017
- McDonald, R., & Strang, J. (2016). Are take-home naloxone programmes effective? Systematic review utilizing the application of the Bradford Hill criteria. *Addiction*, **111**(7), 1177-1187. <https://doi.org/10.1111/add.13326>
- Monteiro, K., Dumenco, L., Collins, S., Bratberg, J., MacDonnell, C., Jacobson, A., ... & George, P. (2017). An interprofessional education workshop to develop health professional student opioid misuse knowledge, attitudes, and skills. *Journal of the American Pharmacists Association*, **57**(2), S113-S117
- Mueller, S. R., Koester, S., Glanz, J. M., Gardner, E. M., & Binswanger, I. A. (2017). Attitudes toward naloxone prescribing in clinical settings: a qualitative study of patients prescribed high dose opioids for chronic non-cancer pain. *Journal of general internal medicine*, **32**(3), 277-283. <https://doi.org/10.1016/j.japh.2016.12.069>
- Peckham, A. M., Niculete, M. E., Steinberg, H., & Boggs, D. L. (2018). A survey of prescribers' attitudes, knowledge, comfort, and fear of consequences related to opioid overdose education and naloxone distribution program. *Journal of public health management and practice*, **24**(4), 310-317. <https://doi.org/10.1097/PHH.0000000000000668>
- Rudd, R. A., Aleshire, N., Zibbell, J. E., & Gladden, R. M. (2016). Increases in drug and opioid overdose deaths—the United States, 2000–2014. *Morbidity and mortality weekly report*, **64**(50-51), 1378-1382. <https://doi.org/10.15585/mmwr.mm6450a3>
- Scholl, L., Seth, P., Kariisa, M., Wilson, N., & Baldwin, G. (2019). Drug and opioid-involved overdose deaths—the United States, 2013–2017. *Morbidity and Mortality Weekly Report*, **67**(51-52), 1419. <https://doi.org/10.15585/mmwr.mm675152e1>
- Sporer, K. A. (2003). Strategies for preventing heroin overdose. *BMJ*, **326**(7386), 442-444. <https://doi.org/10.1136/bmj.326.7386.442>
- Strang, J., McDonald, R., Campbell, G., Degenhardt, L., Nielsen, S., Ritter, A., & Dale, O. (2019). Take-home naloxone for the emergency interim management of opioid overdose: the public health application of an emergency medicine. *Drugs*, **79**(13), 1395-1418. <https://doi.org/10.1007/s40265-019-01154-5>
- Thakur, T., Frey, M., & Chewning, B. (2020). Pharmacist roles, training, and perceived barriers in naloxone dispensing: a systematic review. *Journal of the American Pharmacists Association*, **60**(1), 178-194. <https://doi.org/10.1016/j.japh.2019.06.016>
- Walley, A. Y., Xuan, Z., Hackman, H. H., Quinn, E., Doe-Simkins, M., Sorensen-Alawad, A., ... & Ozonoff, A. (2013). Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ*, 346. <https://doi.org/10.1136/bmj.f174>
- Wermeling, D. P. (2013). A response to the opioid overdose epidemic: naloxone nasal spray. *Drug delivery and translational research*, **3**(1), 63-74. <https://doi.org/10.1007/s13346-012-0092-0>
- Wheeler, E., Jones, T. S., Gilbert, M. K., & Davidson, P. J. (2015). Opioid overdose prevention programs providing naloxone to laypersons—United States, 2014. *MMWR. Morbidity and mortality weekly report*, **64**(23), 631
- Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., ... & Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The lancet*, **382**(9904), 1575-1586. [https://doi.org/10.1016/S0140-6736\(13\)61611-6](https://doi.org/10.1016/S0140-6736(13)61611-6)
- Winstanley, E. L., Clark, A., Feinberg, J., & Wilder, C. M. (2016). Barriers to implementation of opioid overdose prevention programs in Ohio. *Substance abuse*, **37**(1), 42-46. <https://doi.org/10.1080/08897077.2015.1132294>
- Yarlagadda, K., Kim, J., Kanderi, T., Sendil, S., & Nookala, V. K. (2020). Opioid antidote induced pulmonary edema and lung injury. *Respiratory medicine case reports*, **30**, 101107. <https://doi.org/10.1016/j.rmcr.2020.101107>