

TITLE: Naloxone Use and Knowledge from Patients Treated for Opioid Use Disorder

BACKGROUND: Best practices recommend that patients at risk for overdose, including those in treatment for opioid use disorder (OUD), have naloxone on hand in case of relapse or if someone near to the person in treatment overdoses (1). It was estimated that, in 2019, a bystander was present in nearly 40% of opioid and stimulant overdose deaths, further emphasizing the importance of community availability (2). It is not currently known how frequently patients with OUD obtain naloxone, how often it is used, and the extent of barriers to obtaining naloxone such as insurance coverage and price. In our practice, a large telehealth-only OUD treatment practice group, it is routine to co-prescribe a nasal naloxone rescue kit along with the first prescription for buprenorphine. This study surveyed our patients to determine the rate at which patients fill their naloxone prescription, their knowledge about naloxone, their use of naloxone, and – if not filled – why not.

METHODS: This was a survey study of patients treated in our group, a large telehealth-only OUD treatment provider. The program utilizes a smartphone app that patients access for all aspects of care, including video visits with their providers, therapists, peer recovery coaches, and to attend group meetings. The app includes a secure text messaging platform for communication. At the time of this study, there were about 12,000 active patients and around 5,000 more who were no longer in treatment but still had access to the app. All patients who had access to the app were invited via text message that invited participants to complete a brief survey about naloxone. Patients who provided an email address were eligible to win one of two \$200 gift cards. Primary outcomes pertained to use and prescription filling of naloxone. This includes patient knowledge of naloxone, use of naloxone, and whether the patient had filled their prescription for naloxone. If they had not filled the prescription, they were asked to provide a reason for not filling it. Secondary outcomes examined were assessments of naloxone knowledge, use, and prescription filling among different demographics. The study was approved by the Western-Copernicus Group (WCG) institutional review board.

RESULTS: The survey instrument was sent to 17,899 individuals, of whom 12,887 were active in treatment. 701 surveys were completed. Most patients who responded were aged 30-49 (n=451, 64%). There were more female patients than male (55% vs. 44%). Most patients were white race (n=617, 89%) and non-Hispanic/Latino ethnicity (n=610, 89%). Patients resided in 31 different states. About two-thirds of patients (n=478, 69%) predominantly used prescription opioids before starting OUD treatment. Nearly all patients (n=693, 99%) know what naloxone is, and the majority (n=601, 86%) know how to administer it. A quarter of these patients (n=177, 25%) reported either having naloxone used on themselves or using it on someone else in the past. There were 161 patients (23%) who reported taking a naloxone training course. Even though it is routine practice to send a naloxone co-prescription (with 9 refills) along with a first buprenorphine prescription in our practice, 76% (n=533) recalled receiving a prescription. There were 382 patients (of the 533 who recalled receiving a prescription, or 72%) who filled the prescription. Three hundred twenty patients (75%) reported that insurance paid for all or part of it. Of these, 287 reported their co-pay amount: 172 (60%) had no co-pay. The remainder paid a

median of \$10 (interquartile range (IQR) \$7.47-\$20). Fifty-seven patients reported that insurance did not pay for the naloxone. Of these, 42 reported their out-of-pocket cost. For 7 patients (12%) there was no out-of-pocket cost. The remainder paid a median of \$60 (IQR \$33.64-\$95). There were many reasons why patients did not fill the prescription. Many patients already had it (n=55). Others didn't think it was needed (n=54) or reported it was too expensive (n=36). When naloxone was obtained, in 85% of instances, insurance paid for all or part of it. A multivariable analysis found that the following characteristics were more associated with filling a prescription: females were more likely than males (adjusted odds ratio (aOR) 1.76, 95% confidence interval (CI) 1.07-2.87), those who knew how to use naloxone (aOR 2.29 (95% CI 1.18-4.46), and those who had previously had naloxone used on themselves or used it on someone else (aOR 4.95 (94% CI 2.09-11.66)).

CONCLUSIONS: When prescribed naloxone, patients treated in a telehealth treatment program fill the prescription 72% of the time, and when it is filled, 8% use the naloxone, which we interpret as a high rate of use that justifies the practice. Education is needed to teach patients how to administer naloxone and inform those at risk of the benefits of having naloxone on-hand. Prescription benefit cost policy changes (either better insurance coverage, lower copays or lower over-the-counter cost) may assist those who did not fill the prescription because it was too expensive.

TITLE: Improving linkage to addiction treatment with extended-release naltrexone.

BACKGROUND: Patients admitted to an inpatient unit for medically managed alcohol withdrawal (“detox” unit) often fail to successfully link to post-discharge outpatient addiction treatment. While there have been studies looking at several ways to improve this linkage, to our knowledge, there are no published studies that have evaluated whether medication for alcohol use disorder (AUD, MAUD) improves post-discharge outcomes from a detox unit. We sought to evaluate whether continuation or initiation of MAUD is associated with improved rates of successful linkage to post-discharge outpatient addiction treatment by performing a retrospective review of patients admitted for management of alcohol withdrawal.

METHODS: This study took place in an American Society of Addiction Medicine (ASAM) level IV unit for medically managed withdrawal embedded in an academic community hospital in Boston, MA. The unit provides pharmacotherapy for the treatment of alcohol withdrawal and AUD and robust social work support for aftercare planning. All patients receive counseling on all MAUD options and have the option of continuing or initiating MAUD during their hospitalization. This primarily includes the FDA-approved medications: extended-release (XR) naltrexone, oral naltrexone, acamprosate, and disulfiram. Patients requesting XR-naltrexone receive the injection prior to discharge. Patients receiving non-injectable medications receive an outpatient prescription at the time of discharge.

We performed a retrospective electronic chart review of all patients admitted for alcohol withdrawal during the time of September 2021 to November 2022. We defined successful linkage to care as confirmation in our electronic health record of attendance at the planned post-discharge visit within 30-days of discharge.

Analyses were conducted using STATA and descriptive statistics were used to summarize the results. Chi-square or t-test for categorical and continuous variables were used to compare those with and without confirmed linkage to care, and logistic regression was used to conduct adjusted analyses.

RESULTS: Three-hundred and twenty-five unique patient encounters were extracted. A total of 312 encounters remained after thirteen patients were excluded due to having an admitting diagnosis other than alcohol withdrawal. Of the remaining encounters, 76% were White, 15.4% were Black and approximately 8% were categorized as other. The majority of patients were male (71%) and the average age was 51 years. Co-occurring psychiatric conditions were present in most of the patients including depression (55%) and anxiety (49%). The most prevalent co-occurring substance use disorder was tobacco (49%) followed by opioids (19%).

Linkage to care was confirmed in fifty-three patients (17%). Compared to those patients without linkage to care, the patients were noted to drink less (16% vs. 21%, $p=0.0081$), were less likely to have a history of alcohol withdrawal seizures (26% vs. 41%, $p=0.049$), and more likely to have stable housing (84% vs. 74%, $p=0.043$). Otherwise, no significant differences were noted in demographic or clinical variables examined.

MAUD was continued or initiated on 127 patients (41%): gabapentin (27%), PO-naltrexone (18%), acamprosate (17%), XR-naltrexone (14%), topiramate (2%), and disulfiram (2%). XR-naltrexone was the only medication associated with a significantly greater likelihood of successful linkage to formal addiction treatment (28% compared to 11%, $p=0.001$). A logistic regression model was used with age, home status, drinking amount, patient-directed discharges, and receipt of XR-naltrexone entered as covariates. Significant predictors of linkage to care were determined to be those receiving XR-naltrexone prior to discharge (aOR 2.7, 95% CI 1.3-5.6, $p=0.009$) and drinks per drinking day (aOR 0.96, 95% CI 0.92-0.99, $p=0.016$).

CONCLUSIONS: Forty-one percent of patients admitted to the ASAM level IV unit for medically managed alcohol withdrawal were either continued or initiated onto medication for alcohol use disorder. Only XR-naltrexone was associated with improved linkage to post-discharge addiction treatment (aOR 2.7, 95% CI 1.3-5.6, $p=0.009$). XR-naltrexone requires a once-monthly injection which inherently improves adherence and confirmation of adherence compared to oral MAUD formulations. The results of this study suggest that XR-naltrexone may increase the chances that patients discharged from a unit for medically managed withdrawal adhere to follow-up outpatient addiction treatment.

Multiple recent emergency department-based studies have shown similar promising results supporting an association between the administration of XR-naltrexone and higher rates of community-based linkage to care¹⁻³. There is an NIH-funded trial (NCT02478489) awaiting publication that is evaluating post-hospital outcomes of patients with alcohol use disorder who received XR-naltrexone compared to those who were prescribed PO-naltrexone that may provide additional insights on the impact of naltrexone prescribed in the inpatient setting. Overall, more research is needed examining the potential role of MAUD in improving AUD-related outcomes after inpatient withdrawal treatment