

## ■ ORIGINAL CLINICAL RESEARCH REPORT

# Assessment of a Naloxone Coprescribing Alert for Patients at Risk of Opioid Overdose: A Quality Improvement Project

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**BACKGROUND:** Patients taking high doses of opioids, or taking opioids in combination with other central nervous system depressants, are at increased risk of opioid overdose. Coprescribing the opioid-reversal agent naloxone is an essential safety measure, recommended by the surgeon general, but the rate of naloxone coprescribing is low. Therefore, we set out to determine whether a targeted clinical decision support alert could increase the rate of naloxone coprescribing.

**METHODS:** We conducted a before-after study from January 2019 to April 2021 at a large academic health system in the Southeast. We developed a targeted point of care decision support notification in the electronic health record to suggest ordering naloxone for patients who have a high risk of opioid overdose based on a high morphine equivalent daily dose (MEDD)  $\geq 90$  mg, concomitant benzodiazepine prescription, or a history of opioid use disorder or opioid overdose. We measured the rate of outpatient naloxone prescribing as our primary measure. A multivariable logistic regression model with robust variance to adjust for prescriptions within the same prescriber was implemented to estimate the association between alerts and naloxone coprescribing.

**RESULTS:** The baseline naloxone coprescribing rate in 2019 was 0.28 (95% confidence interval [CI], 0.24–0.31) naloxone prescriptions per 100 opioid prescriptions. After alert implementation, the naloxone coprescribing rate increased to 4.51 (95% CI, 4.33–4.68) naloxone prescriptions per 100 opioid prescriptions ( $P < .001$ ). The adjusted odds of naloxone coprescribing after alert implementation were approximately 28 times those during the baseline period (95% CI, 15–52).

**CONCLUSIONS:** A targeted decision support alert for patients at risk for opioid overdose significantly increased the rate of naloxone coprescribing and was relatively easy to build. (Anesth Analg 2022;135:26–34)

## KEY POINTS

- **Question:** Does identifying patients at risk for opioid overdose using an alert in the electronic health record increase naloxone prescribing?
- **Findings:** Compared to baseline, naloxone coprescribing rates increased from 0.28 (95% confidence interval [CI], 0.24–0.31) to 4.51 (95% CI, 4.33–4.68) naloxone prescriptions per 100 opioid prescriptions after alert implementation, increasing the odds of naloxone coprescribing by approximately 28 times those during the baseline period (95% CI, 15–52).
- **Meaning:** A targeted decision support alert for patients at risk for opioid overdose significantly increased the rate of naloxone coprescribing and was relatively easy to build.

## GLOSSARY

**CDC** = Centers for Disease Control and Prevention; **CDS** = clinical decision support; **CI** = confidence interval; **COVID-19** = coronavirus disease 2019; **EHR** = electronic health record; **IRB** = institutional review board; **MEDD** = morphine equivalent daily dose; **OB/GYN** = obstetrics and

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gynecology; **OR** = odds ratio; **OD** = opioid use disorder; **PM&R** = physical medicine and rehabilitation; **VUMC** = Vanderbilt University Medical Center

Each day, 116 people die from opioid overdose in the United States.<sup>1</sup> These deaths are attributed to prescription opioids (ie, oxycodone, hydrocodone, morphine, tramadol, etc), illicit opioids (ie, heroin, illicitly manufactured fentanyl, and analogs), and frequently a combination of both.<sup>2,3</sup> Public health interventions, including changes in state laws and provider education, have contributed to a dramatic reduction in opioid prescriptions, but this reduction has been inconsistent and may not translate to a reduction in overdoses. For example, in 2012, 81.3 opioid prescriptions were dispensed per 100 people in the United States,<sup>4</sup> which decreased significantly to 58.7 opioid prescriptions per 100 people in 2017. However, in Tennessee, there were 107.5 opioid prescriptions dispensed per 100 people in 2016.<sup>5</sup> Despite the overall reduction of opioid prescriptions nationwide, mortality due to prescription opioids has increased by 15% between 2012 and 2018 and doubled when including nonprescription opioids.<sup>1</sup> As such, these opioid overdoses represent a critical public health intervention opportunity.

Naloxone is a competitive opioid antagonist that quickly reverses respiratory depression and sedative effects of opioids. Expanded availability and use of naloxone through community programs and emergency medical services have prevented numerous opioid overdose deaths.<sup>6,7</sup> The Centers for Disease Control and Prevention (CDC) and the US Office of the Surgeon General recommend further increasing availability of naloxone by coprescribing it to patients at risk for opioid overdose.<sup>8</sup>

Several emergency departments have implemented clinical decision support (CDS) tools to identify and alert prescribers of patients at risk of opioid overdose. These tools have demonstrated immediate and impactful changes in naloxone coprescribing, such as a doubling of the number of naloxone prescriptions.<sup>9–14</sup> Features of more successful system changes include alerts that are highly targeted to only display for patients at high risk of overdose, displaying information about the patient, and why the alert was being shown, and are shown as an opportunity for the prescriber to place a naloxone order. Less is known about the effectiveness of these alerts outside of the emergency department.

Following these recommendations to offer naloxone to patients at risk for overdose<sup>8</sup> and based on previous CDS studies, we developed a targeted electronic health record (EHR) alert to increase naloxone coprescribing in these at-risk patients. We hypothesized that by identifying at-risk patients and

notifying the prescriber we would increase the number of naloxone prescriptions (measured per 100 opioid orders), which then could be used in the event of an overdose.

## METHODS

Vanderbilt University Medical Center (VUMC) is a large integrated health system in Nashville, Tennessee, with almost 2 million ambulatory visits per year. VUMC uses Epic (Epic Systems) as its inpatient and outpatient EHR. To increase coprescribing of naloxone, we developed an alert in the EHR, which notifies prescribers when a patient has a high risk of opioid overdose based on a high morphine equivalent daily dose (MEDD)  $\geq 90$  mg, concomitant benzodiazepine prescription, or a history of opioid use disorder or opioid overdose. These risk factors were based on CDC and surgeon general recommendations.<sup>8</sup> The alert displays at the time an opioid or benzodiazepine prescription is signed, gives relevant information to the prescriber (including MEDDs, the reason the alert fired, and problem list risk factors), and allows the prescriber to easily prescribe naloxone nasal spray or autoinjector (Figure 1). The alert continues to appear for future opioid or benzodiazepine prescriptions until naloxone is prescribed or added to the patient's home medication list. Additionally, we added a mechanism for users to submit feedback related to the alert, which then provided additional patient context. Development of the new alert started in October 2019, after which our opioid stewardship group started presenting at meetings around the medical center about the importance of prescribing naloxone. The new naloxone coprescribing alert was implemented in January 2020 across the entire system, with communication emails, announcements, and training materials provided for prescribers.

## Study of the Intervention

To evaluate the CDS alert, we extracted data for outpatient and discharge naloxone and opioid prescriptions from our enterprise clinical data warehouse for 12 months before and 15 months after the alert was implemented (January 2019–April 2021). Our primary outcome was the institutional-level naloxone prescribing rate for the entire period measured preimplementation (January 2019–January 2020) compared to the rate for the entire period postalert implementation (January 2020–April 2021), aggregated by week. To account for increases in clinic volume and population growth over time, the calculated rates were normalized by the number of naloxone prescriptions per 100

opioid prescriptions before analysis, aggregated by week. Secondary outcomes measured included differences in the patient and prescriber populations pre-implementation and postimplementation, as well as a regression model to identify important coefficients that could influence naloxone prescribing, the percentage of at-risk patients with a naloxone prescription over time, and naloxone pharmacy fill rates based on pharmaceutical claims data added to the EHR on subsequent encounters (Medication History, Surescripts). Medication history data are requested at each patient encounter for those with pharmacy benefits listed in the EHR; therefore, only patients with pharmacy insurance benefits listed in the EHR and a subsequent encounter after they were prescribed naloxone were included in this pharmacy fill rate subgroup analysis. The secondary outcomes were measured on a per-patient basis.

### Statistical Analysis

We used descriptive statistics to describe the primary and secondary outcomes and identify potential confounders to be adjusted for in our model. Patient demographics, such as age, race, sex, and ethnicity, as well as opioid overdose risk factors, were compared using the Pearson's  $\chi^2$  test prealert and postalert implementation. To assess the association of alert implementation with the odds of naloxone coprescribing, we used a logistic regression model. We controlled for the patient demographics and opioid overdose risk factors considered in our descriptive statistics. We also included patient insurance type (none, public, private, or both), whether the patient had ever had an oncology visit, provider type, and specialty, and indicators for 3 key time periods: if an observation occurred after the start of education about the importance of naloxone prescribing

**Important (1)** ^

**!** This patient is **at risk for unintentional opioid overdose** and a naloxone prescription is recommended feedback: 😊 😐 😞

**oxycodone-acetaminophen (PERCOCET) tablet 2.5-325 mg**

- MEDD  $\geq$  90 AND there is an unsigned order for an opioid and/or benzodiazepine.
- There is an unsigned order for an opioid and/or benzodiazepine, AND the patient has opioid use disorder or a history of opioid overdose.

**Risk factors from the Problem List:**  
- History of Opioid Use Disorder

Signing this order will affect the patient's Morphine Equivalent Daily Dose (MEDD) for outpatient orders. Review the information below to ensure opioid dosing will remain within appropriate limits.

**Cumulative MEDD (89 mg max recommended)**

AFTER signing: **112.5 mg !**                      Before signing: **90 mg !**

<b>UNSIGNED OUTPATIENT OPIOIDS</b>	<b>MEDD</b>
<p><b>oxycODONE-acetaminophen (PERCOCET) 2.5-325 mg per tablet</b></p> <p>Take 1 tablet by mouth every 4 hours as needed for moderate pain for up to 3 days. Normal, Disp-12 tablet,R-0 Maximum MEDD: 22.5 mg MEDD for this order</p>	22.5 mg
<p><b>OTHER ACTIVE OUTPATIENT OPIOIDS</b></p> <p><b>oxycODONE (OxyCONTIN) 30 mg 12 hr tablet</b></p> <p>Take 1 tablet (30 mg total) by mouth every 12 hours for 7 days., Starting Tue 4/21/2020, Until Tue 4/28/2020, Print</p>	<b>90 mg !</b> (89 mg max recommended)

[What's a MEDD?](#)

<input type="checkbox"/> Order	<input type="checkbox"/> Do Not Order	<input type="checkbox"/> naloxone (NARCAN) 4 mg/actuation nasal spray
<input type="checkbox"/> Order	<input type="checkbox"/> Do Not Order	<input type="checkbox"/> naloxone (EVZIO) 2 mg/0.4 mL auto-injector

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**Figure 1.** Naloxone coprescribing alert. MEDD indicates morphine equivalent daily dose.

(October 27, 2019), after implementation of the alert (January 19, 2020), and during a time when prescribing volume and patient encounters were fluctuating due to the coronavirus disease 2019 (COVID-19) pandemic (March 1, 2020–June 30, 2020). Finally, time in months since the earliest observation included (January 6, 2019) was included to account for the possibility of a linear time trend in addition to potential associations with the discrete time periods previously defined. Interactions between time and the indicators for occurring after the start of education and after alert implementation were considered, to allow for the possibility that the association with time differs between periods; if the *P* value of either interaction term was >.2, we removed it to yield a more parsimonious model with a simple interpretation. The resultant model after *P* value screening was considered as the primary model and was used to estimate the adjusted association between alerts and the odds of naloxone coprescribing. In addition, a

secondary model with interactions between the time period indicators and covariates in the model was also considered to assess if the association between the alert and the odds of naloxone coprescribing differed for specific levels of considered covariates (patient sex, race, ethnicity, opioid overdose risk factors, insurance type, and oncology visit history, and provider type and specialty), with the same *P* value threshold of .2. To account for potential clustering by prescriber in both models, the logistic regression models were fit with a working independence covariance matrix followed by the Huber-White method to obtain robust standard error estimates.<sup>15</sup> We report odds ratios (ORs) and 95% confidence intervals [CIs] constructed using Wald statistics. This model was fit using R 4.0.5 and the package rms version 6.0-1.<sup>16,17</sup>

This study was reviewed and approved by the VUMC institutional review board (IRB), and the requirement for written informed consent was waived.

**Table 1. Patient Demographics Prealert and Postalert Implementation**

Patient demographics	Patients prealert implementation, n (%)	Patients postalert implementation, n (%)	<i>P</i> value <sup>a</sup>
No.	20,334	22,772	
Age (y)			
<18	584 (2.9)	440 (1.9)	<.001
18–34	2827 (13.9)	3342 (14.7)	
35–64	11,192 (55.0)	12,579 (55.2)	
≥65	5731 (28.2)	6411 (28.2)	
Sex			
Female	10,695 (52.6)	12,116 (53.2)	.206
Male	9639 (47.4)	10,656 (46.8)	
Race			
White	17,157 (84.4)	18,836 (82.7)	<.001
Black	2239 (11.0)	2576 (11.3)	
Other	444 (2.2)	673 (3.0)	
Unknown	494 (2.4)	687 (3.0)	
Ethnicity			
Not Hispanic	19,300 (94.9)	21,353 (93.8)	.484
Hispanic	442 (2.2)	512 (2.2)	
Insurance			
None	1421 (7.0)	1678 (7.4)	.003
Public	11,200 (55.1)	12,175 (53.5)	
Private	7301 (35.9)	8391 (36.8)	
Both	412 (2.0)	528 (2.3)	
Highest MEDD			
<90	5592 (27.5)	6174 (27.1)	<.001
90–119	6044 (29.7)	6566 (28.8)	
120–239	5182 (25.5)	5474 (24.0)	
≥240	3516 (17.3)	4558 (20.0)	
Oncology visits			
Never had an oncology visit	12,119 (59.6)	14,287 (62.7)	<.001
Ever had an oncology visit	8215 (40.4)	8485 (37.3)	
Risk criteria			
MEDD ≥90	14,743 (72.5)	16,598 (72.9)	.372
OUD and opioid or benzodiazepine ordered	809 (4.0)	1220 (5.4)	<.001
Opioid and benzodiazepine ordered together	2046 (10.1)	2079 (9.1)	.001
Active benzodiazepine and history of opioid overdose or opioid ordered	7277 (35.8)	7942 (34.9)	.048
Active opioid and benzodiazepine ordered	3860 (19.0)	3938 (17.3)	<.001

Abbreviations: MEDD, morphine equivalent daily dose; OUD, opioid use disorder.

<sup>a</sup>*P* values using Pearson's  $\chi^2$  test comparing prealert and postalert implementation.

## RESULTS

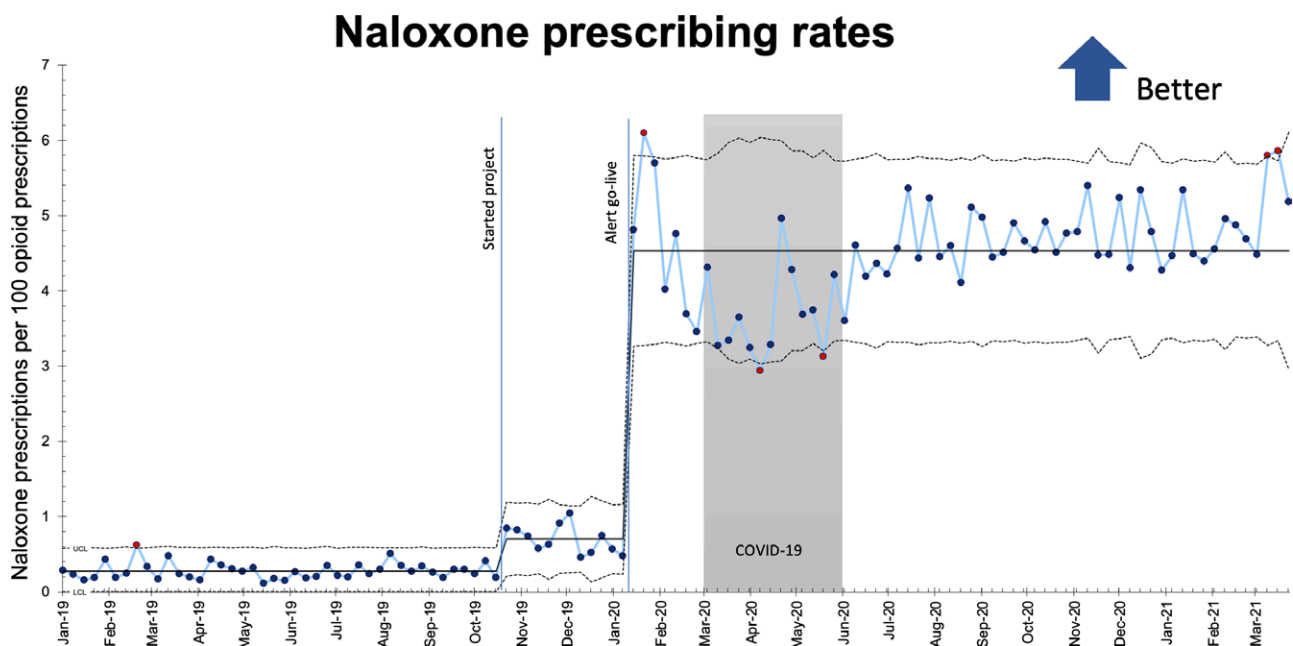
Table 1 shows the patient demographics before and after the alert implementation. There were 20,334 patients considered at risk for opioid overdose in the preimplementation phase and 22,772 patients in the postimplementation phase. The baseline average rate for naloxone prescribing from January to October 2019 was 0.28 (95% CI, 0.24–0.31) naloxone prescriptions per 100 opioid prescriptions. The educational push in October 2019 was associated with a small, but significant, centerline shift in the naloxone prescribing rates (mainly among the interventional pain specialists) increasing to 0.70 (95% CI, 0.58–0.81) naloxone prescription per 100 opioid prescriptions. After implementation of the alert (January 2020), there was an increase in the naloxone prescribing rates to 4.51 (95% CI, 4.33–4.68) naloxone prescription per 100 opioids in the postimplementation phase. A plot of naloxone prescriptions per 100 opioid prescriptions over our study time (Figure 2) showed that the baseline rate of naloxone prescribing from January to October 2019 remained stable, with a small increase in late October (corresponding with the educational efforts with interventional pain specialists). After alert implementation, prescriptions for naloxone increased substantially; they fell during the start of the COVID-19 pandemic but have since somewhat stabilized and are continuing to increase.

In the primary model, neither of the considered time by time period interaction terms in our logistic regression of naloxone coprescribing met the *P* value threshold of .2, suggesting that the slopes in these periods do not differ from the baseline. Thus, our

final model excluded these interaction terms for parsimony. The increase in naloxone prescriptions after alert implementation was statistically significant after controlling for the variables described previously. As shown in Table 2, comparing to baseline, educational efforts from interventional pain specialists increased the odds of naloxone coprescribing by 2.25 (95% CI, 1.5–3.4), and the implementation of the alert system increased the odds by an additional multiplicative factor of 12.25 (95% CI, 7.2–20.9) over educational efforts alone. Overall, after educational efforts and the implementation of the alert system, the odds of naloxone coprescribing were 28 times higher than the baseline period (95% CI, 15–52). We also found that fluctuations due to the COVID-19 pandemic reduced the odds of naloxone coprescribing by a factor of 0.80 (95% CI, 0.67–0.95) while the alert system was in place. There was no significant trending by time in months (OR, 1.0; 95% CI, 0.99–1.05).

We found that patients were more likely to be prescribed naloxone overall if they were without insurance (OR, 1.8; 95% CI, 1.3–2.5) and less likely with increasing age in years (OR, 0.98; 95% CI, 0.98–0.99). Patients who had an MEDD  $\geq 90$  were more likely to be prescribed naloxone (OR, 1.3; 95% CI, 1.1–1.5), as were those who had never had an oncology visit (OR, 0.88; 95% CI, 0.78–0.99).

In our secondary model, none of the interactions between covariates and the posteducation period indicator were significant at the *P* value threshold of .2. However, interactions between the postalert period indicator and sex, race group, Hispanic status, provider type, department, and several variables



**Figure 2.** Naloxone prescribing rates across the study period. COVID-19 indicates coronavirus disease 2019.

**Table 2. Odds Ratios and 95% CIs From Our Main Model of the Association Between Temporal Exposures of Interest and the Odds of Naloxone Coprescribing Using Logistic Regression, Adjusted for Covariates of Interest and With Huber-White Adjusted Robust Standard Errors**

Covariates of interest	Odds ratio (95% CI)	P value <sup>a</sup>
Posteducation efforts	2.25 (1.49–3.41)	<.001
Postalert implementation	12.25 (7.20–20.85)	<.001
During COVID-19 fluctuations	0.80 (0.67–0.95)	.01
Time (in months since earliest observation)	1.02 (0.99–1.05)	.13

In our model, “posteducation efforts” refer to all observations after October 27, 2019, “postalert implementation” refers to all observations after January 19, 2020, and “during COVID-19 fluctuations” refer to observations between March 1, 2020, and June 30, 2020. Out of 115,343 observations, 48,256 occurred before education efforts, 14,311 occurred posteducation efforts and prealert implementation, and 52,776 occurred postalert implementation. Of the 52,776 occurring postalert implementation, 14,594 were during COVID-19 fluctuations. Our outcome of interest was whether naloxone was coprescribed when an opioid was prescribed. The odds ratio for posteducation efforts compares to the baseline period before education efforts (January 6, 2019, the start of the study, to October 26, 2019), while the postalert implementation odds ratio compares to time period before alert implementation (January 6, 2019, to January 18, 2020). The odds ratio for COVID-19 fluctuations compares to all observed times outside of the March 1, 2020, to June 30, 2020, window. Additional covariates considered are related to patient demographics and medical history, as well as provider type and department. For a full summary of these additional variables and their effects, see Supplemental Digital Content 1, Table 1, <http://links.lww.com/AA/D896>. Note that the considered interactions between time and the specified time periods have been omitted from this table, as these terms did not meet our *P* value threshold and were thus excluded from the final model. This table contains the results of our primary model without interaction terms, and thus, the odds ratios represent the average across all groups. Our secondary model that included interactions with a *P* value below a threshold of .2 is detailed in Supplemental Digital Content 1, Table 1, <http://links.lww.com/AA/D896>.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019.

<sup>a</sup>*P* values using the Wald test.

pertaining to opioid and benzodiazepine prescriptions were significant with overall *P* values <.2 and were included in the final secondary model (fully detailed in Supplemental Digital Content 1, Table 1, <http://links.lww.com/AA/D896>). Before alert implementation, having opioid use disorder and having an opioid or benzodiazepine ordered increased the odds of being prescribed naloxone (OR, 1.9; 95% CI, 1.2–3.1), as did having an opioid and benzodiazepine ordered together (OR, 5.4; 95% CI, 1.1–26.8). After alert implementation, having an active benzodiazepine prescription and an active opioid prescription or history of opioid overdose increased the odds of being prescribed naloxone (OR, 2.5; 95% CI, 2.2–2.9).

Prealert implementation, compared to attending physicians, nurse practitioners and physician assistants were less likely to prescribe naloxone (OR, 0.09; 95% CI, 0.03–0.23). After alert implementation, fellows (OR, 1.6; 95% CI, 1.04–2.6) and resident physicians (OR, 1.8; 95% CI, 1.3–2.5) were more likely to prescribe naloxone. Before alert implementation, compared to internal medicine, infectious disease (OR, 7.4; 95% CI, 2.6–20.9) and interventional pain (OR, 9.8; 95% CI, 4.6–21.0) were most likely to prescribe naloxone. After alert implementation, neurosurgery (OR, 6.2; 95% CI, 3.3–11.7) and interventional pain (OR, 4.6; 95% CI, 2.8–7.6) were most likely to prescribe naloxone. Odds ratios and 95% CIs for all specialties as well as all considered covariates and included interactions can be found in Supplemental Digital Content 1, Table 1, <http://links.lww.com/AA/D896>.

Figure 3 shows the proportion of patients considered high risk for overdose that has naloxone prescribed or on their medication list and those that do not. The baseline average in 2019 of 3.7% (95% CI, 3.6–3.9) of at-risk patients with naloxone increased to 17.3% (95% CI, 16.8–17.3; *P* < .001) in the first quarter of 2021 and continues to grow.

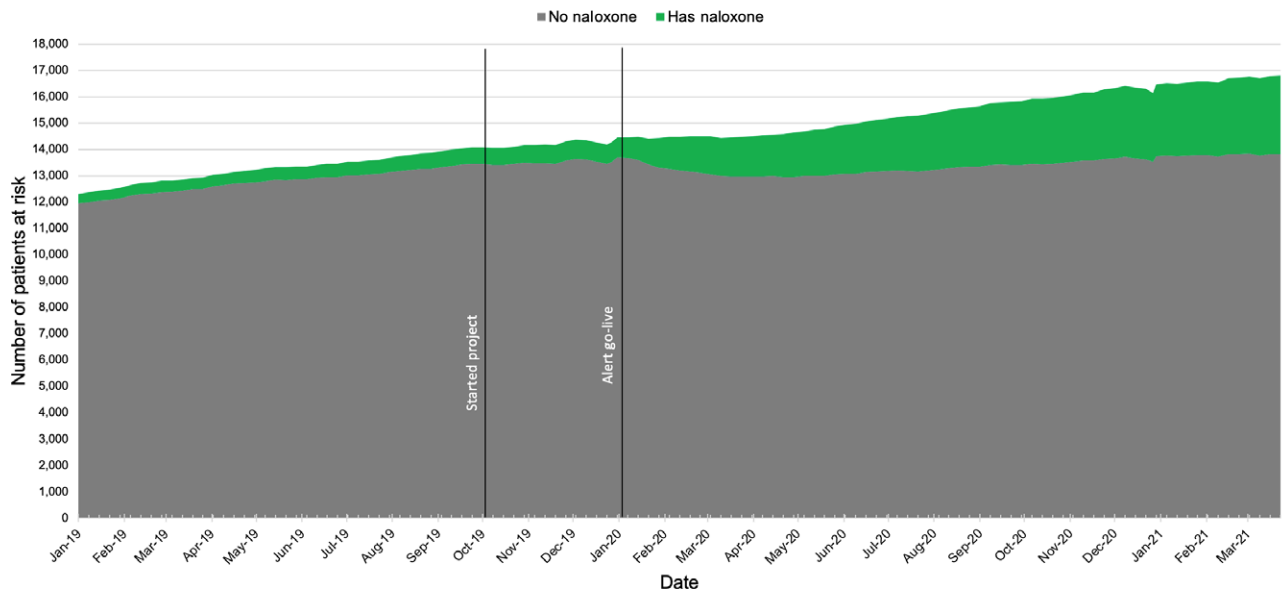
Finally, we looked to see how often the naloxone prescriptions were dispensed at a pharmacy based on external medication history data. The fill history data before the alert implementation were rather sparse given the low number of naloxone prescriptions; however, postimplementation, we had evidence that on average 65.0% (95% CI, 62.7–66.5) of naloxone prescriptions were filled at a pharmacy. On further analysis, and limited follow-up time, about 6% of patients refilled their naloxone.

## DISCUSSION

In this study, we found that an automatic naloxone alert for prescribers managing patients at high risk for opioid overdose resulted in a significant change in the prescription behavior and led to an increase in naloxone coprescribing rates. Our study showed that patients were more likely to be prescribed naloxone if they were young adults, without insurance, or had a high MEDD. From the perspective of the prescriber, resident physicians and fellows, as well as prescribers in the neurosurgery and interventional pain specialties were most likely to prescribe naloxone. Additionally, we found that most patients actually filled their naloxone prescription.

Some potential reasons why younger patients without insurance were more likely to be prescribed naloxone include: (1) at our institution, and others, younger individuals are overrepresented in our addiction consult service, and among those receiving buprenorphine-naloxone treatment.<sup>18,19</sup> Given that we practice in a state that did not expand Medicaid, this age group is also less likely to have insurance. Additionally, job loss from the COVID-19 pandemic has disproportionately impacted young adults (18–29 years of age) and lower-income adults,<sup>20</sup> which may have worsened the insurance coverage situation. (2) When the alert displays for older patients related to

## Patients at risk for opioid overdose with and without naloxone



**Figure 3.** Patients at risk for overdose with and without naloxone.

MEDD or concurrent use of benzodiazepines rather than other risk factors, providers may be less willing to generate potential conflict or concern by proposing naloxone to the patient, whereas with younger patients with opioid use disorder or buprenorphine products, providers may be more apt to prescribe naloxone. (3) Finally, and perhaps least likely, but also of interest, young people (<25 years of age) are at higher risk of doing poorly in outpatient buprenorphine treatment. Prescribers may either consciously or subconsciously realize this vulnerability to the extent that it may interact with reasons 1 and 2 above, so they prescribe naloxone to these younger patients since they have less confidence that the patient will stay in recovery, and they want to provide them with a rescue option.<sup>21,22</sup>

The naloxone coprescribing rates that we saw in our study were higher than those reported elsewhere in the literature. Our study found that 25.4% of patients considered high risk for overdose in the emergency department received a naloxone prescription after the alert was first introduced into clinical care, which then stabilized to 24.2%. Other studies using similar alerts in the emergency department saw that an initial 14% to 21.7% of high-risk patients receive a naloxone prescription postalert implementation.<sup>11-14</sup> Another study that looked at departments across the medical center (outside of the emergency department) saw similar results to ours with 13.5% of high-risk patients receiving naloxone postalert implementation.<sup>9</sup> In our study, study saw a 16-fold increase in naloxone coprescribing, going from a baseline rate of 0.28 naloxone prescriptions per 100 opioid prescriptions to 4.51 naloxone prescriptions

per 100 opioid prescriptions, which has been maintained for more than a year and continues to increase. Some potential positive contributors to the success of the alert may include:

1. The alert is highly targeted and only displays for patients at high risk of overdose.
2. The alert allows prescribers to quickly survey the situation by providing detailed information from the patient chart, including MEDD calculations, details on why the alert triggered, and links to external references.
3. The alert is actionable with a default action to prescribe naloxone, consistent with the surgeon general's recommendation.

The patient demographics for naloxone prescriber were similar to those shown in other studies.<sup>23,24</sup> In some departments, such as oncology, there were very few patients who had an order for naloxone before this alert; however, after the alert implementation, there were many more patients with access to this life-saving medication, even though the overall acceptance of the alert was relatively low. The dramatic increase in naloxone prescriptions for patients <18 years of age is also impactful in an important and often under-recognized patient age group who are at risk for both unintentional respiratory depression, as well as developing opioid use disorder. One provider from rheumatology informed us that he uses the detailed display of the alert to show patients their total MEDD and risk factors to encourage them to reduce their use of opioids and reduce their risk of overdose. This was an unintended benefit of the detailed design of the

alert. Over the course of the study period, there was a general trend of decreasing the amount of morphine milligram equivalence per prescription; while statistically significant, we could not attribute that directly to this alert. MEDDs remained the same prealert and postalert. Additionally, provider feedback allowed us to increase the specificity of the alert, such as preventing it from displaying in scenarios in which 1-time benzodiazepines were prescribed for procedures.

Although we had limited data on naloxone prescription fill rates at pharmacies, we had evidence that more than half of patients who received a naloxone prescription filled it. This is lower than the average 70% to 80% fill rate for medications in general,<sup>25,26</sup> but higher than what other studies have seen for naloxone, with fill rates between 23% and 33%.<sup>27–29</sup> Additionally, we have received anecdotal reports from prescribers where their patients have used the naloxone prescribed during an overdose. One patient revived her boyfriend from an overdose, another patient's mother revived him from a fentanyl overdose, and other patients asked for refills because they had used their naloxone on others in their communities or households. Although the alert is designed to identify those at risk for an overdose, there has also been a life-saving benefit to others around them.

Overall, while the alert increased the prescribing rate of naloxone, there is still a need to provide naloxone to additional at-risk patients. As such, coprescribing or offering to coprescribe naloxone is now required by statute or regulation in at least 8 states. For example, Vermont requires naloxone coprescribing for patients with an MEDD  $\geq 90$  mg and saw a naloxone coprescribing rate increase from 0.2 to 3.2 naloxone prescriptions per 100 opioid prescriptions among Medicare Part D patients.<sup>30</sup> Overall, states that have enacted these legal mandates have seen increased naloxone coprescribing rates (incidence-rate ratio, 7.8 [95% CI, 1.2–49.4;  $P = .03$ ]).<sup>31</sup> We anticipate that this trend will continue to grow across states. Additionally, the Food and Drug Administration is requiring that opioids and medications used to treat opioid use disorder be updated to include information about coprescribing naloxone.<sup>32</sup>

### Limitations

This study is limited in that we do not have dispense data on all prescriptions, only those with pharmacy insurance and a subsequent encounter in our system. We did not capture data if the patient paid for their naloxone prescription without using their pharmacy benefits insurance. Unfortunately, we were unable to determine if this project has had an impact on overdose death rates in our patient population due to the lack of access to state data; however, we have evidence that multiple prescriptions have been used to reverse

an overdose and have been refilled. Additionally, the cost of naloxone prescriptions and the availability of naloxone at that pharmacy could be a barrier for many patients.<sup>33</sup> According to GoodRx, the cash price for generic naloxone is about \$30 per dose, the Narcan kit is about \$130 and has 2 doses, while the price for Evzio can range from \$200 to \$500+ (retail price of \$5460) for 2 doses. However, another study found that 94% of patients with pharmacy insurance had a \$0 deductible for their naloxone prescriptions.<sup>34</sup> Looking at data from our own pharmacies, 62% of naloxone prescriptions had no copay, and 77% were paying \$10 or less for naloxone. There were still 5% of prescriptions that were filled and paid at full price. Additionally, many pharmacies have price reduction or patient assistance programs for those in need. As a prepost implementation study, there is the potential for confounding since the time periods are completely separated in time. Finally, our postimplementation follow-up data included the start of the COVID-19 pandemic in the United States, which may be the cause of the u-shaped graph postimplementation and later increases in alert acceptance and naloxone coprescribing rates.

### CONCLUSIONS

At our institution, an alert suggesting a naloxone prescription for patients at risk for overdose resulted in a significant change in the prescription behavior and led to an increase in naloxone coprescribing rates. We recommend that other organizations implement similar decision support notifications. ■

### DISCLOSURES

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