

ORIGINAL RESEARCH

Toxicology

Evaluation of an emergency department-based approach to reduce subsequent opioid overdoses

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Abstract

Objective: The purpose of this study was to determine the association of a multi-pronged treatment program in emergency department (ED) patients with an acute presentation of opioid use disorder (OUD) on the rate of subsequent opioid overdose (OD). This approach included ED-initiated take-home naloxone, prescription buprenorphine, and an ED-based peer support and recovery program.

Methods: This was a retrospective observational analysis of adult patients presenting to the ED at a large urban hospital system from November 1, 2017 to March 17, 2023. Patients with an ED discharge diagnosis of OD or OUD were included. Outcomes determined were subsequent 90-day OD and 180-day OD death. Post hoc analyses were performed to identify intervention utilization throughout the study period including the COVID-19 pandemic as well as ED characteristics associated with subsequent OD and OD death. Statistical comparisons were made using logistic regression and chi-squared test.

Results: A total of 2634 patients presented to the ED with an opioid OD or diagnosis of OUD. Subsequent 90-day OD decreased significantly over time (11.5%–2.3%, odds ratio [OR] 0.85, confidence interval [CI] 0.82–0.89). No single intervention was independently associated with 90-day OD or 180-day OD death. Resource utilization was stable during the COVID-19 pandemic and increased afterward. A higher buprenorphine fill-rate among all patients and the Black race subgroup was associated with a decrease in 90-day OD.

Conclusions: Subsequent OD and OD death decreased over time after implementation of a multi-pronged treatment program to ED patients with OUD. No single intervention was associated with a decrease of subsequent OD or OD death.

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1 | BACKGROUND

Opioid overdose (OD) fatalities have steadily increased in the United States over the last two decades.¹ The emergency department (ED) is commonly the primary point of entry into the health care system for patients with nonmedical opioid use and is increasingly utilized for repeat care for opioid-related complaints.²

A recent study found that patients with substance-related ED encounters experienced mortality at a rate six times greater than the general ED population.⁴ Others have reported mortality rates ranging from 2% to 5.5% in the year following discharge from the ED after nonfatal OD.^{5,6} These factors suggest that early intervention in the ED is critical to reducing mortality.^{7,8} Effective ED interventions include medication for opioid use disorder with buprenorphine, take-home naloxone, counseling, and referral to treatment before discharge.⁶ ED-buprenorphine has been shown to reduce self-reported opioid use and maintain engagement in treatment.⁹ Take-home naloxone is associated with reduction in fatal overdose rates in some communities.^{10,11} Behavioral interventions with either social work or peer supporters are also potentially effective strategies to increase engagement in treatment for ED patients at high risk for opioid overdose.

The landscape of the opioid crisis in the United States is ever evolving and strategies employed in the ED setting require evaluation over time. For example, during the COVID-19 pandemic, outpatient treatment resources were likely underutilized. However, in contrast to overall emergency visits, OUD visits declined only slightly and returned to baseline after May 2020.¹² The shift from prescription opioids to non-prescription opioid use has been associated with a change in demographics where white males were initially overrepresented, but by 2021, the population became more racially diverse.¹ This shift in the pattern of drug use and demographic of people who use drugs has been accompanied by an increase in utilization of EDs to treat nonfatal drug overdoses.^{3,15,16}

In November 2017, our hospital system implemented an ED-based multi-pronged intervention program for patients presenting to the ED with an acute presentation of OUD. The program included the following available interventions: (1) take-home intranasal naloxone, (2) ED-prescribed buprenorphine, and (3) availability of an ED-peer support and recovery program.

2 | GOALS OF THIS INVESTIGATION

This was an evaluation of a system-wide multi-pronged program for ED patients with an acute presentation of OUD. The aims of this study were to (1) determine the longitudinal association of the program on subsequent 90-day OD and 180-day OD deaths, (2) evaluate the utilization of each program intervention over time, and (3) determine which patients are at highest risk for subsequent OD and death and may benefit the most from intervention.

The Bottom Line

The emergency department (ED) is commonly the primary point of entry into the health care system for patients with opioid use disorder, and the ED has been on the forefront of developing innovative treatments to prevent opioid overdose. With the increase of these programs throughout the country, it is important to evaluate their utilization and effectiveness. This is a retrospective analysis of a system-wide ED program for patients with opioid use disorder to determine its utilization and effectiveness at prevention of subsequent overdose. After implementation, subsequent overdose and death decreased over time, with no single intervention alone improving outcomes. Overall utilization remained low but may be improved by identifying higher-risk patients upon arrival to the ED.

3 | METHODS

3.1 | Study design and setting

This retrospective observational study was performed in a major urban Midwestern hospital system with one large and with three satellite EDs (total visits 108,000/year). Eligible patients presenting to the ED with an acute OUD-related diagnosis were identified by the electronic health record (EHR). Patient demographics and ED interventions were identified retrospectively. The study was approved by the institutional review board, and a request for a waiver of informed consent was granted.

3.2 | Selection of participants

3.2.1 | Inclusion and exclusion

We identified a cohort of patients presenting to the ED with an acute OUD-related diagnosis. The ED discharge diagnosis of opioid OD or OUD (corresponding to ICD10 codes T40.1 × 1A, T40.1 × 2A, F11.10/11/21/23/99/988) was used to identify the cohort for inclusion and represented a patient group in which there was opportunity for ED intervention. Exclusion criteria were as follows: (1) under 18 years old, (2) patients with chronic opioid use presenting for an unrelated complaint, and (3) currently in treatment presenting with a treatment-related complaint. Patients who eloped from the ED after a high-risk presentation were not excluded as these patients had an opportunity for intervention.

3.2.2 | Index visit

During the study period (November 1, 2017 to March 17, 2023), index visits were identified as the earliest included visit based on ED arrival date and time.

3.2.3 | Subsequent visits

Each additional visit was identified as a subsequent visit and manually reviewed by the investigators for opioid OD. Mortality data was collected from (1) the date of death returned by the EHR or (2) the county medical examiner data.

3.3 | Interventions

The ED-based multi-pronged treatment program evaluated in this study includes three main interventions: (1) take-home naloxone, (2) ED-buprenorphine prescription, and (3) an ED-based peer support and recovery program (ED-PSRP). Between 2017 and 2019, take-home naloxone was personally furnished to patients at ED discharge in a kit that included two naloxone 2 mg doses. In 2019, two nasal naloxone 4 mg doses were added and the prefilled naloxone syringes which was necessary to reverse high-potency fentanyl which had become prevalent. ED-initiated buprenorphine was defined as a buprenorphine or buprenorphine/naloxone sublingual tablets or films prescribed at the ED visit.

3.4 | Outcomes and measurements

We identified a subsequent OD within a 90-day period following the index ED visit as the primary outcome with 180-day OD death as the secondary outcome. Outcomes were identified using (1) the identical search method for the subsequent ED visit at the home hospital system as described above for the index visit, (2) county medical examiner data for OD death, and (3) an EHR search of hospital systems that participate in CareEverywhere, a Health information exchange that provides data across hospital systems. Approximately two-thirds of health systems in our region participate in CareEverywhere, providing an opportunity to assess outcomes that occur outside of our health system for most enrolled patients. Using an Structured Query Language query, we identified external encounters of the identified study patients and searched for reason for visit and encounter diagnoses matching those used in our initial identification query.

3.4.1 | Utilization of ED interventions over time

As the timeframe of our cohort encompassed efforts for OUD treatment before, during, and after the COVID-19 pandemic, an analysis was performed to determine treatment utilization over time. In the initial phase of the pandemic, mitigation strategies, that is, suspension of many outpatient and other hospital resources and limiting

patient contact, were put in place. These were subsequently lifted, creating a post-mitigation period, still during the ongoing pandemic. Patients were analyzed according to the following groups: pre-COVID-19 (November 1, 2017 to March 16, 2020), COVID mitigation (March 17 2020 to April 30, 2020), post-mitigation (May 1 2020 to December 31, 2020), and post-COVID-19 (January 1, 2021 to March 17, 2023).

3.4.2 | ED patients with the highest risk of subsequent OD

Post hoc analysis was performed to identify a cohort of patients at highest risk for 90-day OD and OD death that would most benefit from ED interventions. All patient characteristics were identified in the EHR. Age, gender, race, ethnicity, and insurance status were determined. Area deprivation index (ADI) was used for measuring socioeconomic distress.¹⁷ The ADI compiles multiple factors of distress to census tract level: including socioeconomic factors, poverty level, education, single-parent households, and others. Past medical and family history, history of opioid or other substance use disorder, previous prescriptions and total amount of doses dispensed for opioids, benzodiazepines, total amount of buprenorphine dispensed per year (in doses), and previous ED visits for OD were determined (Supporting Information Appendix Table A1).

3.5 | Analysis

To determine the effect of each ED intervention on the 90-day OD and 180-day OD death, univariate regression analysis was first performed, followed by a multivariable regression analysis to identify adjusted independent variables associated with the outcomes. To determine differences in utilization of resources during the pandemic, comparisons were made between four temporal groups (pre-COVID-19, COVID-mitigation, post-mitigation, and post-COVID-19) on ED interventions. Finally, to develop methods used to identify patients at highest risk for 90-day overdose, variables readily available in the EHR upon arrival were compared between patients with a positive and negative outcome.

A sample size calculation was performed a priori to detect a 25% decrease in subsequent OD for a single intervention. Presuming a 2:1 ratio of control to intervention exposure, 2157 total patients would be needed to reject the null hypothesis with a power of 0.8 and a type 1 error rate of 0.05 by continuity-corrected chi-squared statistic. Statistical analysis was performed using IBM SPSS Statistics, version 28.

4 | RESULTS

4.1 | Characteristics of the study subjects

From November 1, 2017 to March 17, 2023, there were 2634 patients presenting to the ED who met inclusion criteria. Patient demographics, insurance, and interventions are shown in Table 1. The majority of the

TABLE 1 Patient characteristics.

Total N	2634
Age in years, median (25% and 75% quartile)	36 (29,45)
Female N (%)	970 (37)
Race N (%)	
White	2005 (76)
Black	359 (14)
Other	12 (0.5)
Unavailable	258 (9.8)
Ethnicity N (%)	
Hispanic	396 (15)
Non Hispanic	2189 (83)
Unavailable	49 (1.8)
Insurance status N (%)	
Medicaid	1818 (69)
Medicare	229 (9)
Commercial	149 (6)
Other	125 (5)
Self-pay	307 (12)
ED length of stay (min), median (25%, 75% quartile)	200 (127,330)
Interventions	
Take-home naloxone	524 (20)
Prescription buprenorphine	486 (18)
Transported to a facility	152 (6)

Abbreviation: ED, emergency department.

patients were male (63%), White (76%), non-Hispanic (83%), and most patients had Medicaid insurance (69%). The average ED length of stay was 277 ± 245 min. A total of 714 (27%) spoke with the ED-PSRP 524 (20%) received take-home naloxone, 486 (18%) received an ED prescription for buprenorphine, and 152 (6%) were transported directly to a treatment facility (Table 1).

4.2 | Main results

4.2.1 | Effect of ED-interventions on 90-day OD and 180-day OD death

There were 130 (4.9%) subsequent 90-day ODs during the study period. The 90-day OD rate decreased significantly over time (Figure 1, in 4-month intervals 11.5%–2.3%, odds ratio [OR] 0.85, confidence interval [CI] 0.82–0.89). The ED interventions of take-home intranasal naloxone (ED-initiated buprenorphine or transport to a facility) were not independently associated 90-day OD.

There was a total of 34 OD deaths within 180 days (1.3%). Figure 2 shows the 180-day OD death rate by 4-month blocks. There was a significant decrease in death rate over time (OR 0.98, CI 0.96–0.996). This

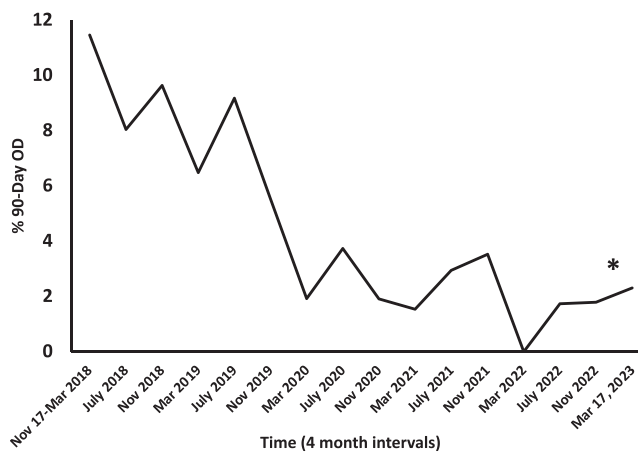


FIGURE 1 Subsequent 90-day opioid overdose (OD). The total number of patients in the cohort per 4-month block and the number of subsequent 90-day OD. The percent of subsequent 90-day OD significantly decreases over time ($*p < 0.001$).

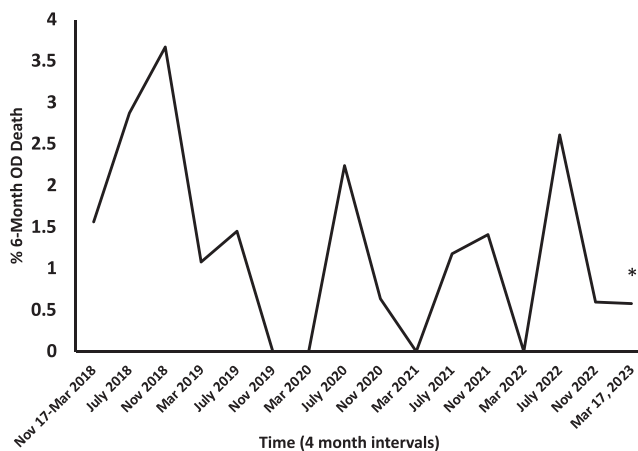


FIGURE 2 Subsequent 6-month opioid overdose (OD) death. The percent of subsequent 6-month OD deaths, and 6-month deaths decreased significantly over time ($*p = 0.021$).

decreasing mortality trend contrasted with the mortality rate within our region, where the State of Ohio had a decrease in OD deaths from 2017 to 2018, but then a 7% increase in OD deaths from 2018 to 2019 and a 25% increase from 2019 to 2020.¹⁸ The ED interventions of take-home intranasal naloxone, ED-initiated buprenorphine, ED-PSRP, or transport to a facility were not independently associated with 180-day OD death.

4.2.2 | Temporal trends in resource utilization

There were 1335 patients presenting to the ED for an acute OUD complaint in the pre-COVID-19 timeframe (1.4 patients/day), 46 patients during COVID-mitigation (1.05 patients/day), 371 patients during post-mitigation (1.2 patients/day), and 882 patients in the post-COVID-19 timeframe (1.1 patients/day). Resource utilization was

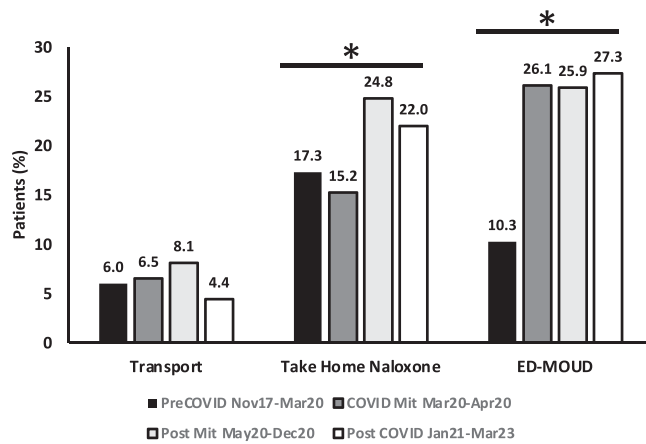


FIGURE 3 Resource utilization during COVID-19 mitigation. The percent of subsequent patients utilizing resources available in the emergency department (ED) in the year prior to COVID-19 mitigation (pre-COVID) and during COVID-19 mitigation (* $p < 0.05$).

increased throughout the study period (Figure 3). There was an increase in the rate of ED-buprenorphine prescriptions and increase take-home naloxone kits distributed. No significant difference was noted in patients directly transported to a treatment facility by ED-peer supporters.

4.2.3 | Patient characteristics associated with 90-day OD and 180-day OD death

Multivariate regression analysis was performed on patient characteristics at the index visit (Supporting Information Appendix Table A2). The following index characteristics were found to be positive independent predictors of OD: (1) number of internal ED visits in the previous ninety days (OR 1.25, CI 1.06–1.48), (2) number of internal ED visits for OD within the past 2 years (OR 1.61, CI 1.12–2.31), (3) number of external ED visits for OD within the past 2 years (OR 1.37, CI 1.08–1.74). Black race was associated with a lower incidence of 91 OD (OR 0.34, CI 0.13–0.86). The number of buprenorphine doses filled was also associated with a reduction of 90-day OD (OR (per dose) 0.98, 0.97–0.99). Figure 3 shows the percent of 90-day OD in patients with less than 28 doses filled (5.4%) and more than 28 doses filled (2.4%, OR 2.32, CI 1.21–4.47).

Patient age (OR 1.03, CI 1.001–1.050), receiving a benzodiazepine in the ED (OR 3.05, CI 1.33–7.00), and a history of OD (OR 2.57, CI 1.22–5.42) were independent risk factors of 180-day OD death after multivariate analysis (Figure 4).

5 | LIMITATIONS

This was a retrospective observational study, and bias may have been introduced as patients self-selected into study groups. The study design was observational and not interventional as it would be unethical

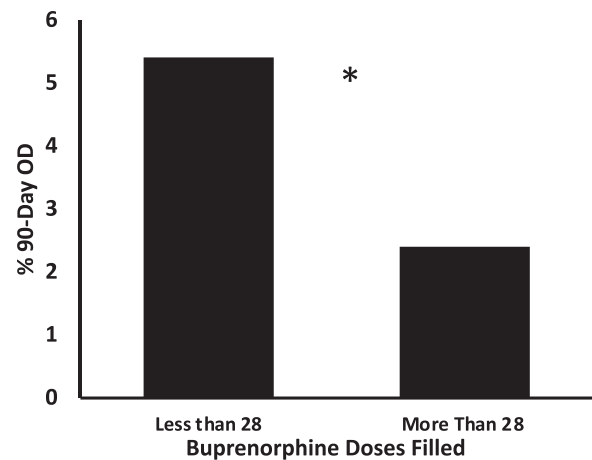


FIGURE 4 Subsequent 90-day opioid overdose (OD) death in patients prescribed medication for opioid use disorder (MOUD). The percent of subsequent 90-OD deaths in patients prescribed more than 28 doses of buprenorphine vs less than 28 doses of buprenorphine (* $p = 0.009$).

ical to deny access to resources based on study randomization. As an observational study, we can only determine associations between the interventions and outcomes observed, although temporal associations between the interventions and outcomes can provide some potential insight into their efficacy. However, although only determining associations, it is important to assess potential impact of these interventions and develop methods of screening for patients who may most benefit from treatment. This was an evaluation of a program at a single health system, which may limit the external applicability of the results.

The identification of patients with opioid use disorder (OUD) or at risk for OUD is a well-described challenge.^{19–21} Studies have been done using a variety of methods including documentation in the EHR and the addition of natural language processing or machine learning to traditional search methods.^{19,20,22} Based on the well-reported shortcomings of solely ICD-10 diagnoses to identify these patients, we developed a search using multiple elements of EHR documentation from the ED visit.^{21,23,24}

For prior buprenorphine use within the previous year, we identified “doses dispensed” as opposed to “prescriptions written.” Both variables are searchable in the EHR, but “doses dispensed” potentially represents a more accurate of buprenorphine the patient received.

While our search was geared to identify all patients appropriate to the study, there are some limitations to the search methods. First, the identification of patients through EHR data is dependent on the consistency and accuracy of provider documentation, which may mean information is limited or missing in some cases. Second, patient mortality data are partially based on local EHR data, which may be incomplete. However, to mitigate this limitation was incorporated regional coroner and EHR data from other hospital systems. However, subsequent visits at non-Epic using organizations, including one large, local hospital system was not available and therefore may have been missed by the query and review. Finally, subsequent visits at outside Epic

organizations may be missed if no automated update or patient contact occurred at our organization after the outside visit occurred.

6 | DISCUSSION

While this study did not identify any one intervention which independently improved patient centered outcomes, the downtrend of 90-day OD and trend toward reduction of 6-month OD death was observed occurred during a time when there was increasing utilization of our system's multi-pronged ED treatment approach. This is in contrast to OD trends nationally and within our larger state of Ohio region during the same study period, suggesting that the system's approach may be benefiting these patients.

The ED has been at the forefront of developing innovative approaches to treat patients with OUD, including providing take-home naloxone to at-risk patients, initiating buprenorphine in the ED, linkage to treatment and in implementing opioid educational programs.^{9,25,26} Take-home naloxone programs are cost effective, feasible, and reduce population-level mortality in communities that implement them.^{27,28} While ED take-home naloxone interventions are feasible,^{25,29} studies have yielded mixed results in reducing patient-level mortality and improving treatment engagement.^{30–32} Variability exists among program access to naloxone in the ED with rates of uptake between 30% and 70% reported in one review.^{33,34} In our study, take-home naloxone was not independently associated with a reduction in the primary outcome of repeat OD at 90 days, although the uptake of this intervention was low at 20% (524/2634) of eligible patients.

Buprenorphine initiation in the ED has been shown to reduce subsequent nonmedical opioid use and increase engagement in treatment,⁹ however rates buprenorphine prescribing in the ED remain low.⁵ Thirteen percent of patients described in this study were given a prescription for buprenorphine at the time of their initial presentation within the study period. The post hoc analysis adds to the literature, noting that filling of buprenorphine prescriptions was associated with a lower 90-day OD rate.

A variety of models for linkage to treatment have previously been implemented in the ED with varying success.^{35–40} Brief interventions have also yielded mixed results.^{9,40} ED-PSRPs with real-time linkage to treatment provide support and facilitate treatment for this population. In 2014, Rhode Island was the first to describe their PSRP outcomes, reporting a 33% increase in take-home naloxone prescriptions to at-risk patients. Peer navigators were accessible with one-third of patients interacting with a peer recovery coach.⁴¹ The ED Leads program in New York describes a blended model utilizing a licensed clinician and a peer counselor team. Linkage and engagement outcomes were promising in this model; however, they failed to fully integrate the teams with majority of patients being evaluated by the licensed clinician.⁴² Substance use navigator (SUN) programs offer a similar intervention model without the requirement for lived experience among SUNs. These programs have been deployed throughout the

country modeled after the Bridge Program in California and are associated with higher rates of engagement, buprenorphine administered after naloxone reversal, inpatient hospital buprenorphine offered, initiation of buprenorphine in pregnant women, and addiction treatment after ED discharge.^{43,44} Although not independently associated with decreases in OD or mortality, the authors feel that the ED-PSRP program examined in the current report was likely an important part of the multi-pronged approach, providing a bridge for patients to be linked to treatment.

Overall, the available ED interventions were not utilized by the majority of patients and implementation could be further improved. Moreover, identification of patients at highest risk for subsequent OD and death incorporated into the EHR, if more uniformly adopted, could provide important information to the provider in real time to offer these interventions and improve utilization.

As opposed to regional and national reports regarding opioid OD and mortality rate, patients treated at our institution demonstrated decreased rates of ODs and deaths, including during the COVID-19 pandemic. We provide system-wide support for providers and patients through a multidisciplinary Office of Opioid Safety (OOS) and Project DAWN (Deaths Avoided with Naloxone) programs. It is possible that as these resources increased in scope immediately prior to 2019, we were well equipped to provide care during the pandemic. The contrast between our experience and others nationally during the COVID pandemic suggests that if adopted and prioritized, these programs can be robust and effective in the face of health care change and challenges.

In conclusion, after implementing a multi-pronged approach to treat ED patients with OUD, 90-day subsequent OD and 180-day OD death rates decreased over time.

AUTHOR CONTRIBUTIONS

Eric N. Reed, Lance D. Wilson, and Joseph S. Piktel conceived the project and designed the study. Eric N. Reed and Joseph S. Piktel obtained research funding. Joan Papp provided content expert guidance and access to participating programs. Eric N. Reed, Jonathan Siff, and Joseph S. Piktel supervised and conducted data collection. Yesol Oh, Kellie LeVine, Estella Bastian, and Kailee Pollock conducted data collection and analysis. Yasir Tarabichi and Jonathan Siff provided informatics support, including coding and data dictionary support. Joseph S. Piktel drafted the manuscript, and all authors contributed substantially to its revision. Joseph S. Piktel takes responsibility for the paper as a whole.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENTS

Partial or complete deidentified datasets and data dictionary will be available upon request from the corresponding author at the time of publication.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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