



Effect of a best practice advisory activated “kit in hand” naloxone distribution program in the emergency department

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ABSTRACT

Purpose: We implemented a “kit in hand” naloxone distribution program at emergency department (ED) discharge activated by electronic health record Best Practice Advisory (BPA). The purpose of this study was to evaluate naloxone kit distribution before and after implementation.

Methods: Retrospective observational study of adult ED patients with unintentional opioid overdose conducted over a six-month period. An intranasal (IN) naloxone kit in hand distribution program activated by BPA was implemented during the study period. Patient demographics and reasons eligible patients did not receive a kit are reported. Multivariable regression was performed to identify differences in patients that received naloxone or were intended to receive it compared to those that were not to identify any biases in distribution.

Results: A total of 349 patients were included; 160 pre- (median age 39.5 years, 74.4 % males, 63.1 % white, 83.7 % non-Hispanic) and 189 post-implementation (median age 41 years, 75.7 % males, 52.9 % white, 81.5 % non-Hispanic). Pre-implementation, 109/160 (68.1 %) patients received a naloxone prescription at discharge with only 25/109 (22.9 %) confirmed to have picked up the naloxone kit and therefore a total of 25/160 (15.6 %) receiving naloxone. Post-implementation, 106/189 (56.1 %) patients left the ED with a naloxone kit in hand and 1/22 additional patients that had a prescription written were confirmed to have picked it up; therefore, a total of 107/189 (56.6 %) receiving naloxone. Reasons for not receiving a naloxone kit in the post-implementation period were patient refusal (6.3 %), patient already had naloxone (1.6 %), or a prescription was written instead (11.6 %). There were instances where kits were intended to be ordered based on clinician notes or naloxone kit was ordered but not dispensed by nursing staff. There were no differences between age, sex, race, ethnicity, or time of discharge from the ED following comparison of those where the clinician intended for the patient to receive naloxone and those where there was not intent to prescribe naloxone in the post-implementation group.

Conclusions: Implementation of a BPA-activated kit in hand naloxone distribution program increases the rate of successful naloxone distribution to patients presenting to the ED following unintentional opioid overdose, a sub-population at very high risk for recurrence of overdose. Opportunities for program improvement were identified as there were instances where kits were intended to be distributed but barriers in the process existed.

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1. Introduction

The emergency department (ED) can serve as a crucial point for intervention in patients presenting with opioid overdoses. In a

retrospective, cross-sectional study using data collected from nearly 1000 hospitals, there were 792,416 adult ED visits in a two-year period involving overdoses with opioids [1]. These patients are at high risk for recurrent overdoses and death. One study reported one-year mortality after a nonfatal opioid overdose treated in an ED was 5.5 %, and 67.4 % of these deaths were attributed to an opioid-related overdose [2]. According to the Centers for Disease Control and Prevention (CDC), the total number of overdose deaths from prescription and recreational

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opioids in the United States has about quintupled over the past decade from 21,089 in 2010 to 107,942 in 2022 [3,4].

Naloxone, a full opioid antagonist, is a life-saving intervention that reverses respiratory depression after opioid overdose. It can be administered intravenously, intramuscularly, or intranasally. Previous reports have commented on successful reversal of opioid overdose with naloxone administration by bystanders and subsequently a lower likelihood for additional medical interventions [5,6]. The CDC recommends that rescue naloxone kits be offered to all patients at high risk for opioid overdose, which includes patients presenting to the ED after an unintentional opioid overdose [7]. However, multiple EDs report a naloxone prescription rate below 10% in high-risk patients, and only 1.1% of commercially insured patients with opioid-related ED encounters filled a prescription for naloxone within 30 days in one report [8–11]. Prescription fill rates may be low due to cost. A study using cost data over a five-year period found the average copayment for naloxone was almost \$25 United States Dollars (USD); more than double the cost for most opioid prescriptions [12]. Furthermore, for patients without insurance, the cost for a naloxone intranasal kit (2-pack) is approximately \$50 USD. Stigma, education, and motivation are also presumed to be other barriers in obtaining naloxone [11].

We conducted a preliminary quality review between October and December 2021 which concluded that 37% of patients treated for unintentional opioid overdoses were given an intranasal (IN) naloxone prescription at discharge, with an unknown prescription fill rate. Given this, we developed a “kit in hand” naloxone distribution program at ED discharge activated by an electronic health record (EHR) Best Practice Advisory (BPA) which has been previously reported as a strategy to improve naloxone distribution [6,10,13,14]. Therefore, the purpose of this study was to evaluate this program's efficacy by comparing the proportion of patients that received naloxone over a 6-month period; 3 months prior to and 3 months after implementation.

2. Methods

2.1. Study setting and design

This was a single-center retrospective, observational study of adult ED patients with unintentional opioid overdose 3 months prior to and 3 months after BPA-activated kit in hand naloxone distribution program implementation at a large, tertiary care academic medical center with >117,000 annual ED encounters. This study met federal and University criteria for exemption by the organization's Research Subjects Review Board.

This program was developed collaboratively by a medical toxicologist physician and clinical toxicologist pharmacist, emergency medicine (EM) physician and nursing leadership, and a supply chain pharmacy representative. A medical informaticist that is also an EM physician helped develop the BPA and naloxone kit orders in the EHR. The BPA activates when an EM clinician enters a discharge diagnosis associated with an International Classification of Diseases (ICD)-10 code related to opioid overdose (codes F.11 and T.40). Once activated, the BPA notifies the clinician the patient is at high risk of fatal opioid overdose and asks them to consider prescribing an IN naloxone kit at ED discharge. If accepted, the BPA auto populates an ED medication order for a naloxone kit in the EHR for the physician to accept. IN naloxone kits, which contain two single-dose 4 mg nasal spray devices, are obtained from the county health department free of charge and stored in the central pharmacy. They are individually labeled to be suitable to provide to a patient at discharge (institution name, address, phone number, patient friendly instructions for use) and stocked in the ED automated dispensing cabinet to allow for quick distribution and patient throughput. Once ordered, an ED nurse obtains the IN naloxone kit, places a patient sticker containing the patient's name and date of birth, on the naloxone kit box, and dispenses the kit directly to the patient. Clinicians were not blocked in the EHR from writing a naloxone prescription at the time of

BPA-activated kit in hand naloxone distribution program implementation, though it was encouraged to use the new kit in hand process. Education on opioid use disorder (OUD) and the new BPA-activated naloxone kit in hand distribution program was provided to EM faculty and resident physicians by an EM physician board certified in medical toxicology and addiction medicine during scheduled ED conferences and staff meetings. As there are scheduled, annual, ED conferences on addiction medicine topics, this was added to that curriculum. Such education was also provided to advanced practice providers, nurses, and EM clinical pharmacists by leadership and through email communication. Prior to this program implementation, clinicians were only able to write a prescription for a naloxone kit and there was no process for direct distribution to the patient in the ED prior to discharge.

2.2. Patient selection

All adult patients (≥ 18 years old) with a chief complaint of “drug overdose” from December 20, 2022 through June 20, 2023 were screened for inclusion. Implementation of the new naloxone distribution program and EHR BPA occurred March 20, 2023 and therefore December 20, 2022 to March 19, 2023 represents the pre-implementation group and March 20, 2023 to June 20, 2023 represents the post-implementation group. Those with confirmed unintentional opioid overdose following EHR review that were discharged directly from the ED were included. If patients had multiple ED presentations meeting inclusion during the study period, each encounter was included. Patient that were (1) incarcerated (naloxone would not be routinely prescribed/given since there is availability at the jail/prison), (2) transferred to the comprehensive psychiatric emergency program unit, (3) transferred to the obstetrics unit, (4) required hospital observation, (5) required hospital admission, or (6) died during the visit were excluded.

2.3. Study AIMS

The primary aim was to compare the proportion of patients presenting to the ED with unintentional opioid overdose receiving naloxone for home use before and after program implementation. Secondary aims were to investigate barriers to distribution for program refinement. We also sought to identify differences in patients that received naloxone or were intended to receive it compared to those that were not to identify any biases in prescribing or distribution.

2.4. Data collection

Patients with the chief complaint “drug overdose” were identified from an EHR generated report. A manual review of the EHR was performed to screen patients for inclusion and data collection. Patient demographic characteristics including age, sex, race, ethnicity, time of day of patient discharge (i.e., day, evening, overnight), disposition (i.e., discharged after being seen/care completed, left without being seen [LWBS], left before evaluation completed [LBEC], left against medical advice [LAMA]) were collected. Receiving a naloxone prescription was collected in the pre-implementation group. Receiving a naloxone kit in hand or prescription at ED discharge was collected in the post-implementation group. In both groups, reasons for not receiving a kit or prescription, if available, were collected (i.e., patient refused, patient already owned one). For patients that had a prescription written, outpatient pharmacies were contacted via telephone by a single investigator to confirm naloxone receipt by determining if the naloxone kit was actually picked up by the patient.

Manual data collection was performed by three investigators using a data dictionary and entered into a standardized data collection form using Research Electronic Data Capture (REDCap). Training for data collection was performed by one investigator prior to the start of data collection, and this investigator reviewed the EHR when questions or clarifications were necessary to reduce variability in data collection.

2.5. Data analysis

Data are reported descriptively as effect estimates with dispersion. To compare the pre- and post-implementation groups, univariate analysis was performed. Specifically, the Wilcoxon rank sum test was used for continuous variables and Chi-squared analysis or Fisher's Exact Test for dichotomous variables, as appropriate based on cell count size. Multivariable regression was performed to identify potential biases related to age, sex, race, ethnicity, or ED time of discharge and EM clinician decision for the patient to receive naloxone or not. Odds ratios (ORs) and 95 % confidence intervals (CIs) on the outcome intent to distribute were calculated on the unadjusted association between all variables of interest. Both the unadjusted effect estimates as well as the fully adjusted model with all covariates were quantified in the logistic regression model. A *p*-value of 0.05 or less was determined to be statistically significant a priori.

3. Results

3.1. Demographics

A total of 587 patient encounters were screened and 349 were included; 160 in the pre-implementation group and 189 in the post-implementation group (Fig. 1). Median age, sex, race, and ethnicity were similar in pre-implementation and post-implementation groups; median age (39.5 years vs. 41 years), male sex (74.4 % vs. 75.7 %), white race (63.1 % vs. 52.9 %), non-Hispanic ethnicity (83.7 % vs. 81.5 %), respectively. There were no differences between time of ED discharge or disposition between groups. Complete patient demographics are in Table 1.

3.2. Primary outcome

More patients in the post-implementation group, 107/189 (56.6 %), compared to the pre-implementation group, 25/160 (15.6 %), were confirmed to have received naloxone ($p < 0.01$). In the pre-implementation group, 109/160 (68.1 %) patients received a naloxone prescription at discharge, however only 25/109 (22.9 %) of patients picked up this prescription. Therefore, although there was intent for patients to receive naloxone in 68.1 % of patients, only 25/160 (15.6 %) were confirmed to have received naloxone. In the post-implementation group, 106

Table 1
Patient demographics.

	Pre-Implementation (n = 160)	Post-Implementation (n = 189)	p-value
Median age, years (IQR)	39.5 (33–51)	41 (31–55)	0.28
Sex, n (%)			0.88
Male	119 (74.4)	143 (75.7)	
Female	41 (25.6)	46 (24.3)	
Race, n (%) ^a			0.07
White	101 (63.1)	100 (52.9)	
Black	51 (31.9)	67 (35.4)	
Asian	0	0	
American Indian or Alaskan native	1 (0.6)	2 (1.1)	
Native Hawaiian or Other Pacific Islander	0	0	
Other	11 (6.9)	20 (10.6)	
No race documented	1 (0.6)	6 (3.2)	
Ethnicity, n (%)			0.9
Hispanic	20 (12.5)	22 (11.6)	
Non-Hispanic	134 (83.7)	154 (81.5)	
No ethnicity documented	6 (3.8)	13 (6.9)	
ED Discharge, n (%)			0.12
Day (0701–1500)	56 (35.0)	53 (28.1)	
Evening (1501–2300)	50 (31.3)	52 (27.5)	
Overnight (2301–0700)	54 (33.7)	84 (44.4)	
Disposition, n (%)			0.31
Discharged after being seen/care completed	154 (96.3)	186 (98.5)	
Left against medical advice	4 (2.5)	1 (0.5)	
Left without being seen	2 (1.2)	1 (0.5)	
Left before evaluation completed	0	1 (0.5)	

Abbreviations: IQR = interquartile range, ED = emergency department.

^a Some patients had multiple races documented.

patients received a naloxone kit dispensed directly in hand because of the new naloxone distribution program. An additional 22 patients had a naloxone prescription written, however only 1/22 picked up naloxone from the outpatient pharmacy. Therefore, although there was intent for patients to receive naloxone in 67.7 % of patients (106 receiving a kit directly and 22 receiving a prescription), only 107/189 (56.6 %) were confirmed to have received naloxone.

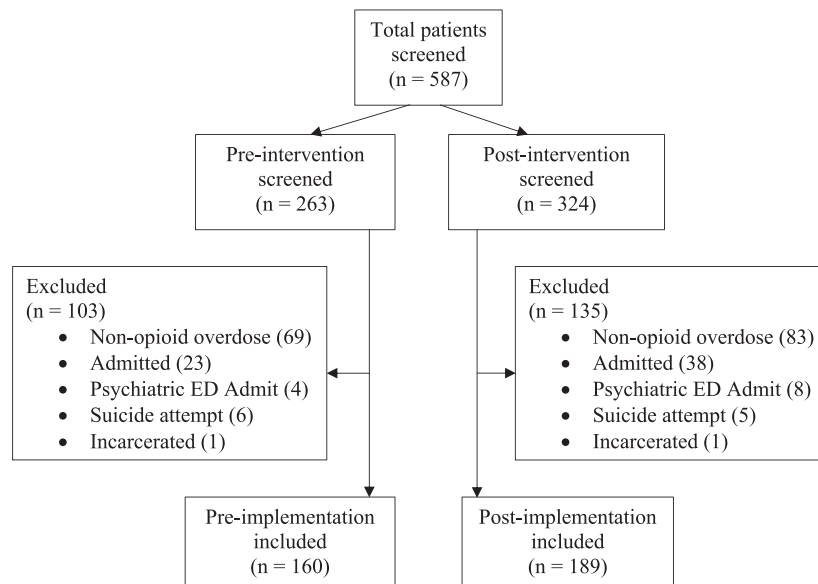


Fig. 1. Consort diagram.

Table 2
Naloxone kit distribution outcomes.

	Pre-Implementation (n = 160)	Post-Implementation (n = 189)
Total patients where there was intent by the clinician to distribute naloxone, n (%)	109 (68.1)	128 (67.7) ^a
Naloxone kit dispensed directly from the ED; “kit in hand”		106 (56.1)
Naloxone prescription	109 (68.1)	22 (11.6)
Total patients receiving naloxone (successful distribution), n (%) ^b	25 (15.6)	107 (56.6) ^c
Naloxone kit dispensed directly from the ED; “kit in hand”		106 (56.1)
Naloxone prescription pick up confirmed	25 (22.9)	1 (4.5)
Documented reasons for not receiving naloxone, n (%)		
Patient already owned naloxone	2 (3.9)	3 (4.9)
Patient refused	1 (1.2)	12 (19.7) ^b
Unknown	48 (94.1)	46 (75.4)
Failures to the post-implementation process, n (%)		
Clinician ordered but kit was not dispensed in the ED		9 (4.8)
Clinician documented they ordered the kit in the progress note but did not		2 (1.1)

Abbreviations: ED = emergency department.

^a $p = 0.94$.^b Represents the number of patients that went home with naloxone either from a kit being dispensed directly in the ED (post-implementation group) or confirmed pick-up on the prescription written at the ED visit (pre- and post-implementation group).^c $p < 0.01$.

A similar number of patients did not receive naloxone in the pre- and post-implementation groups because they self-reported they already owned naloxone. However, more patients refused naloxone in the post-implementation group; 12 vs. 1 patient in the pre-implementation group ($p < 0.01$). Complete naloxone kit distribution results are in Table 2.

3.3. Secondary outcomes

There were barriers to the naloxone kit in hand distribution identified in the post-implementation group (Table 2). In nine patients, naloxone was never documented to be dispensed in the ED by nursing staff after clinician order. For two other patients, the clinician documented in the progress note that they ordered a kit; however, the actual medication order for dispensing was not placed in the EHR and therefore never dispensed to the patient. There were no significant predictors observed between those patients where the EM clinician had intent for the

patient to receive naloxone compared to those where there wasn't in regards to age, sex, race, ethnicity, or ED discharge time (day, evening, or overnight) in the unadjusted or fully adjusted analysis (Table 3).

4. Discussion

We implemented a naloxone “kit in hand” distribution program at ED discharge that was activated by an EHR BPA. The program increased the proportion of patients treated in the ED for unintentional opioid overdose that received naloxone by over 300 %. The program resulted in 56 % of patients leaving the ED with a naloxone kit. Age, sex, race, ethnicity, and time of day ED discharge occurred were not factors that seemed to influence patients that received or were offered naloxone.

Data regarding naloxone distribution rates from the ED are limited and heterogeneous. Multiple studies report a lower rate than ours in the post-implementation period [–8–10,13,15,16]. Samuels et al. found a distribution rate of 35.4 % in two EDs following the implementation

Table 3
Comparison of demographics between patients where the EM clinician intended for the patient to receive naloxone compared to those where they did not in the post-implementation group.

	Intended to receive naloxone (n = 154) ^a	Not intended to receive naloxone (n = 35)	Unadjusted ^b OR (95 % CI)	Fully adjusted model ^c OR (95 % CI)
Median age, years (IQR)	41 (31–53.75)	49 (32.5–57)	1.01 (0.98, 1.04)	1.01 (0.98, 1.04)
Sex, n (%)				
Male	116 (75.3)	27 (77.1)	References	References
Female	38 (24.7)	8 (22.8)	0.90 (0.38, 2.16)	0.91 (0.38, 2.22)
Race, n (%) ^d				
White	85 (55.2)	15 (42.9)	References	References
Other races	69 (44.8)	20 (57.1)	1.64 (0.78, 3.45)	1.76 (0.80, 3.86)
Ethnicity, n (%) ^e				
Hispanic	18 (11.7)	4 (11.4)	References	References
Not Hispanic	136 (88.3)	31 (88.6)	1.03 (0.32, 3.24)	1.39 (0.41, 4.70)
ED Discharge, n (%)				
Day (0701–1500)	40 (26.0)	13 (37.1)	References	References
Evening (1501–2300)	45 (29.2)	7 (20.0)	0.48 (0.17, 1.32)	0.47 (0.17, 1.31)
Overnight (2301–0700)	69 (44.8)	15 (42.9)	0.67 (0.29, 1.55)	0.65 (0.27, 1.53)

Abbreviations: EM = emergency medicine, OR = odds ratio, CI = confidence interval, IQR = interquartile range, ED = emergency department.

^a Patients that received a naloxone kit in hand at ED discharge, a prescription for naloxone, were offered naloxone but already owned a kit or the patient refused or had a failure in the post-implementation process were included in this group for comparison as the EM clinician intended for the patient to receive naloxone.^b Unadjusted effect estimates for each variable individually.^c Fully adjusted model in which all variables are forced into the model regardless of their association with the outcome. Effect estimates presented are adjusted for all other variables listed.^d Race was collapsed into two categories for comparison in the model. Patients were categorized as “Other” if any of their races documented in the chart did not include white. All “Other” races are described in Table 1.^e Patients were categorized as not Hispanic for comparison if they did not select Hispanic as an ethnicity that they identified with.

of a naloxone distribution program for patients at risk of opioid overdose [8]. In a study of adolescents seen in the ED with OUD, Sidlak et al. reported a similar rate of 29 % [15]. Eswaran et al. reported a naloxone distribution rate of 34 % following implementation of a program where after clinician decision for a naloxone kit to be given to the patient, the EM pharmacist managed naloxone dispensing and education to ensure a kit in hand at discharge [16]. Conversely, Jacka et al. report that 69 % of patients that were seen by an addiction response team that bundled behavioral counseling, ED-initiated buprenorphine, and treatment referral received naloxone, however, not all patients that presented to the ED after overdose received the bundled care [17]. These differences may be related to the patient population included, as this study reported rates in opioid overdose patients that received the bundled intervention compared to our population that were all comers with opioid overdose. Also, we included patients that LWBS, LBEC, or LAMA which likely reduced our effect size whereas this study excluded those patients.

There have been a few reports using similar naloxone distribution designs to ours with an EHR screening and clinician prompt approach to order naloxone with varying targeted patient populations [9,10,14,18,19]. Following implementation of an EHR prompt to promote provision of take-home naloxone in nine EDs, Marino et al. reported an increase in naloxone kit distribution at discharge from 10 % to 13 % [9]. This study also attempted to identify patient specific factors associated with naloxone distribution and found younger age and white race were associated with take home naloxone kit distribution in the pre-implementation period, but like our study, in the post-implementation period there were no differences [9]. Another study by Funke et al. reported a more robust increase from 6 % to 29 % after EHR prompt for patients with opioid overdose or OUD-related diagnoses and order set implementation for naloxone prescribing in a single ED [10]. Two studies reported a system-wide intervention to increase naloxone prescribing rates with a component that focused on co-prescribing of naloxone with opioid prescribing in the EHR [16,18]. Devries et al. reported a 10-fold improvement in take-home naloxone prescribing following implementation of a guideline, EHR changes which alerted for opioid prescribing in patients with a known diagnosis of substance abuse or previous opioid overdose, and a robust educational component [18]. Heiman et al. noted an improvement in naloxone prescribing rates from 0.7 % to 4.2 % after coupling high morphine milligram equivalent prescribing with a naloxone kit prescription in the EHR [14]. In both studies, only a portion of patients were ED patients and the patient population being sought after for naloxone distribution was different. Regardless, our study and these ED and health system-wide studies all included a component to leverage the EHR to identify relevant patient populations to improve naloxone distribution rates.

We identified that the EHR BPA did not necessarily change the intent of EM clinicians to provide naloxone to the patient. Although this was not formally assessed, IN naloxone prescriptions in the pre-implementation group were similar to the summative rate of take-home naloxone kits and IN naloxone prescriptions in the post-implementation group. This was likely a consequence of years of educational initiatives targeting both resident physicians and faculty on the topic of ED management of OUD. However, we identified that although intent was there, prescribing naloxone alone is not a viable option to actually improve naloxone distribution as seen with our low prescription pick-up rates. Therefore, the implementation of the BPA coupled with a kit in hand distribution program and EM clinician and staff education seemed to provide the most impact for patients at high risk for unintentional opioid overdose.

This study had limitations. We examined a subgroup of patients at very high risk for recurrent overdose, namely those presenting to the ED with a chief complaint of drug overdose. This distinguishes our study from others which examined more broadly all patients with OUD, OUD-related conditions, or receiving high morphine milligram equivalent prescriptions. Therefore, our results may not be

generalizable to other populations. Additionally, there is the possibility that ICD-10 codes failed to capture all patients with unintentional opioid overdose in the ED which may have led to underreporting. We chose to include patients that presented to the ED with opioid overdose but left LWBS, LBEC, or LAMA. In our experience, unintentional opioid overdose patients have historically high rate of LWBS, LBEC, or LAMA, but are still at risk for recurrent overdose. We felt that it would be in the best interest of these patients and our aim in the ED to at minimum dispense a naloxone kit prior to leaving, therefore our inclusion of these patients may have reduced our effect size. Overall, the sample size is small to identify differences in patients where the EM clinician intended for the patient to receive naloxone compared to cases where they did not, and the confidence intervals are imprecise and should be interpreted cautiously.

Furthermore, we only evaluated a six-month study period and additional post-implementation assessment cycles are needed to determine sustainability of the intervention. Overall, we suspect interclinician practice patterns, off-service trainees unfamiliar with departmental practice working in the ED, and workspace or staffing limitations in the strained current practice environment impacted our results. Specifically, we predict this influenced the number of patients receiving a naloxone prescription rather than a kit in hand in the post-implementation period. We intend to further leverage the EHR to help direct clinicians attempting to write a prescription back to the kit in hand program for patients physically in the ED. Lastly, our data may not be generalizable to all EDs in that there are multiple EM faculty members holding additional board certification in addiction medicine which may have impacted our effect size.

5. Conclusions

EM clinician intent to distribute naloxone was unchanged throughout the study period. However, the proportion of ED patients receiving naloxone following unintentional overdose, a subpopulation at very high risk for recurrence of overdose, was successfully improved by the BPA-activated kit in hand naloxone distribution program. Opportunities for program improvement were identified as there were instances where kits were intended to be distributed but barriers in the process existed.

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CRediT authorship contribution statement

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editing, Methodology, Formal analysis, Conceptualization. **Nancy E. Wood:** Writing – review & editing, Methodology, Conceptualization. **Kenneth R. Conner:** Writing – review & editing, Methodology, Conceptualization. **Nicholas Nacca:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

None.

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