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# Factors associated with post-intubation sedation after emergency department intubation utilizing a national airway registry

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ABSTRACT

*Background:* Previous work has suggested low rates of post-intubation sedation in patients undergoing endotracheal intubation (ETI) in the emergency department (ED) with limited data examining factors associated with sedation use. Utilizing a national database; we sought to determine the frequency of post-intubation sedation and associated factors.

*Methods:* We performed a retrospective analysis of a prospectively collected database (National Emergency Airway Registry (NEAR) from 25 EDs from January 1, 2016 to December 31, 2017). Patients were considered to have received post-intubation sedation if they received any of the following medications within 15 min of ETI completion; propofol, midazolam, diazepam, ketamine, etomidate, fentanyl, and morphine. We calculated odds ratios for post-intubation sedation.

*Results:* Of the 11,748 eligible intubations, 9099 received post-intubation sedation (77.5%) while 2649 did not (22.5%). Pre-intubation hypotension (odds ratio; 95% confidence Interval) (0.27; 0.24–0.31) and post-intubation hypotension (0.27; 0.24–0.31) were associated with lower odds of post-intubation sedation. Patients with a medical indication compared to a traumatic indication for ETI had higher odds of receiving post-intubation sedation (1.16; 1.05–1.28) as did those that underwent rapid sequence intubation (15.15; 13.56–16.93). Use of succinylcholine was associated with a higher odd of post-intubation sedation compared to a long-acting neuromuscular blocking agent (i.e. rocuronium or vecuronium) (1.89; 1.68–2.12).

*Conclusion:* Post-intubation sedation rates in NEAR are higher than previously reported and multiple factors including the indication for intubation and succinylcholine use, are associated with higher odds of receiving post-intubation sedation.



## 1. Background

Endotracheal intubation (ETI) is a critical procedure in the resuscitation of acutely ill and injured patients including those in the emergency department (ED). While much attention has been focused on optimizing airway management strategies, appropriate sedation after intubation is crucial for maintaining patient comfort, especially if a long-acting neuromuscular blocking agent (NMBA) is used during rapid sequence intubation (RSI). Previous studies of intubated patients in the intensive care unit (ICU), have found that up to 82% of patients remembered the pain stemming from the endotracheal tube after extubation [1]. The stress response from the discomfort of the endotracheal tube results in the release of catecholamines that may decrease tissue perfusion secondary to constriction of arterioles [2,3]. Additional effects including hyperglycemia and muscle breakdown can also result from noxious stimuli [2]. Careful attention to sedation is also helpful for improving ventilator response, ventilator free days, hospital length of stay and prevention of ICU delirium [4]. Sedation and pain control are often provided to patients after intubation. As a result, current guidelines emphasize analgesia sedation as opposed to benzodiazepine only strategies in the intubated patient with opioids being the most prevalent analgesic agents used [2,4].

Previous studies have shown variable rates of post-intubation sedation for patients after intubation in the emergency department [5-8]. These have suggested that as few as 1 in 4 patients receive sedation within 15 min of intubation, well within the time frame where the effects of long-acting NBMAs may still be present [9]. Previous work has suggested an association between starting sedation within half an hour of ED ETI and decreased mortality in boarded patients [10]. Limited

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data have examined post-intubation sedation outside single centers and previous studies have had methodologic issues, tempering their findings [7,11]. The National Emergency Airway Registry (NEAR) has previously been used to identify trends in managing the pre-intubation period including rapid sequence intubation, procedure techniques, and intubation success [12]. We sought to examine the rates of post-intubation sedation and identify associated factors utilizing this multicentered dataset in order to better identify patient populations who may be at risk from lack of post-intubation sedation.

## 2. Methods

### 2.1. Study design and setting

We performed a retrospective analysis of a prospectively collected, multicenter database of ED intubation sedation captured in the NEAR registry. Each site has approval from its respective institutional review board.

### 2.2. Methods of measurement and data collection and processing

NEAR is a prospective multi-center database for emergency medicine airway practices [12]. Compliance is monitored by the NEAR Coordinating Center which ensures that ≥90% of the total intubations that took place at all participating sites EDs during the studied timeframe are entered in the database and full description of site compliance has previously been discussed [12]. Characteristics of each intubation are entered by the performing physician onto www.nearstudy.net via a centralized web-based data management database (StudyTRAX; v3.73.002; ScienceTRAX, Macon, GA). Access to the NEAR database is provided to participating hospitals through an institution-specific specific login and password. Data are uploaded directly onto the site of the principal center at the Department of Emergency Medicine at Brigham and Women's Hospital in Boston, Massachusetts which serves as the coordinating location. Study investigators identify and correct data entry errors using quality assurance algorithms described previously [12].

### 2.3. Selection of participants

Patients who underwent endotracheal intubation in the emergency department of participating hospitals and were entered into the database with the data pertaining to the intubation including induction, intubation technique, and post-intubation sedation were included. Multiple medications may be utilized after intubation for sedation including sedative medications (e.g. propofol) and analgesic medications (e.g. fentanyl). For the purposes of our analysis, we included all patients in the dataset where there was documented administration of either a sedative or analgesic medications which we define broadly as 'post-intubation sedation'.

### 2.4. Outcomes and covariates

The NEAR database collects patient demographics, intubation methods, reason for the procedure, airway characteristics, peri-intubation hemodynamics and vital signs, pharmacological interventions, patient outcomes, and complications. Age is collected in years up to age 88. After that, individuals can input the age as 89+. In order to estimate mean age and evaluate the odds of receiving post-intubation sedation, these values were estimated to be 90 (2.36% of the cases). Age <1 year old was considered 0 years old (0.5% of cases). NEAR captures the use of post-intubation medications including sedatives and analgesics through a section for the operator to select medications that were given in the 15 min after intubation. This is a specific field 'Did the patient receive any of the following medications in the 15 minutes after intubation? Check all that apply.' A patient was considered to have received post-intubation sedation if it was recorded that they received any of the following after intubation; propofol, ketamine, etomidate, midazolam, diazepam, fentanyl or morphine. These are the only sedation medications recorded in the dataset. There is also a section in which the operator can indicate no post-intubation medications given. Patients where none of these fields were selected, were excluded (n = 974; 7.7%).

### 2.5. Data analysis

We analyzed the prevalence of post-intubation sedation in the emergency department, as well as which medications were used and characteristics of these patients. We report patient, provider and intubation characteristics between patients who received post-intubation sedation and those that did not. We report the frequency of post-intubation medications using descriptive statistics. We report univariate odds ratios for the use of post-intubation sedation for patient, provider and intubation characteristics. As limited work has previously examined the variables associated post-intubation sedation, we focused our efforts on performing a univariate analysis [13]. Given the potential for withholding of post-intubation sedation in patients in arrest, to evaluate for awakening if the patient has return of spontaneous circulation, we repeated the analysis excluding patients where the indication for intubation was either 'cardiac arrest' or 'traumatic arrest'. All analyses were completed using Stata v 12 (Stata Corp, College Station, TX).

## 3. Results

Of the 12,722 patients in NEAR, 974 did not report on the use of post-intubation sedation leaving 11,748 for analysis of which 9099 received post-intubation sedation (77.5%) while 2649 did not receive sedation (22.5%). Patients receiving sedation had a mean age of 50.8, were frequently intubated using RSI (93%) and intubated for different medical and traumatic conditions compared to those who did not receive sedation (Table 1). The most frequent medical indications for intubation in patients that received sedation were 'non-overdose mental status change' (n = 1705; 25.2%) and 'overdose' (n = 1148; 16.5%) with 'cardiac arrest' being the most frequent indication for intubation in patients that did not receive sedation (n = 1106; 56.7%). The most frequent traumatic indications in patients that received sedation were 'head injury with hemorrhage' (n = 550; 36.3%) and 'polytrauma' (n = 462; 30.5%) while 'traumatic arrest' (n = 189; 27.1%) and 'polytrauma' (n = 154; 22.1%) were the most common indications for patients who did not receive sedation. Of patient that did not receive post-intubation sedation, 36.7% had post-intubation hypotension while 13.6% of patients who received post-intubation sedation had post-intubation sedation.

Several factors were associated with lower odds of receiving post-intubation sedation (odds ratio; 95% confidence interval): pre-intubation hypotension (0.27; 0.24–0.31), post-intubation hypotension (0.27; 0.24–0.31), and being in arrest prior to intubation (0.07; 0.06–0.08) (Table 2). RSI was associated with increased odds of post-intubation sedation (15.15; 13.56–16.93) as was the use of short-acting paralytics (i.e. succinylcholine) compared to long-acting NBMA (rocuronium and vecuronium) (1.89; 1.68–2.12).

### 3.1. Subgroup analysis excluding patients in arrest

When excluding patients in arrest, 8609 received post-intubation sedation (86.4%) while 1352 did not receive sedation (13.6%). Age, gender and estimated weight were similar between groups (Table 3). Pre-intubation (0.3; 0.26–0.35) and post-intubation hypotension (0.29; 0.26–0.34) were associated with lower odds of receiving post-intubation sedation (Table 4). Similar to the full analysis, RSI (4.46; 3.77–5.27) and succinylcholine use (1.95; 1.72–2.22) were associated with higher odds of receiving post-intubation sedation.

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**Table 1**
Intubation characteristics.

| Intubation characteristics | Patients receiving sedation n = 9099 (77.5%) | Patients not receiving sedation n = 2649 (22.5%) |
|---|---|---|
| Mean age (SD) | 50.8 (20.4) | 54.3 (22.1) |
| (missing = 27) | | |
| Male gender | 3056 (33.6) | 905 (34.2) |
| (missing = 2) | | |
| Estimated weight in kg (SD) | 79.4 (24.4) | 78.3 (26.9) |
| (missing = 102) | | |
| Medical indications for intubation* | n = 6940 | n = 1949 |
| (n = 8889) | | |
| Cardiac arrest | 455 (6.6) | 1106 (56.7) |
| Non-overdose mental status change | 1705 (25.2) | 281 (14.4) |
| Overdose | 1148 (16.5) | 114 (5.8) |
| Seizure | 662 (9.5) | 37 (1.9) |
| Shock (sepsis) | 394 (5.7) | 95 (4.9) |
| Traumatic indications for intubation* (n = 2839) | n = 2141 | n = 698 |
| Combative/agitated | 265 (17.5) | 17 (2.4) |
| Head injury with hemorrhage | 550 (36.3) | 146 (20.0) |
| Head injury without hemorrhage | 222 (14.6) | 39 (5.6) |
| Polytrauma | 462 (30.5) | 154 (22.1) |
| Traumatic arrest | 17 (1.1) | 189 (27.1) |
| Pre-intubation hemodynamics[a] | n = 8569 | n = 1361 |
| (n = 9930) | | |
| Hypertensive (SBP >140 mmHg) | 3195 (37.3) | 317 (23.3) |
| Normotensive (SBP100–140 mmHg) | 4212 (49.2) | 545 (40) |
| Hypotensive (SBP <100 mmHg) | 1162 (13.6) | 499 (36.7) |
| No treatment | 214 (2.5) | 102 (7.5) |
| Treated with IV fluids | 595 (6.9) | 233 (17.1) |
| Treated with vasopressors | 353 (4.1) | 164 (12) |
| Technique[b] | | |
| RSI | 8465 (93) | 1241 (46.8) |
| Sedation only | 152 (1.7) | 27 (1) |
| Paralytic only | 188 (2.1) | 149 (5.6) |
| No medications | 294 (3.2) | 1232 (46.5) |
| RSI paralytic n = 10,035 | | |
| (missing = 8) | n = 8646 | n = 1389 |
| Rocuronium | 4081 (47.2) | 873 (62.9) |
| Succinlycholine | 4538 (52.5) | 513 (36.9) |
| Vecuronium | 27 (0.3) | 3 (0.2) |
| Adverse events | | |
| Hypoxia (missing = 1943) | 787 (9.3) | 120 (9.1) |
| Post-intubation hypotension | 1312 (14.9) | 567 (39.3) |
| (SBP <100 mmHg) | | |
| (missing = 1504) | | |
| Medications[c] | | |
| Diazepam | 96 (8.7) | |
| Midazolam | 2069 (22.7) | |
| Ketamine | 663 (7.3) | |
| Fentanyl | 3874 (42.6) | |
| Morphine | 20 (0.2) | |
| Etomidate | 46 (0.5) | |
| Propofol | 6002 (66) | |

Percentages are of patients with values. Totals may not equal 100 due to rounding.
SD – standard deviation.
SBP – systolic blood pressure.
RSI – rapid sequence intubation.
ICU – intensive care unit.
ED – Emergency Department.
* For clarity, only the top 5 most frequent indications are shown. *P*-values are for top five indications. There were 67 cases where the indication for intubation was missing.
[a] Blood pressures presented are for patients age 13 and older. Not applicable for patients in arrest.
[b] Technique utilized on the first attempt.
[c] Totals may not equal 100% as patients may have received multiple post-intubation medications for sedation.

**Table 2**
Odds ratios for post-intubation sedation in all patients.

| Odds ratio of post-intubation sedation | Odds ratio (95% CI) |
|---|---|
| Age (in years) | 0.99 (0.99–0.99) |
| Gender | 0.97 (0.89–1.07) |
| Estimated weight in kg | 1 (1–1) |
| Pre-intubation systolic blood pressure | 0.27 (0.24–0.31) |
| (Hypotension vs not hypotensive) | |
| Indication (medical vs traumatic) | 1.16 (1.05–1.28) |
| In arrest prior to intubation (medical or traumatic) | 0.07 (0.06–0.08) |
| Technique (RSI vs not RSI) | 15.15 (13.56–16.93) |
| Paralytic type (short acting vs long acting)[a] | 1.89 (1.68–2.12) |
| Post-intubation hypoxia | 1.02 (0.83–1.24) |
| Post-intubation hypotension | 0.27 (0.24–0.31) |

RSI – rapid sequence intubation.
kg – kilograms.
[a] Long acting paralytics included rocuronium and vecuronium while succinylcholine was considered short acting paralytic.

## 4. Discussion

In this retrospective study of a multi-center database, nearly 80% of patients received post-intubation sedation; higher than previously reported rates [6,7]. Sedation rates were even higher (86.4%) after excluding patients in arrest who may have had specific clinical reasons for not receiving initial sedation. After excluding patients in arrest, it is unknown why the remaining 13.6% were not provided sedation however, there may have been specific clinical factors that lead the provider to elect not to provide post-intubation sedation such as patients intubated for 'head injury with hemorrhage' where sedation may be held for serial neurologic examinations. Several factors were associated with higher odds of receiving post-intubation sedation including ETI technique, specifically RSI, paralytic choice, and indication for intubation.

Current recommendations are for patients to receive post-intubation sedation and the vast majority of patients who undergo ED intubation receive post-intubation sedation. Pre- and post-intubation hypotension, and non-RSI technique, were associated with decreased odds of receiving post-intubation sedation. While tempting to associate the latter two with patients in either cardiac or traumatic arrest, these findings persisted after excluding these groups. In addition, a significant portion of patients where no medications were utilized to facilitate intubation (RSI, sedation, or paralytic) were not provided post-intubation sedation. While the exact reason for these findings is unknown, it may suggest that these patients had severe neurologic impairments and unresponsiveness (e.g poly-trauma with coma) whereby the treating provider may not have wanted to mask awakening. How to balance patient comfort with appropriate sedation for neurologic examination is unknown. Additional work will be needed to examine the ideal timing and depth of sedation in patients with neurologic conditions as providers may be reluctant to administer sedation that may mask awakening however, withholding sedation can induce profound negative physiologic effects.

Pre- and post-intubation hypotension was both associated with lower odds of post-intubation sedation. Based on these findings, physicians may be hesitant to prescribe sedation in hypotensive patients due to fear of worsening the hypotension. In our study, it is possible that this is related to the most common medication used for sedation after ETI; propofol, which can worsen hypotension. Other medications such as ketamine may be utilized in patients with tenuous blood pressures and future work will be needed to understand why providers select specific post-intubation medications as ketamine was infrequently utilized in this dataset (7.3% of those with sedation).

Prior studies, conducted at single center institutions, showed lower rates of post-intubation sedation [5,6]. Why these rates differ is unknown however, previous work has suggested increasing rates of sedation over time [7]. Our data may be the results of temporal trends and an increasing awareness of the importance of post-intubation sedation. Our study of post intubation practices utilizes the NEAR database that collects data from 25 hospitals and may better represent the current

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**Table 3**
Intubation characteristics of patient not in arrest.

| Intubation characteristics | Patients receiving sedation n = 8609 (86.4%) | Patients not receiving sedation n = 1352 (13.6%) |
|---|---|---|
| Mean age (SD) | 50.3 (20.4) | 51.1 (22) |
| (missing = 23) | | |
| Male gender | 2887 (33.5) | 483 (35.7) |
| (missing = 2) | | |
| Estimated weight in kg (SD) | 79.2 (24.2) | 77.4 (25) |
| (missing = 74) | | |
| Pre-intubation hemodynamics[a] | n = 8305 | n = 1182 |
| n = 9487 | | |
| Hypertensive (SBP > 140 mmHg) | 3117 (37.5) | 295 (25) |
| Normotensive (SBP100–140 mmHg) | 4090 (49.3) | 492 (41.6) |
| Hypotensive (SBP < 100 mmHg) | 1098 (13.2) | 395 (33.4) |
| No treatment | 204 (2.5) | 74 (6.3) |
| Treated with IV fluids | 571 (6.9) | 205 (17.3) |
| Treated with vasopressors | 323 (4.7) | 116 (9.8) |
| Technique[b] | | |
| RSI | 8188 (95.1) | 1100 (81.4) |
| Sedation only | 141 (1.6) | 24 (1.8) |
| Paralytic only | 159 (1.9) | 62 (4.6) |
| No medications | 121 (1.4) | 166 (12.3) |
| RSI paralytic n = 9961 | | |
| (missing = 5) | n = 8609 | n = 1352 |
| Rocuronium | 3914 (46.9) | 738 (63.5) |
| Succinlycholine | 4403 (52.8) | 662 (38.2) |
| Vecuronium | 25 (0.3) | 5 (0.3) |
| Adverse events | | |
| Hypoxia (missing = 595) | 766 (9.3) | 108 (9.5) |
| Post-intubation hypotension (SBP <100 mmHg) | 1249 (14.7) | 454 (36.8) |
| (missing = 206) | | |
| Medications[c] | | |
| Diazepam | 91 (1.1) | |
| Midazolam | 1913 (22.2) | |
| Ketamine | 615 (7.1) | |
| Fentanyl | 3621 (42.1) | |
| Morphine | 17 (0.2) | |
| Etomidate | 42 (0.5) | |
| Propofol | 5802 (67.4) | |

Percentages are of patients with values. Totals may not equal 100 due to rounding.
SD – standard deviation.
SBP – systolic blood pressure.
RSI – rapid sequence intubation.
ICU – intensive care unit.
ED – Emergency Department.
[a] Blood pressures presented are for patients age 13 and older. Not applicable for patients in arrest.
[b] Technique utilized on the first attempt.
[c] Totals may not equal 100% as patients may have received multiple post-intubation medications for sedation.

**Table 4**
Odds ratios for post-intubation sedation excluding patients presenting in either cardiac or traumatic arrest.

| Odds ratio of post-intubation sedation | Odds ratio (95% CI) |
|---|---|
| Age (in years) | 1 (1–1) |
| Gender | 0.91 (0.81–1.02) |
| Estimated weight in kg | 1 (1–1.01) |
| Pre-intubation systolic blood pressure (Hypotension vs not hypotensive) | 0.3 (0.26–0.35) |
| Indication (medical vs traumatic) | 1.84 (1.63–2.08) |
| Technique (RSI vs not RSI) | 4.46 (3.77–5.27) |
| Paralytic type (short acting vs long acting)[a] | 1.95 (1.72–2.22) |
| Post-intubation hypoxia | 0.98 (0.79–1.21) |
| Post-intubation hypotension | 0.29 (0.26–0.34) |

RSI – rapid sequence intubation.
kg – kilograms.
[a] Long acting paralytics included rocuronium and vecuronium while succinylcholine was considered short acting paralytic.

state of the practice. Similar to previous studies of post intubation sedation, we identified 1390 cases (11.8%) where patients received a NMBA for intubation and did not have a sedation medication documented, defined as a sedative medication given within 15 min of intubation [5]. Of these, 63% (876/1390) involve long-acting NMBAs (i.e. rocuronium or vecuronium) whose effect can persist well beyond the 15-minute time period captured by the NEAR dataset and have a half-life much greater then sedation medications typically used for RSI such as etomidate. Prior studies have suggested that a significant number of patients experience ongoing paralysis after the sedation medicine used in RSI is no longer active due to the very short clinical half-life of most induction agents [5]. Our findings suggest that short-acting neuromuscular blocking agents decrease the risk of not receiving sedation compared with long-acting NMBAs is particularly. This is particularly worrisome since this suggests that patient movement is a late reminder to initiate of post-intubation sedation, a strategy with unfortunate implications for patients receiving long-acting NMBAs. Additional work is needed to understand why a portion of ED patients do not receive post-intubation sedation and what efforts can be taken to help reduce the discomfort of intubation and negative effects that lack of sedation can incur.

### 4.1. Limitations

There are multiple limitations to our study. The NEAR database is based on physician reporting which can suffer from recall bias. Factors pertaining to patient vitals, choice of sedation medication, and patient characteristics are all self-reported by the practitioner. NEAR maintains a standard of registry-wide compliance of ≥90% which assures that the data entered into the system correspond to the overall intubation practices of the participating institutions however, due to the separate reporting system for NEAR, we are unable to verify each data element entered into the database. There is potential for both underreporting, due to recall bias, and for over reporting as there is potential for data entry into NEAR to prompt providers to administer post-intubation sedation if the dataset is completed shortly after the intubation is performed although we believe these limitations to be infrequent. NEAR also represents a set of EDs that are engaged in airway research at academic medical centers and these data may not represent post-intubation sedation rates in other settings such as community EDs. NEAR includes data primarily from United States EDs that utilize medication combinations that may differ from other countries; predominantly propofol and fentanyl. How these results generalize to other countries where other medications may be utilized will require further study. There is the potential for another provider to order post-intubation sedation (e.g. trauma team) while the ED provider entered data into NEAR. Limited work has previously examined the variables associated post-intubation sedation. While multivariable models can help to understand complex associations, this requires an understanding of valid, potential factors that can be inputted into a complex model. As such we performed a univariate analysis and future work will be needed to develop multivariable models to better understand post-intubation sedation characteristics more broadly [13]. The frequency with which non-emergency department providers ordered sedation during the time while a provider was entering data in NEAR, is unclear. The NEAR data form directly asks what medications were administered within 15 min of ETI. How many patients received sedation after that time period is unknown. Many of the intubations were performed by trainees at academic institutions with advanced resources (e.g. specialists, specialty care units, additional nursing staff, etc). How these data generalize to community practice, is unknown. As NEAR only reports if a patient receives specific medications, there may be other medications that were used for sedation (e.g. barbiturates, dexmedetomidine, etc.) although we believe the incidence of these medications to be rare. We are unable

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to determine the appropriateness of post-intubation sedation as level of sedation is not reported in the dataset. A prospective study will be needed to evaluate the appropriateness of the sedation. As the dataset only records if these medications were administered, we do not know the dosing or frequency (e.g. single dose or continuous infusion) of the administered medications.

## 5. Conclusion

Post-intubation sedation rates in NEAR are higher than previously reported. Factors including pre- and post-intubation hypotension are associated with lower odds of receiving post-intubation sedation while the use of RSI and succinylcholine are associated with higher odds of receiving post-intubation sedation.

## Financial disclosure

OL, DG, CK, AF, and JNC have no financial conflicts of interest to disclose.

RMW and CAB have potential financial conflicts of interest. They are both partners in Airway Management Education Center, LLC.

CAB is a member of the scientific advisory board for Verathon Inc. Verathon had no input into the study design, analysis, or decision to publish this work.

## Conflict of interest

The authors have no other conflicts of interest to disclose.

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## Presentation

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## Author contributions

RMW conceptualized, designed, built and managed the NEAR project since its inception. CAB co-managed the NEAR registry and had oversight of all aspects of NEAR. OL, DG, CK, AF, JNC, and CAB designed the data analysis for this manuscript. JNC drafted the manuscript, and all authors contributed substantially to its revision. JNC takes responsibility for the paper as a whole.

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