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Comparing Quick Sequential Organ Failure Assessment Scores to End-tidal Carbon Dioxide as Mortality Predictors in Prehospital Patients with Suspected Sepsis

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Introduction: Early identification of sepsis significantly improves outcomes, suggesting a role for prehospital screening. An end-tidal carbon dioxide ($ETCO_2$) value ≤ 25 mmHg predicts mortality and severe sepsis when used as part of a prehospital screening tool. Recently, the Quick Sequential Organ Failure Assessment (qSOFA) score was also derived as a tool for predicting poor outcomes in potentially septic patients.

Methods: We conducted a retrospective cohort study among patients transported by emergency medical services to compare the use of $ETCO_2$ ≤ 25 mmHg with qSOFA score of ≥ 2 as a predictor of mortality or diagnosis of severe sepsis in prehospital patients with suspected sepsis.

Results: By comparison of receiver operator characteristic curves, $ETCO_2$ had a higher discriminatory power to predict mortality, sepsis, and severe sepsis than qSOFA.

Conclusion: Both non-invasive measures were easily obtainable by prehospital personnel, with $ETCO_2$ performing slightly better as an outcome predictor. [West J Emerg Med. 2018;19(3)446-451.]

INTRODUCTION

Early identification and treatment of sepsis, including timely administration of intravenous fluids and antibiotics, has shown to significantly improve outcomes.[1-3] Many septic patients receive their initial care from prehospital personnel, providing an opportunity for early detection.[4,5] Hallmarks of severe sepsis include hypoperfusion, lactic acidosis, and organ failure. Exhaled end-tidal carbon dioxide ($ETCO_2$) has a negative correlation with serum lactate levels and a similar predictive value for poor outcomes in suspected sepsis.[6] In fact, prehospital $ETCO_2$ values of ≤ 25 mmHg may predict mortality and severe sepsis as part of a screening tool for potentially septic patients.[7,8] Recently, the Quick Sequential Organ Failure Assessment (qSOFA) score was derived as a tool for predicting poor outcomes, defined as mortality or admission to the intensive care unit (ICU) for ≥ 3 days, in patients with suspected sepsis.[9]

The qSOFA score is calculated by using altered mental status (defined by Glasgow Coma Scale [GCS] < 15), systolic blood pressure (SBP) ≤ 100 mm Hg, and respiratory rate (RR) ≥ 22 breaths per minute. Retrospective analysis suggests a qSOFA score of two or greater is associated with a high risk of poor outcomes. This score can be quickly calculated without the need for laboratory values, so it may have utility in the prehospital environment. This study aims to compare the use of $ETCO_2$ ≤

25 mmHg with qSOFA score of ≥ 2 as a predictor of mortality or diagnosis of severe sepsis in prehospital patients with suspected sepsis.

METHODS

Design and Setting

We conducted a retrospective cohort study among patients transported by a single emergency medical services (EMS) system to several regional hospitals during a one-year period from July 2014 through June 2015 in Orange County, Florida. The institutional review board at the participating hospitals approved the study protocol.

Inclusion criteria consisted of any case where a "sepsis alert" was activated by prehospital personnel. Per the Orange County EMS system (OCEMS) protocols, a sepsis alert is called when an adult patient (≥ 18 years) has a suspected infection, two or more of the following systemic inflammatory response syndrome (SIRS) criteria (temperature > 38° C or < 36° C, heart rate > 90 beats/min, or respiratory rate > 20 breaths/min) and an $ETCO_2$ level ≤ 25 mmHg. The protocol was established immediately prior to the study period; during the roll-out time, education was provided in the form of a short, online training module. However, there were variations in protocol compliance. For example, in 42% of the sepsis alerts, $ETCO_2$ values were > 25 mmHg. For the purposes of this study, the activation of the "sepsis alert" protocol defined our cohort of subjects with "suspected sepsis." Exclusion criteria included pediatric patients (< 18 years old) and patients without available hospital records.

Data Collection

Initial out-of-hospital data documented by first-arriving EMS personnel including SBP, respiratory rate (RR) and $ETCO_2$, were obtained using LIFEPAK® 15 multi-parameter defibrillator/monitors. Prehospital measurement of $ETCO_2$ is a standard practice performed by paramedics in the OCEMS via Microstream™ capnography using LIFEPAK® 15 devices (PhysioControl, Redmond, WA). $ETCO_2$ was recorded when capnographic wave peaks were at a constant end-tidal for 3-5 respirations as directed by protocol. All included patients were spontaneously breathing at the time of evaluation.

We obtained patient age, gender, race, $ETCO_2$, RR, SBP, and GCS from prehospital run reports. Patient mortality, admission to hospital or ICU, initial ED vital signs, pertinent past medical history, principal and admitting diagnoses defined by *International Classes of Disease, Ninth Revision, Clinical Modification* (ICD-9) codes, were obtained from the hospital chart. qSOFA scores (GCS < 15, SBP ≤ 100 mm Hg, and RR ≥ 22 breaths per minute) were calculated from the data collected from prehospital run reports. We used the ICD-9 principal diagnosis to define the diagnosis of "sepsis" or "severe sepsis." The chart reviewers were not blinded to the primary or secondary outcomes; however, only objective, complete data were abstracted from the charts. Records were linked by manual archiving of EMS and hospital data.

The primary outcome was the relationship between $ETCO_2$ and qSOFA scores and hospital mortality. The secondary outcome was diagnosis of sepsis or severe sepsis upon hospital admission.

Analysis

We described data using means and proportions with 95% confidence intervals (CI). Data were assessed for variance and distribution and comparisons between groups were performed using Fisher's exact test and independent sample t-tests with pooled or separate variance as appropriate. We constructed receiver operating characteristics (ROC) curves to assess the performance of $ETCO_2$, and qSOFA for predicting severe sepsis and mortality. Significance was set at 0.05. We analyzed data using STATA (StataCorp, College Station, TX).

RESULTS

Over the study period, 330 sepsis alerts were activated, 289 patients had complete prehospital and hospital records allowing for analysis for the primary outcome, and 287 patients had enough available records for analysis of the secondary outcome. Of the 203 patients with a final diagnosis of sepsis, 86 had a final diagnosis of severe sepsis, and among those 25 patients died. Patients with severe sepsis had lower $ETCO_2$ values and higher serum lactate levels (see Table). There was a varied distribution of qSOFA scores; however, those with a score of 3 were more likely to be diagnosed with severe sepsis (see Table).

We constructed ROC curves to determine the accuracy of prehospital $ETCO_2$ levels and qSOFA scores for predicting outcomes when a sepsis alert was activated. The area under the ROC curve predicting mortality was 0.69 for $ETCO_2$ (95% CI [0.59-0.80]; p=0.001) and 0.57 for qSOFA (95% CI [0.44-0.69]; p=0.277, see Figure 1A). Combining $ETCO_2$ and qSOFA scores resulted in an area under the ROC curve of 0.70 (95% CI [0.59-0.82]; p=0.001). The area under the ROC curve predicting sepsis was 0.66 for $ETCO_2$ (95% CI [0.59-0.72]; p<0.001) and 0.61 for qSOFA (95% CI [0.54-0.68]; p=0.002, see Figure 1B). Combining $ETCO_2$ and qSOFA scores resulted in an area under the ROC curve of 0.68 (95% CI [0.62-0.74]; p<0.001). The area under the ROC curve predicting severe sepsis was 0.78 for $ETCO_2$ (95% CI [0.72-0.84]; p<0.001) and 0.69 for qSOFA (95% CI [0.62-0.75]; p<0.001, see Figure 1C). Combining $ETCO_2$ and qSOFA scores resulted in an area under the ROC curve of 0.81 (95% CI [0.75-0.86]; p<0.001).

To better establish the effectiveness of the designed cut-off values for both outcome predictors, we performed comparisons between $ETCO_2$ ≤ 25 mmHg and qSOFA scores of ≥ 2. Sensitivity and specificity for $ETCO_2$ as a mortality predictor was higher, 80% (95% CI [59-92]) vs. 68% (95% CI [46-84]), and 42% (95% CI [36-48]) vs. 40% (95% CI [34-46]), respectively, than qSOFA score. Using both $ETCO_2$ and qSOFA scores resulted in a sensitivity of 60% (95% CI [39-78]) and a specificity of 62% (95% CI [55-67]). Using

Table. Demographics of patients with a final diagnosis of sepsis.

	Sepsis N=203	Severe sepsis N=86	Total N=289	P value
Age (n=289)	69 (SD18)	74 (SD15)	70 (SD17)	0.034
Gender (female) (n=289)	108 (53%)	41 (48%)	149 (52%)	0.440
Admitted (n=287)	193 (96%)	85 (100%)	278 (97%)	0.062
Admitted to ICU (n=285)	49 (25%)	50 (59%)	99 (35%)	<0.001
Hospital mortality (n=288)	9 (5%)	16 (19%)	25 (9%)	<0.001
Admitting diagnosis (n=287)				
Abdominal/GI	14 (7%)	2 (2%)	16 (6%)	
Altered mental status	19 (10%)	6 (7%)	25 (9%)	
Cardiac/vascular	3 (2%)	1 (1%)	4 (1%)	
Respiratory	35 (17%)	8 (9%)	43 (15%)	0.009
Infection	85 (42%)	60 (70%)	145 (52%)	
Neurologic	3 (2%)	0 (0)	3 (1%)	
Metabolic/endocrine	9 (5%)	2 (2%)	11 (4%)	
Renal/urinary	26 (13%)	4 (5%)	30 (11%)	
Other	7 (4%)	3 (4%)	10 (4%)	
At least 2 SIRS criteria	187 (93%)	84 (98%)	271 (94%)	0.108
qSOFA score				
0	12 (6%)	2 (2%)	14 (5%)	
1	84 (41%)	17 (20%)	101 (35%)	<0.001
2	94 (46%)	40 (47%)	134 (46%)	
3	13 (6%)	27 (31%)	40 (14%)	
$ETCO_2$ [95% CI]	28 [27-29]	19 [18-22]]	25 [24-16]	<0.001
Lactate (n=228)	1.9 [1.8-2.1]	5.4 [4.8-6.2]	3.2 [2.8-3.5]	<0.001
HCO_3 (n=259)	24 [23-24]	20 [19-22]	23 [22-23]	<0.001

ICU, intensive care unit; *GI*, gastrointestinal; *SIRS*, systematic inflammatory response syndrome; *qSOFA*, quick Sequential Organ Failure Assessment.

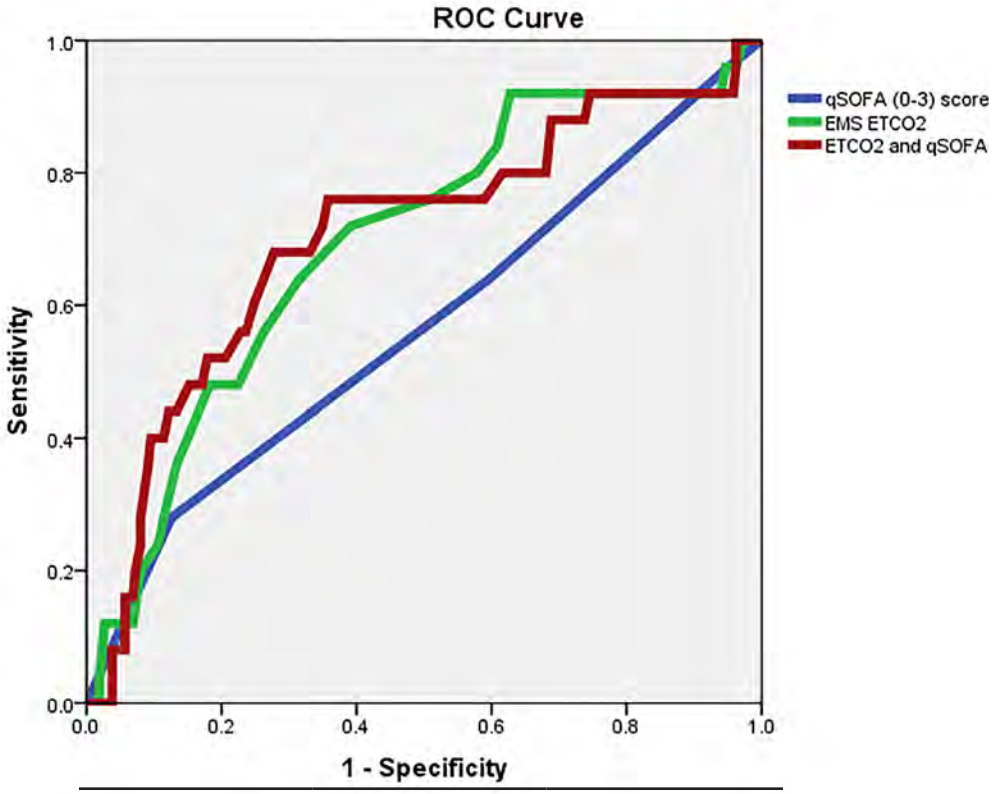
either $ETCO_2$ or qSOFA score increased the sensitivity of our screening tool to 88% (95% CI [68-97]); however, this resulted in a specificity of just 20% (95% CI [16-26]).

DISCUSSION

While both $ETCO_2$ values and qSOFA scores are easily obtainable within the current system, this study suggests that $ETCO_2$ may have a higher discriminatory power to predict mortality and severe sepsis in potentially septic prehospital patients. Adding qSOFA scores to the $ETCO_2$ protocol for identifying sepsis slightly increased sensitivity, but dramatically decreased specificity; thus, it did not add value to the existing screening tool. However, these data suggest that qSOFA may be predictive of sepsis and severe sepsis, providing an outcome predictor in austere environments or where capnography is unavailable.

Studies have shown relationships between $ETCO_2$ and disease severity in patients with shock,[11] sepsis,[7,8,12] and trauma.[13-15] $ETCO_2$ is decreased due to respiratory compensation (hyperventilation) in acidotic states, and poor perfusion of alveoli in the setting of cryptic and frank shock. One advantage of $ETCO_2$ relative to serum lactate is that it can be measured immediately and noninvasively, making it a simple, clinically useful outcome predictor for prehospital providers. The qSOFA score uses several traditionally measured variables to predict organ failure and shares the advantage of immediate and non-invasive calculation. Some of the overlap in predictive value between the two measures may be due to the inclusion of hyperventilation (which may lead to reduced $ETCO_2$) in the calculation of the qSOFA score. The current study suggests that while qSOFA scores may assist in predicting sepsis and severe sepsis in the prehospital setting, $ETCO_2$ levels had a slightly higher discriminatory power for poor outcomes.

The qSOFA score was created as part of the approach taken



	AUROC	P value
qSOFA (0-3)	0.57 (0.44-0.69)	0.277
EMS $ETCO_2$	0.69 (0.59-0.80)	0.001
qSOFA and $ETCO_2$	0.70 (0.59-0.82)	0.001

Figure 1A. Receiver operating characteristic (ROC) curves for predicting mortality.
AUROC,area under receiver operating characteristic curve; *qSOFA*, quick Sequential Organ Failure Assessment, *EMS*, emergency medical services; *$ETCO_2$*, end-tidal carbon dioxide.

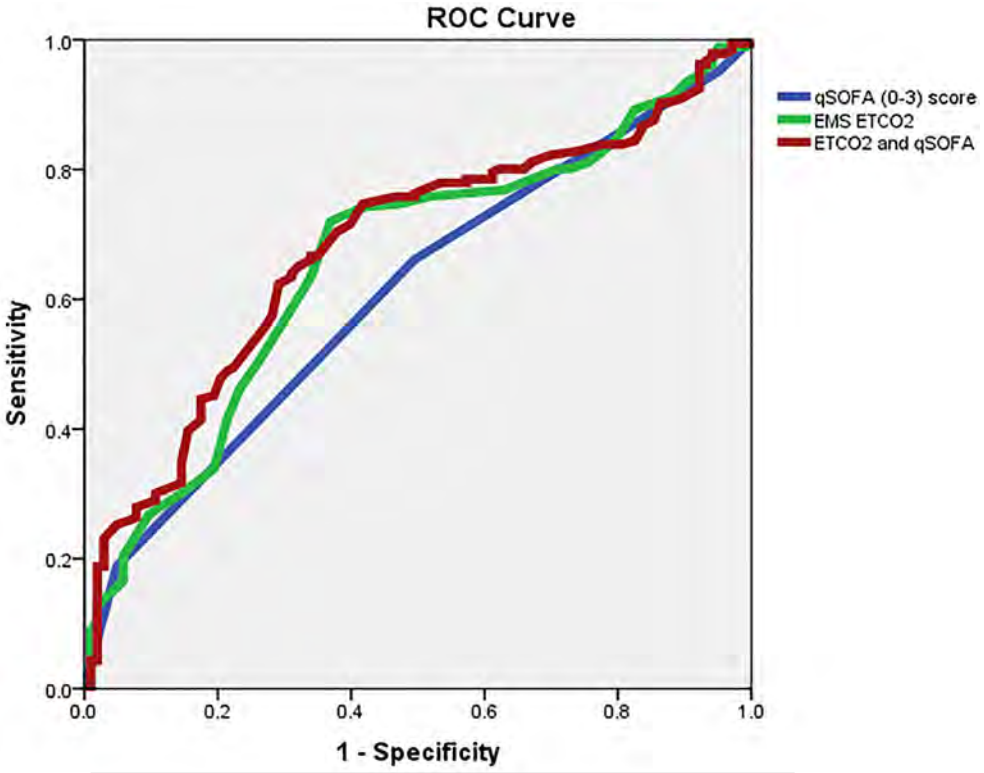
by the Third International Consensus Definitions for Sepsis and Septic Shock to redefine sepsis, with an emphasis on using organ failure to measure severity rather than systemic inflammation.[10] Traditional sequential organ failure analysis (SOFA) score is calculated using variables that include laboratory analysis, and is trended over time. Interestingly, increased SOFA scores correlate with decreased $ETCO_2$ levels in patients with suspected sepsis.[12] The qSOFA score was created to provide a tool for emergency providers without access to all of the variables required for SOFA scoring. This study suggests the qSOFA score may be useful as a prehospital sepsis screening tool. The redefined definitions no longer separate the disease process into "sepsis" and "severe sepsis," only recognizing "sepsis and "septic shock."[10] Since the current data were collected and analyzed prior to this refined definition, we used ICD-9 codes for "sepsis" and "severe sepsis." While the current study suggests both $ETCO_2$ and qSOFA may assist prehospital providers in identifying septic patients, further study is necessary to determine the utility of prehospital outcome predictors in relation to the new definitions.

LIMITATIONS

There are several limitations to this study. First, the qSOFA scores were retrospectively calculated. In addition, the sepsis alert protocol used was in the initiation phases during data collection, so suspicion of sepsis may not have been as high by paramedics as it is now that more training has been provided. Of note, the most difficult and subjective portion of diagnosing sepsis - both in the field and in the hospital - remains the clinical diagnosis of suspected infection, which neither $ETCO_2$ nor qSOFA alone can assist with.

CONCLUSION

The findings of the current study suggest that $ETCO_2$ performed slightly better than qSOFA scoring as a predictor of mortality from severe sepsis and the diagnosis of severe sepsis in prehospital patients with suspected sepsis. Further, prospective validation is necessary to determine the utility of qSOFA as an outcome measure applied to a wide cohort of potentially septic, prehospital patients.



	AUROC	P value
qSOFA (0-3)	0.61 (0.54-0.68)	0.002
EMS $ETCO_2$	0.66 (0.59-0.72)	<0.001
qSOFA and $ETCO_2$	0.68 (0.62-0.74)	<0.001

Figure 1B. Receiver operating characteristic (ROC) curves for predicting sepsis.
AUROC,area under receiver operating characteristic curve; *qSOFA*, quick Sequential Organ Failure Assessment, *EMS*, emergency medical services; *$ETCO_2$*, end-tidal carbon dioxide.

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This work is in memory of Dr. Salvatore Silvestri.

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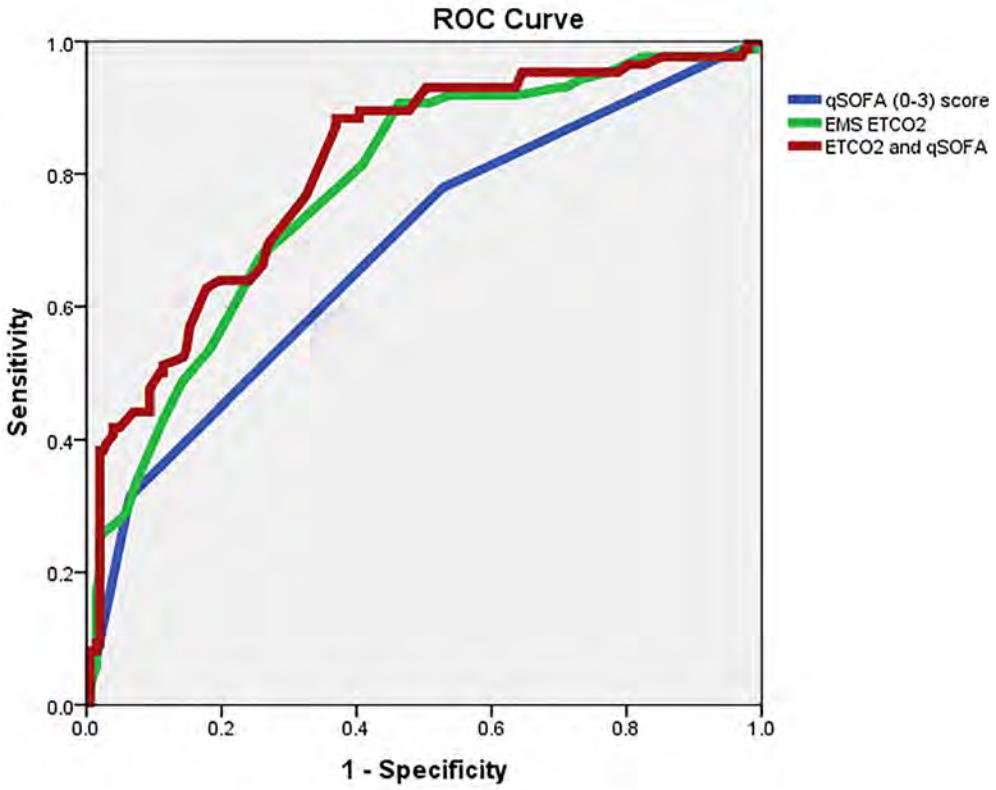

	AUROC	P value
qSOFA (0-3)	0.69 (0.62-0.75)	<0.001
EMS $ETCO_2$	0.78 (0.72-0.84)	<0.001
qSOFA and $ETCO_2$	0.81 (0.75-0.86)	<0.001

Figure 1C. ROC curves for predicting severe sepsis.
AUROC,area under receiver operating characteristic curve; *qSOFA*, quick Sequential Organ Failure Assessment, *EMS*, emergency medical services; *$ETCO_2$*, end-tidal carbon dioxide.

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Severely Elevated Blood Pressure and Early Mortality in Children with Traumatic Brain Injuries: The Neglected End of the Spectrum

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Introduction: In adults with traumatic brain injuries (TBI), hypotension and hypertension at presentation are associated with mortality. The effect of age-adjusted blood pressure in children with TBI has been insufficiently studied. We sought to determine if age-adjusted hypertension in children with severe TBI is associated with mortality.

Methods: This was a retrospective analysis of the Department of Defense Trauma Registry (DoDTR) between 2001 and 2013. We included for analysis patients <18 years with severe TBI defined as Abbreviated Injury Severity (AIS) scores of the head ≥3. We defined hypertension as moderate for systolic blood pressures (SBP) between the 95th and 99th percentile for age and gender and severe if greater than the 99th percentile. Hypotension was defined as SBP <90 mmHg for children >10 years or < 70mmHg + (2 x age) for children ≤10 years. We performed multivariable logistic regression and Cox regression to determine if BP categories were associated with mortality.

Results: Of 4,990 children included in the DoDTR, 740 met criteria for analysis. Fifty patients (6.8%) were hypotensive upon arrival to the ED, 385 (52.0%) were normotensive, 115 (15.5%) had moderate hypertension, and 190 (25.7%) had severe hypertension. When compared to normotensive patients, moderate and severe hypertension patients had similar Injury Severity Scores, similar AIS head scores, and similar frequencies of neurosurgical procedures. Multivariable logistic regression demonstrated that hypotension (odd ratio [OR] 2.85, 95 confidence interval [CI] 1.26-6.47) and severe hypertension (OR 2.58, 95 CI 1.32-5.03) were associated with increased 24-hour mortality. Neither hypotension (Hazard ratio (HR) 1.52, 95 CI 0.74-3.11) nor severe hypertension (HR 1.65, 95 CI 0.65-2.30) was associated with time to mortality.

Conclusion: Pediatric age-adjusted hypertension is frequent after severe TBI. Severe hypertension is strongly associated with 24-hour mortality. Pediatric age-adjusted blood pressure needs to be further evaluated as a critical marker of early mortality. [West J Emerg Med. 2018;19(3)452–459.]

INTRODUCTION

Within the United States, an estimated 50,000 children are hospitalized and 3,000 die each year following traumatic brain injury (TBI).[1] TBI accounts for almost one-half of all deaths in children older than one year of age and is a leading cause of lost productive life-years in the U.S. Increased recognition of TBI in children as a major cause of childhood morbidity and mortality has led to advances in injury prevention and emphasizes the need for new therapies to improve long-term outcomes.[1-3] Despite this, substantial knowledge gaps remain in the early management of pediatric patients with TBIs.

A foundational aspect in the management of severe TBIs is optimization of systemic hemodynamics, as both hypotension and hypoxia have been shown to be associated with adverse outcomes.[4-6] Cerebral perfusion is principally determined by the systemic blood pressure (BP) and intracranial pressure (ICP). Maximizing cerebral perfusion pressure through reductions in ICP and elevations in mean arterial pressure (MAP) are the basis for current treatment algorithms for adults with TBIs.[5-7] After restoration of euvolemia by volume administration, vasopressors are used to increase MAP to maintain a cerebral perfusion pressure of at least 40 mmHg.[8-10] It is unclear whether hypertension or "supernormal" BP is of any benefit, or potentially harmful, in pediatric patients.

Although hypertension during the first 72 hours after injury has been associated with improved outcomes in children with TBIs,[11] emerging evidence in adult TBIs has identified an association between early episodes of hypertension and increased mortality.[12-14] Elevated BP can lead to breakdown of the blood brain barrier and increase cerebral edema through hydrostatic forces.[15] Although vasopressors are used at times to maximize cerebral perfusion, cerebral edema coupled with exogenous vasopressors can lead to a reduction in blood flow to at-risk brain regions that were initially non-ischemic.[16] This suggests a complex relationship between systemic BP, particularly at extremes, and TBI outcomes.

We hypothesized that age-adjusted BP elevation is associated with worse outcomes in hospitalized children with TBIs. We analyzed the Department of Defense Trauma Registry (DoDTR) that contained data from 2001 to 2013 to describe associations between emergency department (ED) BP and outcomes in children with TBIs cared for at U.S. military hospitals in Iraq and Afghanistan.

Population Health Research Capsule

What do we already know about this issue?
In children with traumatic brain injuries, hypotension is associated with increased mortality. No studies have described an association between hypertension and mortality in these children.

What was the research question?
Among children with severe traumatic brain injuries (TBIs), is age-adjusted hypertension associated with mortality?

What was the major finding of the study?
Age-adjusted hypertension is common and strongly associated with 24-hour mortality among children with severe TBIs.

How does this improve population health?
Our findings suggest that age-adjusted hypertension is equally predictive of morality as hypotension in these children. Future work is needed to understand the mechanisms behind this finding.

MATERIALS and METHODS

Study Design, Setting, Population

This study was initiated and conducted under a protocol approved by the San Antonio Military Medical Center Institutional Review Board. This was a retrospective study of patients <18 years old entered into the DoDTR from 2001 to 2013 in Iraq and Afghanistan. This registry has been described in detail in prior publications.[17-18] Briefly, the registry is a prospectively collected dataset of all military and civilian patients from military conflicts in which the U.S. participated. While in the theatre of war, trained nurses abstracted patient data into the DoDTR with no knowledge of future studies. There were no patient records available to obtain any further information.

For this study, we excluded patients with non-traumatic mechanisms of injury (drowning and asphyxiation), primary thermal injuries, and with an absent pulse or missing BP measurement. We used AIS scores to define severity of TBI to overcome any potential language barriers that may have confounded arrival Glasgow Coma Scale (GCS) scores, and to allow for the identification of a comparison group of patients with isolated thoracic and abdominal trauma. Patients were considered to have a severe isolated TBI if their Abbreviated Injury Scale (AIS) of head, neck, and cervical spine was ≥3 and all remaining AIS scores were <3. We identified a comparison group of children with non-TBI trauma as having an AIS-head <3 with AIS of the chest, abdomen, or pelvic region ≥3.

Variables Collected and Outcome Measures

The primary outcome measures were 24-hour mortality and mortality prior to discharge. Demographic and physiologic data elements collected from the registry included age, sex, weight, arrival BP, heart rate, oxygen saturation, and temperature. Injury

mechanism, the injury severity score, AIS scores, and the GCS score were collected as markers of injury severity. We also collected total resuscitation fluids administered, ED intubation, neurosurgical interventions, total number of hospital days, number of days of mechanical ventilation, intensive care unit (ICU) length of stay, 24-hour mortality, and survival to hospital discharge. Only the arrival BP is included in the DoDTR.

We generated age- and gender-adjusted BPs using the American Heart Association Guidelines for the Diagnosis of Pediatric Hypertension.[19] The DoDTR dataset does not include height as an independent variable; therefore, we used the 50th percentile for height for a given age and gender based on World Health Organization (WHO) child growth standards. Moderate hypertension was defined as the 95th to 99th percentile for age and sex and severe hypertension was defined as greater than the 99th percentile. Hypotension was defined as a systolic blood pressure (SBP) <90mmHg for children older than 10 years, or less then 70mmHg + (2 x age) for children 10 years and younger. We defined a neurosurgical procedure as any procedure that required access to the cranium.[20] Age-adjusted rates of bradycardia were calculated using Pediatric Advanced Life Support definitions.[21]

Data Management and Statistical Analysis

We transferred all data into STATA version 12.0 (College Station, TX) for statistical analyses. All frequency data are presented as prevalence estimates with 95% confidence intervals (CI). Normally distributed continuous data were reported as mean with standard deviations (SD), and ordinal or non-normally distributed continuous data were described with medians with interquartile ranges. We performed bivariable analysis of categorical variables using the χ^2 test, and we analyzed continuous variables using Student's-t test, or one-way analysis of variance with Bonferroni correction, as appropriate. We performed multivariable logistic regression to estimate associations between demographics, arrival BP, and 24-hour survival, adjusting for other variables and potential confounders. We used a Cox-proportional hazards model to determine the association of BP with in-hospital mortality, using a time unit of days. Individual characteristics considered for the model were age, sex, mechanism of injury, ED GCS score, arrival oxygen saturation, arrival BP category, ISS, ED intubation, neurosurgical intervention, and whether mechanical ventilation was required. In our regression models, we used stepwise variable inclusion; however, we forced patient demographics and injury mechanisms into the final models.

To minimize bias and preserve study power, we used multiple imputation for missing values (STATA 12.0, College Station, TX). Arrival oxygen saturation was missing for 21.2% of patients and arrival GCS scores were missing in 7.6%. To perform the multiple imputation, we used a multivariable normal model to derive 10 datasets. Included in the model were the following variables: age, gender, AIS-head, ISS, arrival oxygen saturation, arrival SBP, ED intubation, volume of blood product transfused, neurosurgical procedure, days on ventilator, ICU days, total hospital days, death within the first 24 hours, and in-hospital mortality. We performed a sensitivity analysis using only complete cases to examine the assumptions of our imputation on arrival GCS and mortality.

RESULTS

Characteristics of Study Population

During the study period, 4,990 patients <18 years were included in the DoDTR. Of these, 632 patients (12.7%) were excluded for drowning or thermal burns, and 311 (6.2%) were excluded for missing SBP. Of the remaining 4,047 patients, 1,933 (47.8%) either had minor head injuries or had severe torso and pelvic injuries associated with their TBIs and were excluded from analysis. This left 740 patients (18.3%) with severe, isolated TBIs as defined by AIS, and 1,374 patients (34.0%) with isolated torso and pelvic injuries without an associated severe TBI (Figure 1).

Main Results

Patients 0-2 years old had the highest incidence of severe hypertension (17, 50.0%) and patients 14-18 years old had the highest incidence of normotension (64, 65.3%) upon arrival to the ED (Table 1). There were no significant differences in rates of bradycardia across all BP categories. Patients who were hypotensive upon arrival to the ED had lower GCS scores, higher ISS, higher AIS-head, and were intubated more often than those who were not hypotensive on arrival (Table 1). There were no significant differences in ED GCS, ISS, AIS-head, or ED intubation between normotensive, moderate hypertensive, and severely hypertensive patients on post-hoc comparisons (Table 1).

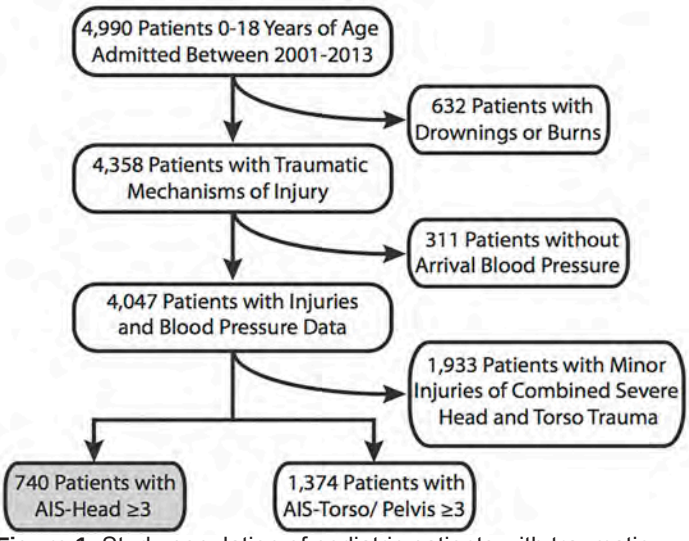

Figure 1. Study population of pediatric patients with traumatic brain injury.
AIS, Abbreviated Injury Severity.

Table 1. Patient demographics and injury characteristics stratified by blood pressure group.

	Hypotensive (N=50)		Normotensive (N=385)		Moderate hypertension (N=115)		Severe hypertension (N=190)		P value
Age (years) (N,%)									<0.01
0-2	1	2.9	15	44.1	1	2.9	17	50.0	
2-5	8	6.0	56	42.1	24	18.1	45	33.8	
5-10	20	7.1	138	48.9	45	16.0	79	28.0	
10-14	16	8.3	112	58.0	26	13.5	39	20.2	
14-18	5	5.1	64	65.3	19	19.4	10	10.2	
Sex (N,%)									0.81
Male	36	72.0	288	74.8	84	73.0	135	71.1	
Female	14	28.0	97	25.2	31	27.0	55	28.9	
Mechanism (N,%)									0.15
Blast	18	36.0	125	32.5	38	33.0	68	35.8	
Blunt	12	24.0	162	42.1	52	45.2	75	39.5	
Penetrating	20	40.0	98	25.5	25	21.7	47	24.7	
ED GCS (median, IQR)	3	3,6	9	3,9	9	3,15	9	3,15	<0.01
Arrival O_2 saturation (mean, 95% CI)	95.1	91.5-98.8	97.4	96.5-98.3	98.1	97.1-99.0	97.1	96.0-98.3	0.23
Bradycardic in ED (N,%)	1	2.0	6	1.6	1	0.9	8	4.2	0.15
ISS (mean, 95% CI)	21.6	18.9-24.7	17.3	16.3-18.3	15.9	14.6-17.2	16.4	15.3-17.5	<0.01
AIS head (mean, 95% CI)	4.3	4.0-4.5	3.7	3.6-3.8	3.6	3.5-3.8	3.7	3.6-3.8	0.83
ED intubation (N,%)	33	66.0	148	38.4	36	31.3	58	30.5	<0.01
Neurosurgical procedure (N,%)	18	36.0	136	35.3	41	35.7	68	35.8	0.99
Ventilator days (median, IQR)	1.5	1,3	1	0,2	1	0,2	1	0,2	<0.01
ICU days (median, IQR)	2	1,5	2	1,4	2	1,4	2	1,4	<0.01
Hospital days (median, IQR)	2.5	1,6	3	2,7	3	1,6	3	1,6	<0.01
Died in 1st 24 hours (N,%)	13	26.0	23	6.0	6	5.2	24	12.6	<0.01
Died in hospital (N,%)	23	46.0	57	14.8	12	10.4	38	20.0	<0.01

ED, emergency department; *GCS*, Glasgow Coma Scale; *IQR*, interquartile range; *CI*, confidence interval; *ISS*, injury severity score; *AIS*, Abbreviated Injury Severity; *ICU*, intensive care unit.

Evaluation of 24-hour mortality and in-hospital mortality in an unadjusted analysis demonstrated a U-shaped distribution with hypotensive patients having the highest 24-hour and in-hospital mortality followed by patients with severe hypertension (Table 1, Figure 2).

Figure 3 demonstrates a Kaplan-Meier survival curve for each BP group. When compared to normotensive patients and patients with moderate hypertension, patients with severe hypertension had increased 24-hour mortality, which plateaued to mirror normotensive patients by 14 days. To determine if BP categories were associated with early mortality, we performed a multivariable logistic regression analysis to adjust for demographics and injury severity. Hypotension and severe hypertension were associated with increased 24-hour mortality (Table 2). A sub-analysis of patients presenting with a GCS ≤8 also demonstrated a

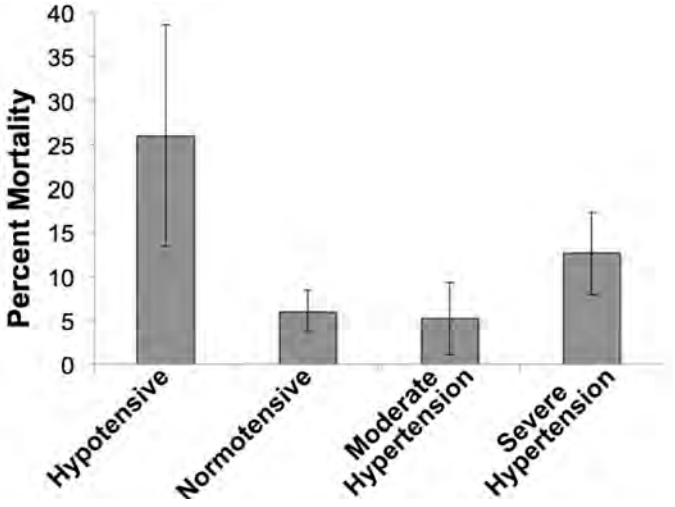

Figure 2. 24-hour mortality by blood pressure category (%, 95CI).

Table 2. Multivariable logistic regression of mortality within first 24 hours.

	Odds ratio	95% CI	P
Age	1.0	0.93-1.07	1.0
Penetrating injury	0.98	0.53-1.81	0.95
ED GCS	0.72	0.65-0.80	<0.01
AIS head	1.69	1.21-2.36	<0.01
ED intubation	0.28	0.15-0.54	<0.01
Blood pressure			
Hypotensive	2.85	1.26-6.47	0.01
Normotensive		Reference	
95th-99th percentile	0.89	0.33-2.40	0.81
>99th percentile	2.58	1.32-5.03	<0.01

CI, confidence interval; *GCS*, Glasgow Coma Scale; *AIS*, Abbreviated Injury Scale; *ED*, emergency department

U-shaped association between presenting BP and 24-hour mortality (Supplemental Table 1). In a Cox regression of in-hospital mortality adjusted for demographics and injury severity, hypotension and severe hypertension were associated with mortality, but once deaths within the first 24 hours were removed, arrival BP categories were no longer associated with in-hospital mortality (Table 3). A sensitivity analysis using complete cases demonstrated similar associations between BP categories and 24-hour mortality (Supplemental Table 2).

Finally, to determine if the association between hypertension and mortality was specific to patients with TBIs, we identified a second cohort of patients with isolated severe torso and abdominal trauma. In multivariable logistic regression analyses and Cox regression analysis severe hypertension was not associated with 24-hour mortality (Supplemental Table 3) or overall mortality (Supplemental Table 4).

DISCUSSION

The present study demonstrates that age-adjusted BP greater than the 99th percentile is common in children with severe TBIs, affecting approximately one-quarter of patients. Furthermore, BP greater than the 99th percentile in children with isolated severe head injuries is associated with 24-hour mortality, and neither hypotension nor severe hypertension is associated with in-hospital mortality after accounting for early deaths. The strength of this association coupled with conflicting reports on the consequences of hypertension in pediatric TBI, reinforces the importance of continued investigation into the causes and effects of hypertension after TBI.

Analyses of hemodynamic parameters in critically injured children present substantial challenges due to the wide variation in age-adjusted normal BPs. For example, the upper limit of normal BP varies from 110 mmHg in a one-year-old female to 143 mmHg in a 17-year-old male.[19] The need to account for differences in physiology based on age is essential in pediatric outcomes research. Prior pediatric TBI studies have demonstrated that age-adjusted hypotension, as compared to a fixed BP cutoff, is associated with worse outcomes,[6,22] and in this manuscript we reported a rate of pediatric hypertension that is higher than rates reported in adult patients suffering from TBIs. The International Mission for Prognosis and Analysis of Clinical Trials in TBI Study, which combined results from nine large, randomized, controlled trials of adult patients with TBIs, reported that the incidence of hypertension varies from 10.3-36.5% with an average of 22%.[13] By comparison, in the current pediatric cohort, the overall incidence of age-adjusted hypertension upon arrival to the ED was much higher.

Table 3. Cox regression analysis of in-hospital mortality.

	All patients			Excluding 24 hour deaths		
	Hazard ratio	95% CI	P value	Hazard ratio	95% CI	P value
Age	1.00	0.96-1.05	0.77	1.00	0.94-1.06	0.97
Penetrating injury	1.14	0.78-1.65	0.50	1.25	0.74-2.11	0.40
ED GCS	0.79	0.74-0.84	<0.01	0.82	0.75-0.91	<0.01
AIS head	1.56	1.26-1.93	<0.01	1.62	1.19-2.20	<0.01
ED intubation	0.57	0.37-0.86	<0.01	0.90	0.46-1.74	0.75
Blood pressure						
Hypotensive	1.82	1.10-3.01	0.02	1.52	0.74-3.11	0.26
Normotensive			Reference			
95th-99th percentile	0.84	0.44-1.58	0.58	0.76	0.32-1.84	0.55
>99th percentile	1.65	1.09-2.52	0.02	1.22	0.65-2.30	0.54

CI, confidence interval; *GCS*, Glasgow Coma Scale; *AIS*, Abbreviated Injury Scale; *ED*, emergency department.

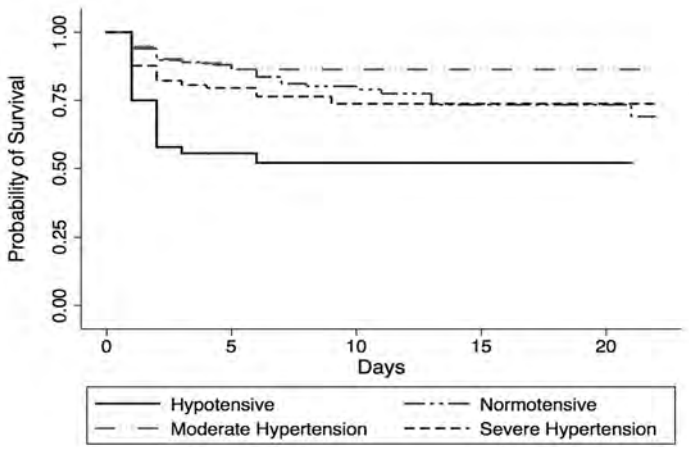

Figure 3. Kaplan Meier curve by blood pressure category.

Traditionally, children are thought to have a well-preserved ability to maintain vascular tone and BP even in the setting of early shock. It may be that these same cardiovascular mechanisms produce an exaggerated BP response to TBI, resulting in a high frequency of age-adjusted hypertension after TBI. If this effect is age-specific, with infants more greatly affected than older children, it would further explain the age-dependent frequency of severe hypertension that we observed. In our study, infants constituted the largest percentage of patients in both hypertension groups. Although one would assume that this is a protective mechanism to preserve cerebral blood flow, the etiology of the association with higher mortality is not clear and requires further study.

Within the field of adult neurotrauma, there is continued debate surrounding hypertension and TBI. Prior research has demonstrated that once a patient has been stabilized in the ICU, maximizing cerebral perfusion pressure with permissive hypertension or induced hypertension results in improved outcomes.[8,16,23-25] Emerging evidence challenges this conventional wisdom. A large retrospective analysis of the National Trauma Data Bank demonstrated an increase in mortality with ED SBPs ≥140 mmHg on adjusted analysis.[12] Similar studies using the European Trauma Database as well as the IMPACT dataset demonstrated an association between hypertension and mortality on bivariable analysis; however, this association was largely mitigated after adjusting for demographic and injury characteristics.[13,14] Our findings are consistent with those of Zafar et al., which suggest an underlying pathology of early systemic BP after TBI that may be under-appreciated.

Changes in cerebral perfusion are thought to follow a distinct time course after TBI; an initial period of hypoperfusion during the first 6-12 hours is followed by a period of hyperemia, and finally a phase of hypoperfusion returns characterized by vasospasm and recurrent ischemia.[26,27] This pattern of cerebral blood flow suggests that early episodes of hypertension could be neuroprotective by increasing cerebral perfusion pressure and overcoming periods of low flow. While characterization of cerebral blood flow and cerebral perfusion often occurs in the ICU setting after patients have been stabilized and may have undergone neurosurgical intervention, the BP measurements we report were recorded upon ED arrival, and likely represent an earlier phase of injury not described in previous studies.

The consequences of hypertension at this early time point may be different than hypertension several hours later after clot stabilization and the onset of increased ICP. Early hypertension may destabilize developing blood clots, increase vasogenic edema, and lead to increased ICP, while late elevations in SBP may maximize perfusion in the setting of increased ICP. Prospective trials with intensive, continuous SBP and ICP monitoring will be required to fully understand the role of BP early after TBI.

One of the only other studies to specifically investigate the role of hypertension in pediatric neurotrauma outcomes demonstrated that hypertension in the first 72 hours following severe TBIs (with GCS scores ≤8) was associated with improved outcomes.[11] In that particular study, a non-age adjusted SBP of 135 mmHg was associated with an 18.8-fold increase in survival.[11] A BP threshold of 135 mmHg is greater than the 99th percentile for boys younger than 14 years and girls younger than 16 years,[19] and stands in contrast to the current study's findings. To limit ambiguity in the current study, patients with isolated and predominant head injuries were identified in order to reduce confounding of the hemodynamic effects and outcomes resulting from substantial non-cranial injuries. The inclusion of severe thoracic and abdominal trauma within the patient population studied by previous investigators may partially explain the improved outcomes in patients with hypertension. These discordant findings between studies emphasize the need for prospective analysis of patient hemodynamics and outcomes after TBIs in children.

Similar to other studies, we have demonstrated a strong association between hypotension on ED arrival and mortality.[4,6,12-14] This patient population differed significantly from the other populations in several critical ways. First, the hypotensive patients had higher ISS, higher incidence of endotracheal intubation while in the ED, as well as lower arrival GCS scores. In general, this was a sicker patient population. The hypotensive patients also had a non-statistically significant higher frequency of penetrating trauma as the cause of injury when compared to the other groups, and in total these differences were associated with worse outcomes across all measured parameters including time on the ventilator, time in the ICU, and mortality. What is surprising is that once injury severity, GCS, and the need for emergent intubation were included in the regression

models, both hypotension and severe hypertension had similar magnitudes of effect on mortality. Although the mechanisms of hypotension on poor outcomes have been linked to poor perfusion and tissue ischemia, further work is needed to understand potential mechanisms to explain the effect of hypertension on TBI.

The lack of radiographic analysis within the trauma database prevented estimation of the size of brain injury or the rate of cerebral herniation that may have accompanied hypertension. Rates of bradycardia, a proxy for cerebral herniation in the setting of hypertension, were not significantly different across all BP categories, suggesting hypertension was not independently associated with bradycardia and was not the result of cerebral herniation. Furthermore, inclusion of bradycardia within the regression models was not associated with increased mortality and did not change the point estimates for the severe hypertension group. Consequently, it was not included in the final regression models.

LIMITATIONS

This study is subject to several limitations. In addition to the inherent issues of its retrospective design, the study patient population and the types of medical facilities within Iraq and Afghanistan differ from civilian medical centers and may limit the generalizability of our findings. Furthermore, due to a lack of published pediatric BP normal ranges in Iraq and Afghanistan, we had to use BP norms derived from U.S. pediatric BP to define BPs as moderate and severe hypertension. The DoDTR also lacks height as a recorded variable; therefore, we used the 50th percentile for age based on WHO standards. Differences in normal rates of childhood heights in Afghanistan may have led to bias within the dataset. However, if bias was introduced based on smaller heights of Afghani children, it would bias more children into the moderate and severe hypertension groups.

The prehospital phase of care for patients within the current study was likely longer and the resuscitation during transport may not have been as intensive as practiced within the U.S. Although all military treatment facilities are equipped with both adult and pediatric BP cuffs, from this dataset we were unable to determine if the pediatric equipment was used for BP pressure reading. In addition, the DoDTR only includes a single BP reading taken upon arrival, which limited any ability to correlate changes in BP with outcomes.

Furthermore, it is unknown what level of resources was available to each individual patient. Resources were often limited based on type of facility as well as the number of other casualties, greatly limiting our ability to fully evaluate the frequency of neurosurgical interventions in each BP category.In addition, the DoDTR could not provide an accurate description of long-term outcomes or follow-up for host national patients. We have attempted to correlate early hypertension with cerebral herniation and increased ICP through the presence of bradycardia. The lack of intracranial monitoring and of sufficient available ICP data for complete evaluation, however, prevents adjustment for increased ICP. Limitations not withstanding, this study demonstrates important associations between initial arrival hemodynamics and short-term outcomes, which necessitates further investigation.

CONCLUSION

In conclusion, we have demonstrated that in children with severe TBIs, marked age-adjusted hypertension is common and associated with early mortality. Early systemic hemodynamics after pediatric TBI requires further analysis to determine optimal resuscitation strategies.

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Clinical Ultrasound Is Safe and Highly Specific for Acute Appendicitis in Moderate to High Pre-test Probability Patients

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Introduction: Clinical ultrasound (CUS) is highly specific for the diagnosis of acute appendicitis but is operator-dependent. The goal of this study was to determine if a heterogeneous group of emergency physicians (EP) could diagnose acute appendicitis on CUS in patients with a moderate to high pre-test probability.

Methods: This was a prospective, observational study of a convenience sample of adult and pediatric patients with suspected appendicitis. Sonographers received a structured, 20-minute CUS training on appendicitis prior to patient enrollment. The presence of a dilated (>6 mm diameter), non-compressible, blind-ending tubular structure was considered a positive study. Non-visualization or indeterminate studies were considered negative. We collected pre-test probability of acute appendicitis based on a 10-point visual analog scale (moderate to high was defined as >3), and confidence in CUS interpretation. The primary objective was measured by comparing CUS findings to surgical pathology and one week follow-up.

Results: We enrolled 105 patients; 76 had moderate to high pre-test probability. Of these, 24 were children. The rate of appendicitis was 36.8% in those with moderate to high pre-test probability. CUS were recorded by 33 different EPs. The sensitivity, specificity, and positive and negative likelihood ratios of EP-performed CUS in patients with moderate to high pre-test probability were 42.8% (95% confidence interval [CI] [25-62.5%]), 97.9% (95% CI [87.5-99.8%]), 20.7 (95% CI [2.8-149.9]) and 0.58 (95% CI [0.42-0.8]), respectively. The 16 false negative scans were all interpreted as indeterminate. There was one false positive CUS diagnosis; however, the sonographer reported low confidence of 2/10.

Conclusion: A heterogeneous group of EP sonographers can safely identify acute appendicitis with high specificity in patients with moderate to high pre-test probability. This data adds support for surgical consultation without further imaging beyond CUS in the appropriate clinical setting. [West J Emerg Med. 2018;19(3)460–464.]

INTRODUCTION

Acute appendicitis is inflammation of the appendix that can lead to perforation, abscess, other serious infections and death. Over 280,000 appendectomies are performed in the United States annually.[1] Although widespread availability of computed tomography (CT) has allowed more accurate diagnosis of acute appendicitis before reaching the operating room, this has come at the price of increased radiation exposure, increased cost and longer emergency department (ED) lengths of stay.[2-4]

Due to these risks, it is common to perform ultrasound examinations as the initial imaging modality in children to diagnose acute appendicitis.[5] Nonetheless, ultrasonography for appendicitis is not available in many EDs, and in most departments the availability of diagnostic ultrasonography is

limited by the time of day.[6,7] Even when available, the accuracy of formal radiology ultrasound may be much lower in community practice than in academic centers where it is commonly studied.[8]

Previous studies have demonstrated excellent specificity of point-of-care or clinical ultrasound (CUS) for acute appendicitis among small cohorts of highly trained sonographers,[9-15] and incorporation of clinical risk-stratification with sonography has been shown to safely enhance diagnostic accuracy in a variety of settings.[16-20] However, the accuracy of ultrasound is highly dependent on the skills of the operator. This may be a barrier to implementation of CUS for appendicitis in new settings. The goal of this study was to determine if a heterogeneous group of emergency physicians (EP) could diagnose acute appendicitis on CUS. We hypothesized that EP sonographers could diagnose acute appendicitis with high specificity using a combination of clinical risk assessment, CUS, and self-assessment of image acquisition and interpretation.

METHODS

Study Design

This was a prospective observational study on a convenience sample of adult and pediatric patients presenting to the ED with signs and symptoms concerning for acute appendicitis. Patients were enrolled from three large urban academic EDs between July 2014 and September 2016. The study sites consisted of two adult centers with a combined annual census of approximately 205,000, and one pediatric center with an annual volume >40,000 patient visits. The study protocol was approved by the institutional review board.

We included any patient with suspected acute appendicitis who underwent a diagnostic EP-performed CUS. Children and pregnant women were included. We excluded patients if CUS images were obtained after formal radiology imaging, or if data collection forms had missing information (including patient demographic information, pre-test or post-test probability, or interpretation).

Study Protocol

CUS was performed at the discretion of the treating clinician after history and physical examination. Prior to CUS, the treating physician recorded pre-test probability of appendicitis on a 10-point visual analog scale (VAS) using clinical gestalt. Following ultrasound, the sonographer filled out a standardized data collection form including the ultrasound diagnosis (appendicitis, indeterminate, or no appendicitis) and confidence in ultrasound interpretation on a 10-point VAS.

Sonographers included emergency medicine residents, ultrasound fellows, and board-certified emergency medicine faculty. All sonographers underwent a structured, 20-minute CUS training on appendicitis including didactics and hands-on scanning of one live model. CUS was performed after parenteral analgesics using a linear 5-10 MHz probe (Zonare ZS3 or Z.One Pro, Mindray Zonare, Mountain View, CA). The patient was in a supine position with hips flexed to relax the abdominal musculature. Graded compression was applied over the patient's maximal site of pain in the right lower quadrant of the abdomen. The presence of a dilated (>6 mm diameter), non-compressible, blind-ending (in long axis) tubular structure was considered a positive study. Secondary signs of appendicitis were not assessed. Non-visualization or indeterminate studies were considered negative.

Outcome

The primary outcome was the diagnostic accuracy of CUS for acute appendicitis in patients with moderate and high pre-test probability. We used unstructured clinical assessment on VAS to determine pre-test probability, as clinical judgment has been shown to outperform clinical decision tools such as the Alvarado score.[21] Pre-test probability of appendicitis was grouped into categories of low (1-3), moderate (4-6), and high (7-10). The criterion standard for diagnosis was surgical pathology results for those patients who went to the operating room, and chart review at hospital discharge and one week post-index ED visit for patients who did not go to the operating room. Local and statewide electronic medical records (EMR) were reviewed for repeat ED visits or hospitalizations for missed cases. We defined a missed case of acute appendicitis as a discharge diagnosis or surgical pathology diagnosis of acute appendicitis after the index visit.

Data Analysis

The expected rate of appendicitis was 35%.[11-13] We expected specificity to be 85%, based on prior studies demonstrating a specificity ranging from 71 to 91%.[17] A sample size of 75 patients with moderate to high pre-test probability of appendicitis was planned to demonstrate specificity within 10% of the expected value. This calculation assumes a power of 0.80 and alpha of 0.05. We calculated sensitivity, specificity, and positive and negative likelihood ratios with 95% confidence intervals (CI). Twenty percent of studies were randomly selected for blinded review by a fellowship-trained expert to calculate observed agreement and inter-rater reliability between EP sonographers' interpretations using Cohen's unweighted kappa. The expert reviewer was blinded to sonographer identity, sonographer interpretations, and clinical data.

RESULTS

During the study period 122 patients underwent CUS. Seventeen studies were excluded for missing data on the data collection form, including missing or incorrect patient medical record numbers, missing sonographer interpretation or pre-test probability. Of the remaining 105 patients, 76 (72%) had moderate or high pre-test probability (see Figure). Of these 76 patients, 28 (36.8%) had acute appendicitis (Table 1).

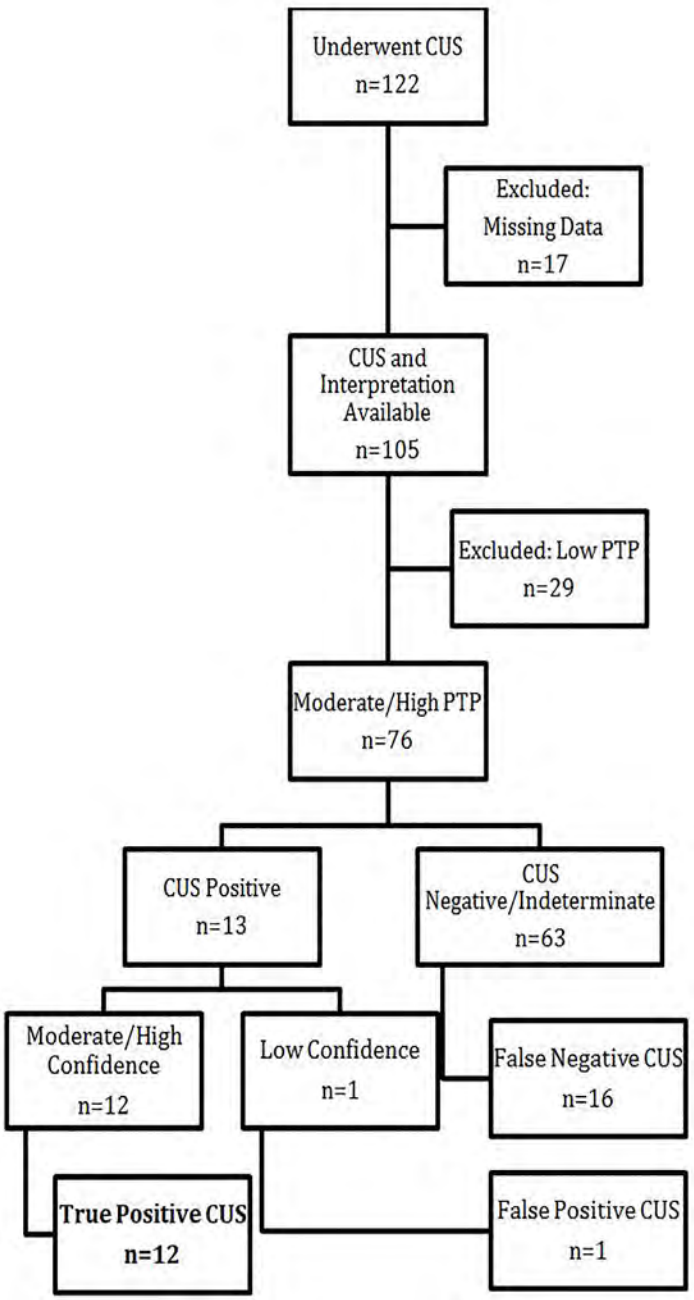

Figure. Flow chart of patients with moderate to high risk appendicitis and use of clinical ultrasound. Among patients with moderate to high risk of appendicitis, clinical ultrasound identified 12/28 cases of acute appendicitis. Among positive CUS scans, all tests with high sonographer confidence were true positives. *CUS*, clinical ultrasound; *PTP*, pre-test probability

There were 27 children, of whom 24 had moderate or high pre-test probability for appendicitis. Two pregnant women underwent CUS and both had a low pre-test probability. At one-week, EMR follow-up there were no missed cases of acute appendicitis.

Table 1. Patient characteristics with moderate to high pre-test probability.

	Appendicitis (n=28)	No appendicitis (n=48)
Age, mean	23.9 ±13.1	28.7 ±16.1
Age <18	12	12
Sex (M)	69.6%	59.5%
BMI	24.5 ±6.6	26.3 ±4.7
Symptom duration (d)	1.1 ±1.1	1.5 ±1.6
Fever	32.1%	27.1%
Vomiting	50.0%	41.7%
Rebound	46.4%	27.1%
Migration	82.1%	27.1%
Anorexia	78.6%	56.3%
White blood cells	12.9 ±3.8	10.7 ±5
Alvarado score	4.6 ±1.4	2.2 ±1.3
Formal radiology imaging	90%	90%

The sensitivity and specificity of EP-performed CUS in patients with moderate to high pre-test probability were 42.8% (95% CI [25-62.5%]) and 97.9% (95% CI [87.5-99.8%]) (Table 2). The positive and negative likelihood ratios were 20.6 (95% CI [2.8-149.9]) and 0.58 (95% CI [0.42-0.8]). In 31 studies sonographers reported high confidence in image acquisition and interpretation (6 or higher on a 1-10 VAS). Of these studies, the sensitivity and specificity improved to 80% and 100%, respectively. The 16 false negative scans all were interpreted as indeterminate; for all 16, appendicitis was confirmed by CT at the index visit. There was one false positive ultrasound. For this study the sonographer reported low confidence in image interpretation (2 out of 10). This patient had a CT that demonstrated an obstructing ureteral stone at the right ureterovesical junction. Two patients proceeded directly to the operating room for appendectomy based on a positive CUS with no further imaging.

Thirty-three different sonographers performed CUS with a range of 1-13 scans per sonographer. Residents performed 40 (52.6%) of the CUS and identified five (41.7%) of the true positives. Inter-rater reliability was high, with 100% agreement and kappa = 1 (95% CI [1-1]).

DISCUSSION

Our study demonstrates that a heterogeneous group of EPs can diagnose acute appendicitis by CUS with high specificity in the appropriate clinical context. In our study, most sonographers had performed an average of 100 prior CUS examinations. Pre-enrollment training was limited to 20 minutes of didactics and hands-on training with a healthy model.

Table 2. Sensitivity and specificity by level of training.

	Faculty	Fellow	Resident	Total
N	25	11	40	76
Sensitivity	50%	75%	31%	43%
Specificity	100%	100%	96%	98%

Recent research has shown diagnostic accuracy can be improved by combining clinical assessment with sonography.[16-20] Therefore, we identified patients with moderate to high pre-test probability. Since ultrasound accuracy is highly dependent on the skill of the sonographer, we also collected data on sonographer confidence. Higher confidence in the ultrasound diagnosis yielded improved sensitivity and specificity of the results. This suggests that confidence in image acquisition and interpretation is an important predictor of diagnostic accuracy for CUS.

These results are consistent with prior studies demonstrating high specificity and moderate sensitivity of EP-performed CUS for acute appendicitis. In a meta-analysis of 21 studies, Fields et al. showed high specificity of 92% and relatively high sensitivity of 80% for CUS by EPs.[15] Our sensitivity is lower than that reported by Fields et al. because the authors excluded non-diagnostic studies from analysis. These results further support the use of CUS as a first-line imaging modality in patients with suspected appendicitis. CUS has potential advantages as compared to CT with reduced time to diagnosis, reduced costs, reduced radiation and contrast dye exposure, and shorter ED stays.[2,4]

LIMITATIONS

The generalizability of this study is limited by the use of a convenience sample design and small number of subjects. There may be spectrum bias based on the inclusion criteria. EP sonographers were not blinded to patient history or physical exam, which could impact real-time interpretation of the images. However, this reflects pragmatic use of CUS in EDs during the early adoption period. The rates of acute appendicitis in this cohort are consistent with prior studies, suggesting that physicians used CUS in a group of patients similar to those seen in routine clinical practice. Follow-up was limited to one-week chart review, but it is unlikely any patients were missed due to use of a statewide-linked EMR. Although highly specific, the sensitivity of 42.8% does not support the use of CUS to rule out acute appendicitis in moderate to high pre-test probability patients.

CONCLUSION

A heterogeneous group of EPs can safely identify acute appendicitis on CUS with high specificity and a positive likelihood ratio of 20. Clinical risk stratification and appraisal of image quality and interpretation may improve diagnostic accuracy. Surgical consultation without further imaging beyond CUS may be supported in the appropriate clinical setting. This data does not support the use of CUS to rule out appendicitis when there is persistent clinical concern.

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Modification of Daly's Do-it-yourself, Ultrasound-guided Pericardiocentesis Model for Added External Realism

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Comment on:

Daly R, Planas JH, Edens MA. Adapting gel wax into an ultrasound-guided pericardiocentesis model at low cost. *West J Emerg Med*. 2017;18(1):114-6.

We were happy to discover the article by Daly and colleagues describing a low-cost, pericardiocentesis training model (Figure 1).[1] We have struggled to find a cost-effective means of demonstrating and practicing ultrasound-guided pericardiocentesis with our emergency medicine residents. We greatly appreciated their ingenuity in building upon and improving previous do-it-yourself models.[2,3] We were especially impressed with their addition of a plastic Halloween skeleton thorax and 250 mL normal saline bag to act as the pericardial sac. In that same spirit, we have devised a modification of their model that offers the benefit of more-realistic external landmarks.

We followed their instructions with several exceptions. Instead of the square-shaped plastic container that they used for a chest wall mold, we used a plastic, manikin dress-form torso (Amazon, $25; https://tinyurl.com/amazondressform). We cut the back of the dress form out with tin snips and turned it upside down to act as a mold. We also used ballistics gel (Amazon, $60; https://tinyurl.com/amazonballisticsgel) instead of gel wax. Ballistics gel does not require the addition of a substance such as flour to simulate the echogenicity of human tissue. Ballistics gel is clear, so we added an optional flesh-colored dye (Humimic, $30; https://humimic.com/product-category/dye/). Like wax gel, ballistics gel can be removed and re-melted to create a new model after repeated needle aspirations. We melted the ballistics gel in a Hamilton-Beach 7-quart cooker (Amazon, $30; https://tinyurl.com/amazonHBcooker) for several hours on the "high" setting, then stirred in the dye and poured the ballistics gel into the turned-over torso (Figure 2). Unlike the Daly model, we did not need to add flour or strain off foam. We placed ice underneath the torso to prevent melting or deforming of the hard plastic torso shell, but this may have been unnecessary.

Figure 1. Original ultrasound-guided pericardiocentesis model from Daly R. et al. *West J Emerg Med.* 2017;18(1):114-6.

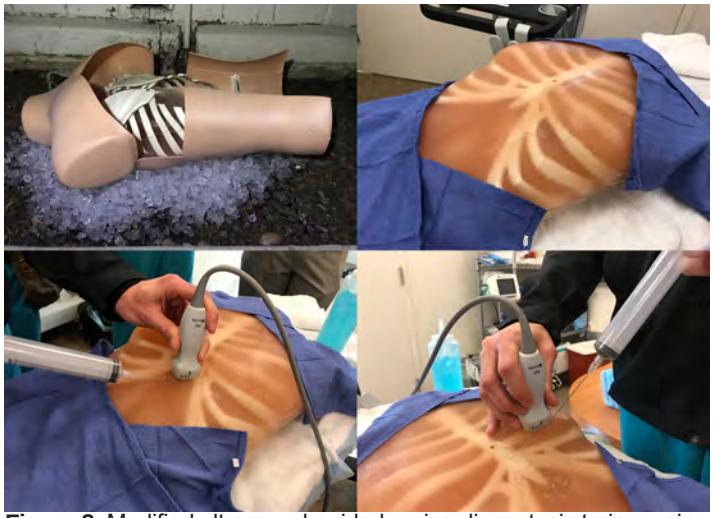

Figure 2. Modified ultrasound-guided pericardiocentesis trainer using a plastic dress form torso turned upside down to act as a mold.

Like the Daly model, we were able to build our model for less than $200. The additional benefit we found was that our model created a realistic chest surface and external landmarks. Our residents were able to practice ultrasound-guided sub-xiphoid and parasternal approaches as well as the blind, landmark-based pericardiocentesis technique. Training programs planning to utilize Daly's brilliant innovation may wish to follow our lead to further increase realism.

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Appropriateness of Extremity Magnetic Resonance Imaging Examinations in an Academic Emergency Department Observation Unit

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Introduction: Emergency departments (ED) and hospitals face increasing challenges related to capacity, throughput, and stewardship of limited resources while maintaining high quality. Appropriate utilization of extremity magnetic resonance imaging (MRI) examinations within the emergency setting is not well known. Therefore, this study aimed to determine indications for and appropriateness of MRI of the extremities for musculoskeletal conditions in the ED observation unit (EDOU).

Methods: We conducted this institutional review board-approved, retrospective study in a large, quaternary care academic center and Level I trauma center. An institutional database was queried retrospectively to identify all adult patients undergoing an extremity MRI while in the EDOU during the two-year study period from October 2013 through September 2015. We compared clinical history with the American College of Radiology (ACR) Appropriateness Criteria® for musculoskeletal indications. The primary outcome was appropriateness of musculoskeletal MRI exams of the extremities; examinations with an ACR Criteria score of seven or higher were deemed appropriate. Secondary measures included MRI utilization and imaging findings.

Results: During the study period, 22,713 patients were evaluated in the EDOU. Of those patients, 4,409 had at least one MRI performed, and 88 MRIs met inclusion criteria as musculoskeletal extremity examinations (2% of all patients undergoing an MRI exam in the EDOU during the study period). The most common exams were foot (27, 31%); knee (26, 30%); leg/femur (10, 11%); and shoulder (10, 11%). The most common indications were suspected infection (42, 48%) and acute trauma (23, 26%). Fifty-six percent of exams were performed with intravenous contrast; and 83% (73) of all MRIs were deemed appropriate based on ACR Criteria. The most common reason for inappropriate imaging was lack of performance of radiographs prior to MRI.

Conclusion: The majority of musculoskeletal extremity MRI examinations performed in the EDOU were appropriate based on ACR Appropriateness Criteria. However, the optimal timing and most-appropriate site for performance of many clinically appropriate musculoskeletal extremity MRIs performed in the EDOU remains unclear. Potential deferral to the outpatient setting may be a preferred population health management strategy.[West J Emerg Med. 2018;19(3)467–473.]

INTRODUCTION

Access to timely healthcare in the United States remains a challenge for many individuals.[1] One potential downstream result of decreased access to primary and ambulatory care is increased utilization of emergency departments (ED).[2] Population health management efforts are thus increasingly focused on EDs, with programs aimed at reducing unnecessary ED visits and optimizing appropriate site of care, including the use of ED observation units (EDOU), mobile observation units, and intensive home health programs.[3-5]

EDOUs were developed to optimize care for patients who need further evaluation and management but who do not meet criteria for discharge or inpatient admission.[6] EDOUs have demonstrated benefits in terms of clinical workflow and cost-effectiveness.[7] However, while EDOUs may provide for a more appropriate and less costly site of care for non-acute patients, they may inadvertently encourage performance of diagnostic workups that may be better suited for outpatient evaluation.

As advanced diagnostic imaging (ADI) has become a critical component of optimal healthcare delivery in the emergency setting, the growth in utilization of advanced imaging has far outpaced trends in general ED use. For example, the use of computed tomography and magnetic resonance imaging (MRI) in the emergency setting increased three-fold over a 10-year period ending in 2007, despite the lack of a commensurate increase in the rate of life-threatening conditions.[8] Improving appropriate use of ADI is imperative within a healthcare landscape that is increasingly focused on healthcare cost and quality. To that end, the implementation of clinical decision-support (CDS) tools has been demonstrated as highly valuable in improving appropriate ADI use. [9-11]However, while CDS systems for imaging utilization currently focus on appropriateness, they may not adequately provide guidance on appropriate timing (e.g. acuity) and setting of imaging (e.g., inpatient, outpatient, emergent).

Given that a large proportion of ED visits are due to musculoskeletal complaints, MRI is potentially an important diagnostic tool in the emergent setting. The superior ability of MRI to delineate soft tissue injury and bone marrow edema is important in characterizing many musculoskeletal conditions.[12,13] However, as healthcare organizations face increased challenges related to capacity, throughput and appropriate site of care, stewardship of limited and high-cost resources while ensuring excellent clinical outcomes is paramount. Thus, the goal of this study was to assess appropriateness of musculoskeletal extremity MRI examinations in an EDOU at a large academic medical center, based on relevant American College of Radiology (ACR) Appropriateness Criteria® (AC).

Population Health Research Capsule

What do we already know about this issue?
Availability and utilization of magnetic resonance imaging (MRI) in emergency departments has significantly increased; while clinical appropriateness of these studies is not well understood.

What was the research question?
To assess clinical appropriateness of extremity MRI exams performed in an emergency department (ED) observation unit, based on American College of Radiology Appropriateness Criteria.

What was the major finding of the study?
Majority of extremity MRIs performed in the ED observation unit were appropriate based on ACR criteria; questions remain about optimal timing and site of imaging.

How does this improve population health?
Consideration of timing and site of imaging when assessing imaging appropriateness in emergent settings may improve efficiency without compromising care quality

METHODS

Human Subjects Compliance

This retrospective, Health Insurance Portability and Accountability Act–compliant study was approved by the institutional review board, including waiver of patient consent.

Study Site

We performed the study at a 999-bed, quaternary care academic center and Level I trauma center. Approximately 111,000 ED visits occur at the institution annually, and approximately 105,000 diagnostic imaging studies are performed and interpreted in the ED radiology division annually. Approximately 10% of ED visits result in further evaluation within the EDOU.

Collection of Patient Data

We queried an institutional database to identify all adult patients evaluated in the EDOU who underwent an MRI of the extremity (Table 1) while in the EDOU during the study period of October 1, 2013, through September 30, 2015. Patients undergoing MRI in the ED prior to admission to the EDOU were excluded. However, we included patients undergoing MRIs that were ordered while the patient was in ED status, but were performed while the

Table 1. Distribution of musculoskeletal extremity MRI exam by body part.

Body part	Number of exams (% of total)
Upper extremity	18 (20%)
Shoulder	10 (11%)
Arm	3 (3%)
Wrist	2 (2%)
Elbow	2 (2%)
Humerus	1 (1%)
Lower extremity	70 (80%)
Foot	27 (31%)
Knee	26 (30%)
Leg	10 (11%)
Femur	5 (6%)
Ankle	2 (2%)
Total	88

MRI, magnetic resonance imaging.

patient was in the EDOU. Patients undergoing MRI of the spine (cervical, thoracic, lumbar, sacrum), pelvis and hip were excluded. For included patients, we also queried the institutional database to determine patient demographic information including age and sex.

Chart review of clinical documented findings within the electronic medical record (EMR) (Partners Healthcare Longitudinal Medical Record, Boston, MA) was performed through use of a data abstraction form designed to capture the following data elements: (1) clinical indication for MRI; (2) appropriateness score of the MRI based on relevant appropriateness criteria; (3) whether surgery was performed, based on review of operative reports; (4) imaging finding categories; and (5) whether subspecialty consultation was performed in the ED, based on documented separate clinical notes from consultants. Chart review was performed by a radiology resident (RG) and radiology fellow (MG). Conflicting data was adjudicated through consensus.

Outcome Measures

The primary outcome measure was appropriateness of musculoskeletal MRI exams of the extremities, based on relevant ACR AC.[14] The ACR AC represent an expert panel's summation of the currently available evidence into a comprehensive set of evidence-based imaging guidelines. The guidelines provide appropriateness scores of various imaging or treatment options for common clinical scenarios. Scores are represented on an ordinal scale from 1 to 9, with 1, 2, and 3 categorized as "usually not appropriate" (i.e., the risks of doing the procedure likely outweigh the benefits); 4, 5, and 6 as "may be appropriate" (i.e., the risk and benefit balance is equivocal); and 7, 8, and 9 as "usually appropriate" (i.e., the benefits of the procedure likely outweigh the risks).

The ACR AC were used retrospectively for this study as they were not part of a clinical CDS system available to physicians at the time of order entry. In cases where a plain radiograph was the most appropriate first exam prior to MRI, the MRI was considered the appropriate second exam only if the radiograph was performed during the ED visit or within seven days prior to the ED visit. We characterized studies dichotomously as "appropriate" for ACR AC scores from 7-9 and "not appropriate" for ACR AC scores of less than seven, a methodology that has been used previously.[15] For MRI studies categorized as appropriate by this criterion, we then determined if the selected study was the most appropriate option or whether an alternative study with a higher ACR AC score could have been performed.

Secondary outcome measures included data elements within the data abstraction form, which were described in the previous section.

Statistical Analyses

Data were imported into Stata 14 (StataCorp, College Station, TX) for further analysis. We used summary statistics to describe the distribution of MR examination by extremity, the distribution of indications for MRI exams, and the additional outcome measures discussed above.

RESULTS

A total of 22,713 patients were evaluated in the EDOU during the study period. Of those patients, 4,409 had at least one MRI performed, and 88 met inclusion criteria for having a musculoskeletal extremity MRI examination, representing 2.0% of all patients undergoing an MRI exam in the EDOU. Forty-eight (55%) extremity MRI exams were ordered while the patient was still in the ED, and 40 (45%) were ordered while the patient was in the EDOU. The mean age of patients included in the cohort was 60 years (standard deviation: 18.2, range 20-99 years); 55% were women.

Frequency and Distribution of MRI Examinations and Indications

MRI examinations were of the lower extremity in 70 patients (80%) and upper extremity in 18 patients (20%). The most common exams were of the foot (27/88; 31%), knee (26/88; 30%), shoulder (10/88; 11%) and leg (10/88; 11%). Thirty-nine (44%) of the exams were performed with intravenous (IV) gadolinium. The most commons indications were suspected infection (42/88; 48%) and acute trauma (23/88; 26%). MRI examination types and indications are detailed in Figure 1 and Table 1, respectively.

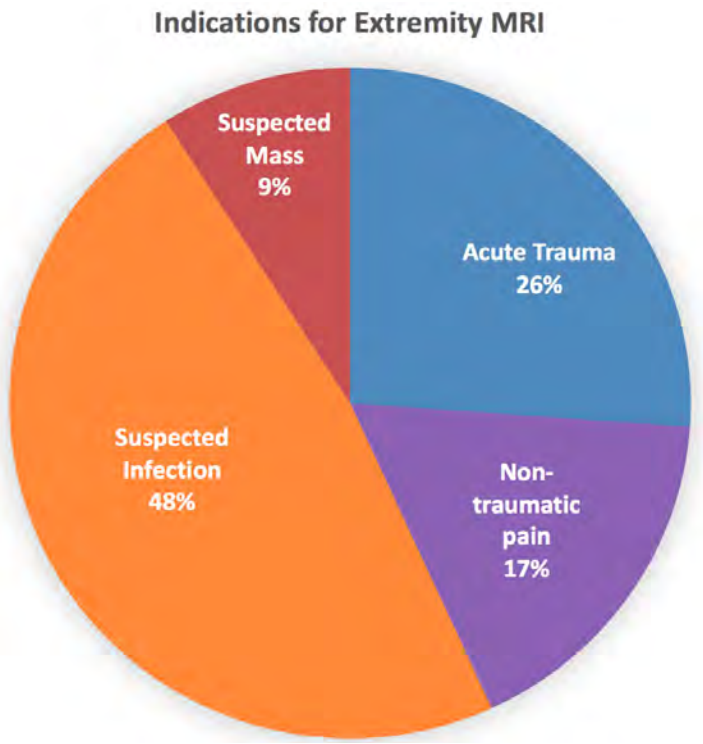

Figure 1. Distribution of indications for musculoskeletal extremity magnetic resonance imaging (MRI) in the emergency department observation unit.

Appropriateness

Of the musculoskeletal extremity MRI exams performed, 73 (83%) were deemed appropriate (ACR AC score 7-9). Of exams that were appropriate, 60 (68% of total exams) were the most appropriate option according to the ACR AC. Of the 13 appropriate exams that were not the most appropriate exam, the most common reason was the absence of IV gadolinium, where the exam with the highest ACR AC score would have been an MRI with and without gadolinium. None of these patients had a clear contraindication to the use of gadolinium (allergy or renal dysfunction) based on chart review. In 10 cases (11%), the radiology report for the initial plain radiograph recommended an MRI for further evaluation, and all of the subsequently performed MRIs were appropriate by ACR AC. In 15 of the exams designated as not appropriate, the reason for this designation was the lack of a plain radiograph performed within seven days prior to the MRI study. By strict interpretation of the ACR AC, the fact that the MRI was the first exam performed in these instances led the appropriateness score to be 1 ("usually not appropriate"). The distribution of most appropriate, appropriate, and not appropriate exams, grouped by body part, is depicted in Figure 2.

Imaging Findings and Additional Outcomes

The most common MRI findings were ligamentous injury (33/88; 38%), joint effusion (14/88; 16%), fluid collection

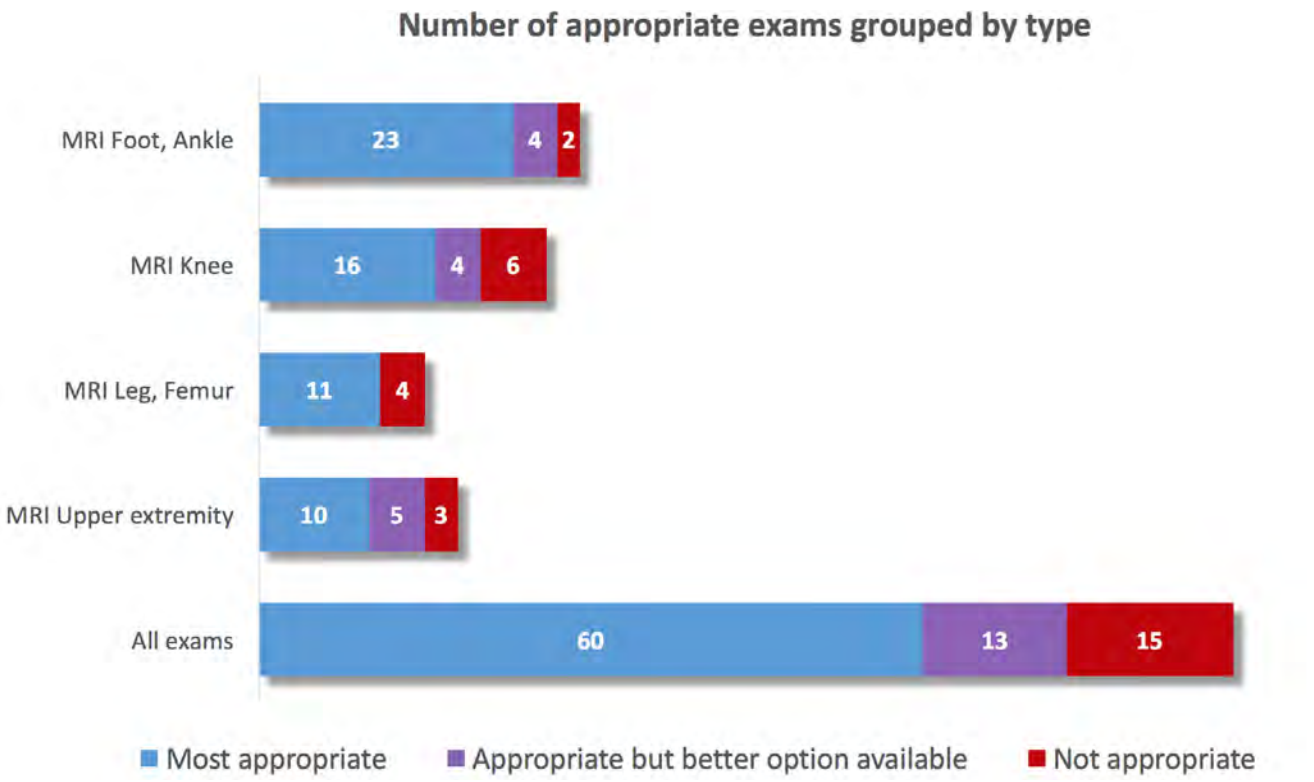

Figure 2. Distribution of magnetic resonance imaging (MRI) appropriateness by body part.

(12/88; 14%), fracture (11, 13%), and osteomyelitis (10/88; 11%), further detailed in Table 2. Nine out of 11 cases of osteomyelitis involved the lower extremity, seven of which involved the foot. The most common consultations obtained while in the EDOU were orthopedic surgery (42/88; 48%), general surgery (5/88; 6%), infectious disease (5/88; 6%), and rheumatology (5/88; 6%), further detailed in Table 3. The most frequent patient disposition following the EDOU visit was home (56/88; 64%), followed by inpatient admission (31/88; 35%) and transfer to a rehabilitation facility (1/88; 1%). Eleven patients (13%) received operative intervention during the same hospital stay.

DISCUSSION

In this study, we found that musculoskeletal extremity MRI exams represent a very small minority of all MRIs performed in the EDOU. Further, we found that the majority of the musculoskeletal MRIs were appropriate based on ACR AC. Several important conclusions can be drawn. First, our findings demonstrated that although musculoskeletal MRI examinations are not among the commonly ordered MRI exams in the EDOU, clinical providers are typically using a high-cost imaging resource appropriately based on current ACR guidelines. This finding may suggest that within our institution, implementation of CDS systems that require their use prior to ordering may not be of value for this subset of MRI examinations in the EDOU. However, the experience within our institution within this small subset of MRIs performed in the EDOU may not be representative of the larger landscape of MRI use within emergent settings. Multiple prior studies have been shown previously to reduce inappropriate use of advanced diagnostic imaging.[9,10]

Second, our study found that nearly half of all patients undergoing musculoskeletal extremity MRI had an orthopedic consultation. Musculoskeletal MRI has roles in evaluation of both traumatic and non-traumatic indications and can be a value-added service in the emergency setting, particularly in guiding management decisions that may alter patient disposition. [12,16,17]These findings suggest that ED providers often collaborate with orthopedic consultants when patients undergo musculoskeletal MRIs. Interestingly, review of clinical notes demonstrated instances in which orthopedic consultants recommended short-term outpatient follow-up and to forego MRI within the ED or EDOU. However, MRI exams were still ultimately performed in these cases, which remained appropriate by ACR AC.

In addition to determining whether imaging, and what type of imaging exam, is appropriate, decisions regarding appropriate timing and location (e.g. acute, emergent, outpatient) are complex. Clinical providers must also account for clinical criteria that may not be included within appropriateness criteria, social situations and/or the ability to obtain appropriate follow-up. However, availability of MRI services in the ED setting may also create incentives to perform exams because of availability.

The development of CDS tools for advanced imaging that incorporate timing of imaging and site of care may be of value in the acute setting. Over time, EDs have become increasingly involved in population health management and primary care.[18] Deferral of non-urgent (even if technically clinically appropriate) advanced imaging studies to the outpatient setting may help alleviate capacity and resource limitations in the ED. Staying within the EDOU to undergo an MRI and waiting for interpretation may not be in the best interest of the patient if short-term management and disposition will not be altered, given that EDOU stays are often subject to co-insurance.[19] However, to better optimize the timing and site of care of advanced diagnostic imaging, EDs and hospitals will need to enhance integration with outpatient providers and services to ensure that imaging is well-coordinated and accessible in the ambulatory setting.[20] Further, within the context of patient experience, the actual and perceived timeliness of results within the ED setting (compared with outpatient follow-up) will also present challenges regarding managing patient expectations while attempting to optimize site of care.[18,21]

Table 2. Prevalence of findings on musculoskeletal extremity MRI exams.

Findings	Number of patients (%)
Ligamentous injury	33 (38%)
Joint effusion	14 (16%)
Fluid collection	12 (14%)
Fracture	11 (13%)
Osteomyelitis	10 (11%)
Mass	5 (6%)
Septic arthritis	2 (2%)

MRI, magnetic resonance imaging.

Table 3. Prevalence of consultations obtained in the ED observation unit for patients undergoing musculoskeletal MRI.

Subspecialty	Number of patients (%)
Orthopedic surgery	42 (48%)
General surgery	5 (6%)
Infectious disease	5 (6%)
Rheumatology	5 (6%)
Podiatry	3 (3%)
Oncology	2 (2%)

ED, emergency department; *MRI,* magnetic resonance imaging.

LIMITATIONS

This retrospective study had a number of important limitations. The study was conducted in a single large, quaternary care academic medical center serving an urban population and with 24-hour MRI services in the ED, which may limit its generalizability to other sites. In addition, this study did not quantify patients who presented with musculoskeletal complaints and did not undergo an MRI, which limits assessment of overall rates of MR utilization. The determination of exam appropriateness was based on receiving a score of 7, 8 or 9, which has been used in previous studies assessing appropriateness. However, exams with lower appropriateness scores may in fact have been an appropriate examination. Lastly, exams found to be inappropriate may have had recent prior radiographs outside of our healthcare system, but they may not have been available within the EMR or picture archiving and communication system.

CONCLUSION

The majority of MRI musculoskeletal extremity exams performed in the EDOU were clinically appropriate based on ACR Appropriateness Criteria. However, optimal timing and most- appropriate site for performance of many clinically appropriate musculoskeletal extremity MRIs performed in the EDOU remains unclear.

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Comments on "Knowledge Translation of the PERC Rule for Suspected Pulmonary Embolism: A Blueprint for Reducing the Number of CT Pulmonary Angiograms"

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To the Editor:

We read with enthusiasm the recent publication of Drescher et al. and applaud their department's commitment to embedding evidence-based medicine (EBM) for best practice in the diagnosis of pulmonary embolism (PE) in their culture through education and computerized decision support (CDS)1. Our healthcare system had similar findings with implementing a CDS tool for our emergency departments (ED), which utilizes the revised Geneva criteria for risk stratification as opposed to Well's criteria.

We designed a CDS tool using the revised Geneva criteria to first risk stratify patients with suspected PE to low, moderate, or high risk. The tool next directed providers to use the Pulmonary Embolism Rule-out Criteria (PERC) for low risk, and if not PERC negative or if moderate risk, order d-dimer testing. The tool indicates that high-risk patients and those with positive d-dimer are appropriate for computed tomography pulmonary angiograms (CTA). The tool was inserted in the electronic medical record (EMR) at six EDs in a single healthcare system using the same EMR (Cerner Corporation, North Kansas City, Missouri.) After obtaining IRB approval, we studied the effect of the EMR CDS tool. We hypothesized that post-implementation the number of CTAs performed would decrease and the diagnostic yield would increase.

Total CTA utilization proportionally decreased post implementation with 4,981 CTAs of 311,313 (1.6%) visits in 2014 compared to 4,608 CTA of 307,200 (1.5%) for 2015, p =0.001. The proportion of patients with a positive study of all those who had CTA was not significantly different from 2014 to 2015 (5.7% vs. 6.6%, p=0.68). In the post-implementation group, the percent positive CTA was 6.7% when the EMR tool was used (263 positive of 3,926) but not significant in comparison to when it wasn't used [5.7% (39 positive of 682), p=0.34].

Although our study suffered from similar limitations in its observational nature we also found that implementation of a PE decision-support tool in the EMR across multiple EDs was associated with reduced CTA utilization and that diagnostic accuracy of CTA for suspected PE did not significantly improve with the decision-support tool. Given the large potential impact in reducing radiation exposure when applied at the system level we support the authors' conclusion that implementation of EBM has demonstrated efficacy for reducing departmental CTA utilization.

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Multicenter Study of Albuterol Use Among Infants Hospitalized with Bronchiolitis

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Introduction: Although bronchiolitis is a common reason for infant hospitalization, significant heterogeneity persists in its management. The American Academy of Pediatrics currently recommends that inhaled albuterol not be used in routine care of children with bronchiolitis. Our objective was to identify factors associated with pre-admission (e.g., emergency department or primary care) use of albuterol among infants hospitalized for bronchiolitis.

Methods: We analyzed data from a 17-center observational study of 1,016 infants (age <1 year) hospitalized with bronchiolitis between 2011-2014. Pre-admission albuterol use was ascertained by chart review, and data were available for 1,008 (99%) infants. We used multivariable logistic regression to identify infant characteristics independently associated with pre-admission albuterol use.

Results: Half of the infants (n=508) received at least one albuterol treatment before admission. Across the 17 hospitals, pre-admission albuterol use ranged from 23-84%. In adjusted analysis, independent predictors of albuterol use were the following: age ≥2 months (age 2.0-5.9 months [odds ratio (OR) 2.09, 95% confidence interval (CI) {1.45-3.01}] and age 6.0-11.9 months [OR 2.89, 95% CI {1.99-4.19}]); prior use of a bronchodilator (OR 1.89, 95% CI [1.24-2.90]); and presence of wheezing documented in pre-admission chart (OR 3.94, 95% CI [2.61-5.93]). By contrast, albuterol use was less likely among those with ≥7 days since the start of breathing problem (OR 0.66, 95% CI [0.44-1.00]) and parent-reported fever (OR 0.75, 95% CI [0.58-0.96]).

Conclusion: Variation in pre-admission albuterol use suggests that local practice had a strong influence on use, but that patient characteristics also influenced the decision. While we agree with current guidelines in recommending against albuterol for all infants with bronchiolitis, our understanding of possible subgroups of responders may improve through investigation of infants with the identified characteristics. [West J Emerg Med. 2018;19(3)475–483.]

INTRODUCTION

Bronchiolitis is the most common cause for hospitalization of infants in the United States, with over 100,000 hospitalizations annually, representing approximately 3% of all children during their first year of life.[1,2] In recent years, the number of annual visits to the emergency department (ED) for bronchiolitis has been increasing.[3] Infants with bronchiolitis also have been found to have an increased likelihood of developing asthma.[4-8] Bronchiolitis, therefore, affects a significant proportion

of the population and is linked to further development of disease in that population. Nevertheless, clinical management of bronchiolitis is still highly variable.[9-11] Although the variation of treatment for bronchiolitis is well-established and is a driving factor behind current clinical guidelines, little is known about how patient characteristics are associated with this variation.

The American Academy of Pediatrics (AAP) has published clinical guidelines, most recently updated in 2014, which recommend against the routine use of all pre-admission medications.[12] Recent analyses on practice variation in the management of bronchiolitis have also taken a broad approach, establishing that variation occurs in the use of several therapies and diagnostic tests across different hospitals.[9,13,14] In the current analysis, we have focused on a single therapy, inhaled albuterol, and the factors associated with its use. We conducted a secondary analysis of data from a prospective multicenter, multiyear study of over 1,000 infants. Our aim was to assess the variation across the 17 participating hospitals and identify patient characteristics independently associated with pre-admission albuterol use. We hypothesized that albuterol use would be common, with significant local variation, and associated with patient characteristics that suggest chronic breathing problems (e.g., older infant age, previous respiratory hospitalization, family history of asthma).

Population Health Research Capsule

What do we already know about this issue?
Bronchiolitis is a major cause of infant hospitalization but heterogeneity persists in its management. Current guidelines recommend against routine use of albuterol.

What was the research question?
What patient characteristics are associated with clinician use of pre-admission albuterol?

What was the major finding of the study?
Older age, prior use of a bronchodilator, and documented wheezing were associated with receiving pre-admission albuterol.

How does this improve population health?
Our understanding of variation in albuterol use and possible subgroups of responders may improve through investigation of infants with the identified characteristics.

METHODS

Study Design

As part of the Multicenter Airway Research Collaboration, a clinical research program focusing on respiratory/allergy emergencies, the Emergency Medicine Network (www.emnet-usa.org) is conducting a multicenter, prospective cohort study that enrolled infants for three consecutive fall/winter seasons from 2011-2014. The total number of hospitals participating is 17, spread across 14 U.S. states. Evaluation and treatment of patients was at the discretion of the healthcare providers on site. Investigators enrolled patients using a standardized protocol. Inclusion criteria for the study were the following: an attending physician's diagnosis of bronchiolitis (as defined by the AAP: an acute respiratory illness with some combination of rhinitis, wheezing, cough, tachypnea, crackles and retractions[15]); age of <1 year; a parent/guardian with the ability to give informed consent who spoke English or Spanish within 24 hours of admission; and complete contact information that was not expected to change for at least 12 months. Exclusion criteria included transfer to a participating hospital >48 hours after original admission, >24 hours since transferring to a participating hospital, a parent/guardian refusing collection or future use of biospecimens, insurmountable language barrier, certain chronic conditions (e.g., known heart-lung disease, immunodeficiency), gestational age <32 weeks, or the patient had met the primary endpoint of the initial five-year grant (U01 AI-087881) at the time of enrollment (i.e., two or more treatments with corticosteroids in six months, or four or more episodes of wheezing in one year). All participating hospitals had approval of their local institutional review board.

Data Collection

Investigators completed a structured interview with parents/guardians to assess patients' demographic characteristics and history, and to obtain detailed information regarding the bronchiolitis episode for which they were admitted. Further clinical data on the patient's evaluation, treatment and course of illness was obtained via the patient's medical records. These data were abstracted from the medical record and entered into a standardized form by staff at EMNet. This chart review included the primary outcome of the current analysis, inhaled albuterol at any point during the entire pre-admission visit (e.g., in the ED of the enrolling hospital, the ED of another hospital, the primary care provider's office, given during transfer, or another location such as an outpatient clinic or urgent care). With this variable, we specifically sought to identify whether or not a clinician chose to administer albuterol. Staff at EMNet Coordinating Center manually reviewed all data for any inconsistencies or missing information and then queried hospitals for clarification.

Nasopharyngeal Aspirate and Virology

Nasopharyngeal aspirates were collected following a standardized procedure within 24 hours of admission for each participant.[16] All samples were placed on ice and stored at -80ºC. Polymerase chain reaction assays were performed as either singleplex or duplex two-step, real-time polymerase chain reactions. Aspirates were tested for a panel of common respiratory viruses, including respiratory syncytial virus (RSV) types A and B and rhinovirus (RV). The virology protocol is described elsewhere.[16]

Statistical Analyses

We performed all analyses using Stata 14.1 (Stata Corp, College Station, TX). Data are presented as proportions with 95% confidence intervals (CI) and medians with interquartile ranges (IQR). To examine factors potentially associated with the primary outcome – pre-admission albuterol use among infants hospitalized for bronchiolitis – we performed unadjusted analyses using chi square, Fisher's exact test, or Wilcoxon rank-sum test, as appropriate. All *P*-values were two-tailed, with $P<0.05$ considered statistically significant.

We conducted multivariable logistic regression to evaluate independent predictors of pre-admission albuterol use. We selected clinically relevant factors a priori for inclusion in the model without regard for statistical significance (e.g., age, sex, parent-reported previous use of bronchodilator). Other factors were evaluated for possible inclusion in the model if found to be suggestively associated with the outcome in unadjusted analyses ($P<0.20$). The final regression model used logistic regression with clustered standard errors to adjust for potential non-independence of observations within hospitals, analyzing data as a panel by site. We reported results as odds ratios (ORs) with 95% CIs.

RESULTS

Among 1,016 enrolled infants admitted to hospitals with bronchiolitis, 1,008 (99%) had data regarding pre-admission albuterol use and formed our analytic cohort. In this cohort, the median age was 3.2 months (IQR, 1.6-6.0 months), 603 (60%) were male, 426 (42%) were non-Hispanic White, 803 (80%) had no prior history of breathing problems, and the most commonly detected viruses were RSV (n=814, 81%) and RV (n=212, 21%) (Table 1). Additionally, 445 infants (44%) had previously used a bronchodilator prior to the pre-admission visit (e.g., for past breathing problems or the index problem).

For most infants, the pre-admission visit was in the ED of the enrolling hospital (n=831, 82%). For the other infants, their pre-admission was in another hospital ED prior to transfering to the enrolling hospital (n=119, 12%), at their primary care provider's office (n=35, 4%), or in other clinics (e.g., an outpatient clinic or urgent care) (n = 23, 2%). In our cohort, 508 infants (50%) were identified as having been administered inhaled albuterol during their pre-admission visit. Across hospitals, the proportion of pre-admission albuterol usage ranged from 23-84% ($P<0.001$; Figure).

Unadjusted associations between patient characteristics and pre-admission albuterol use are shown in Table 1. Several groups of infants were found to have a higher proportion of pre-admission albuterol use, including older infants (≥2 months of age), infants with a history of breathing problems, and infants with previous use of a bronchodilator (i.e., any parent-reported use of a bronchodilator in the infant's life) (all $P<0.001$). Likewise, infants whose parents reported symptoms of breathing faster than normal ($P=0.007$), wheezing, retractions, or having stopped breathing in the 24 hours prior to the pre-admission visit (all $P<0.001$) also were more likely to have received pre-admission albuterol. Although pre-admission albuterol use was not associated with the most common bronchiolitis viruses (RSV and RV), infants with human metapneumovirus were more likely to have received pre-admission albuterol compared to infants without human metapneumovirus ($P=0.02$; Table 1).

Several of the unadjusted associations with pre-admission albuterol persisted in the multivariable analysis (Table 2). Compared to infants <2 months of age, those 2.0-5.9 months were more likely to have received pre-admission albuterol (OR 2.09, 95% CI [1.45-3.01]); and infants 6.0-11.9 months were the most likely to have received it (OR 2.89, 95% CI [1.99-4.19]). Other significant predictors of pre-admission albuterol use were previous use of a bronchodilator (OR 1.89, 95% CI [1.24-2.90]) and pre-admission chart documentation of wheeze (OR 3.94, 95% CI [2.61-5.93]).Factors inversely associated with pre-admission albuterol use included the following: ≥7 days since the start of index breathing problem prior to pre-admission (OR 0.66, 95% CI [0.44-1.00]); and parent-reported fever (OR 0.75, 95% CI [0.58-0.96]). To create a more parsimonious final model, we excluded detection of human metapneumovirus since it was not associated with pre-admission albuterol in adjusted analyses ($P=0.85$).For completeness, we also examined inpatient data on albuterol use (i.e., albuterol receipt after the primary outcome of pre-admission albuterol use). Among 508 infants who received pre-admisson albuterol, 193 (38%) were also treated with inhaled albuterol during the first 24 hours of admission; among the 500 infants who did not receive pre-admission albuterol, only 77 (15%) went on to be treated with inhaled albuterol during their first 24 hours of inpatient stay ($P<0.001$).

DISCUSSION

Among infants hospitalized for bronchiolitis in the U.S. from 2011-2014 we found that albuterol was a commonly used pre-admission treatment. Albuterol use varied more than three-fold across hospitals, ranging from 23-84% of infants. We also identified several patient characteristics that were independently associated with an increased likelihood of pre-admission albuterol use: older age, history of bronchodilator use, and pre-admission chart documentation of wheeze. By contrast, other factors were

Table 1. Characteristics of infants hospitalized for bronchiolitis and pre-admission albuterol use.

Characteristics	All (n=1008) n (%)	Did not receive pre-admission albuterol (n=500) n (%)	Received pre-admission albuterol (n=508) n (%)	P-value
Age at enrollment in months, median (IQR)	3.2 (1.6-6.0)	2.3 (1.3-4.0)	4.5 (2.5-7.2)	<0.001
Age at enrollment in months				<0.001
<2.0 months	305 (30%)	214 (43%)	91 (18%)	
2.0-5.9 months	451 (45%)	208 (42%)	243 (48%)	
≥6 months	252 (25%)	78 (6%)	174 (34%)	
Sex				0.43
Male	603 (60%)	293 (59%)	310 (61%)	
Female	405 (40%)	207 (41%)	198 (39%)	
Race/ethnicity				0.27
Non-Hispanic white	426 (42%)	226 (45%)	200 (39%)	
Non-Hispanic black	239 (24%)	116 (23%)	123 (24%)	
Hispanic	305 (30%)	140 (28%)	165 (32%)	
Other	38 (4%)	18 (4%)	20 (4%)	
Insurance				0.34
Private	388 (39%)	197 (40%)	191 (38%)	
Public	601 (60%)	290 (58%)	311 (61%)	
None	17 (2%)	11 (2%)	6 (1%)	
Parental history of asthma for either or both parents	343 (34%)	157 (31%)	186 (37%)	0.08
Premature birth (≤37 weeks)	185 (18%)	97 (19%)	88 (17%)	0.39
Number of breathing problems prior to admission				<0.001
0	803 (80%)	420 (84%)	383 (75%)	
1	159 (16%)	71 (14%)	88 (17%)	
2	46 (5%)	9 (2%)	37 (7%)	
Previous use of bronchodilator	445 (44%)	158 (32%)	287 (57%)	<0.001
Number of days since start of current breathing problem prior to pre-admission				0.35
0-6 days	879 (87%)	431 (86%)	448 (88%)	
≥7 days	129 (13%)	69 (14%)	60 (12%)	
Symptoms in 24 hours prior to arrival at hospital, as reported by parents				
Cough	968 (96%)	477 (95%)	491 (97%)	0.31
Runny nose	685 (68%)	333 (67%)	352 (69%)	0.36
Fever	501 (50%)	239 (48%)	262 (52%)	0.23
Hoarseness	552 (55%)	261 (52%)	291 (57%)	0.11
Breathing faster than normal	883 (88%)	424 (85%)	459 (90%)	0.007
Wheezing	728 (72%)	323 (65%)	405 (80%)	<0.001
Retractions	724 (72%)	341 (68%)	383 (75%)	0.01
Stopped breathing	85 (8%)	57 (11%)	28 (6%)	0.001
Pre-admission visit				
Presence of apnea				<0.001
No or not documented	952 (94%)	459 (92%)	493 (97%)	
Yes	56 (6%)	41 (8%)	15 (3%)	

IQR, interquartile range; *ED*, emergency department; *bpm*, beats per minute; *ABG*, arterial blood gas; *IV*, intravenous; *CPAP*, continuous positive airway pressure; *ICU*, intensive care unit; *RSV*, respiratory syncytial virus; *RV*, rhinovirus; *hMPV*, human metapneumovirus.
Data are presented as n (%) unless otherwise specified.
*Pathogens tested: RSV types A and B; RV; hMPV, parainfluenza virus types 1, 2, and 3; coronaviruses OC43, 229E, HKU1, and NL63; enterovirus; bocavirus type 1, influenza virus types A and B; adenovirus; *B. pertussis; and M. pneumoniae.*

Table 1. Continued.

Characteristics	All (n=1008) n (%)	Did not receive pre-admission albuterol (n=500) n (%)	Received pre-admission albuterol (n=508) n (%)	P-value
Presence of wheezing				<0.001
No	361 (36%)	262 (52%)	99 (19%)	
Yes	599 (59%)	202 (40%)	397 (78%)	
Not documented	48 (5%)	36 (7%)	12 (2%)	
Initial respiratory rate per minute, median (IQR)	48 (40-60)	48 (40-60)	49 (40-60)	0.23
Initial oxygen saturation by pulse oximetry				0.47
<90%	91 (9%)	40 (8%)	51 (10%)	
90%-93.9%	154 (16%)	75 (15%)	79 (16%)	
≥94%	747 (75%)	378 (77%)	369 (74%)	
Virology				
Number of pathogens detected*				0.003
0	27 (3%)	16 (3%)	11 (2%)	
1	699 (69%)	368 (74%)	331 (65%)	
≥2	282 (28%)	116 (23%)	166 (33%)	
RSV	814 (81%)	409 (82%)	405 (80%)	0.40
RV	212 (21%)	102 (20%)	110 (22%)	0.63
hMPV	56 (6%)	19 (4%)	37 (7%)	0.02

IQR, interquartile range; *RSV*, respiratory syncytial virus; *RV*, rhinovirus; *hMPV*, human metapneumovirus.
Data are presented as n (%) unless otherwise specified.
*Pathogens tested: RSV types A and B; RV; hMPV, parainfluenza virus types 1, 2, and 3; coronaviruses OC43, 229E, HKU1, and NL63; enterovirus; bocavirus type 1, influenza virus types A and B; adenovirus; *B. pertussis; and M. pneumoniae.*

associated with decreased likelihood of pre-admission albuterol use: symptoms present seven days or longer; and parent-reported fever within 24 hours prior to arrival at the hospital.

Our findings suggest that variation in pre-admission albuterol use is strongly influenced by local policy and/or culture. This is consistent with previous literature, which has established local variation across many therapies, including albuterol, in the management of infants hospitalized for bronchiolitis.[9,10,17,18] Local policies are shaped in part by the AAP national guidelines on bronchiolitis, which include recommendations on albuterol use. In an earlier version of the AAP guidelines, published in 2006 (prior to study enrollment), a trial of α- or β-adrenergics remained an "option" for all patients with bronchiolitis.[15] Local variation in albuterol use for bronchiolitis persisted, as shown in recent studies and supported by our data, which was collected from 2011-2014.[17,19] The most recent AAP guidelines were published in November 2014 and now state that "[c]linicians should not administer albuterol (or salbutamol) to infants and infants with a diagnosis of bronchiolitis."[12] As our data showed, a large majority of infants who receive bronchodilators for bronchiolitis will do so in the pre-admission setting first, so this recommendation especially affects clinicians working in the hospital ED. The evidence behind this recommendation is therefore important context for our observations of chosen therapies for albuterol.

The AAP's updated recommendation against albuterol use for bronchiolitis is based on "greater evidence" that showed no benefit in bronchodilator use. Specifically referenced was a 2014 Cochrane meta-analysis of 30 randomized controlled trials (RCT) assessing bronchodilators for "bronchiolitis," based on diverse definitions and clinical populations. This meta-analysis found that bronchodilators used for bronchiolitis were not effective in improving oxygen saturation, nor in reducing the need for hospitalization, and did not shorten length of illness in the hospital or home. Based on these outcomes, the authors concluded that bronchodilators were "not effective in the routine management of bronchiolitis."[11] The analysis had been updated from a meta-analysis previously published in 2006, which had concluded that bronchodilators produced a "modest improvement" in clinical scores.[20] This clinical improvement was not found in the most recent analysis, and may have contributed to the shift in the AAP's recommendation. Both analyses, however, were limited by significant heterogeneity, and noted that all of the included trials were small and that standardized outcomes were not available across the 30 RCTs.[21-26] Furthermore, while the meta-analysis authors' conclusion was to consider bronchodilators ineffective in treating bronchiolitis, they did distinguish that this recommendation in practice

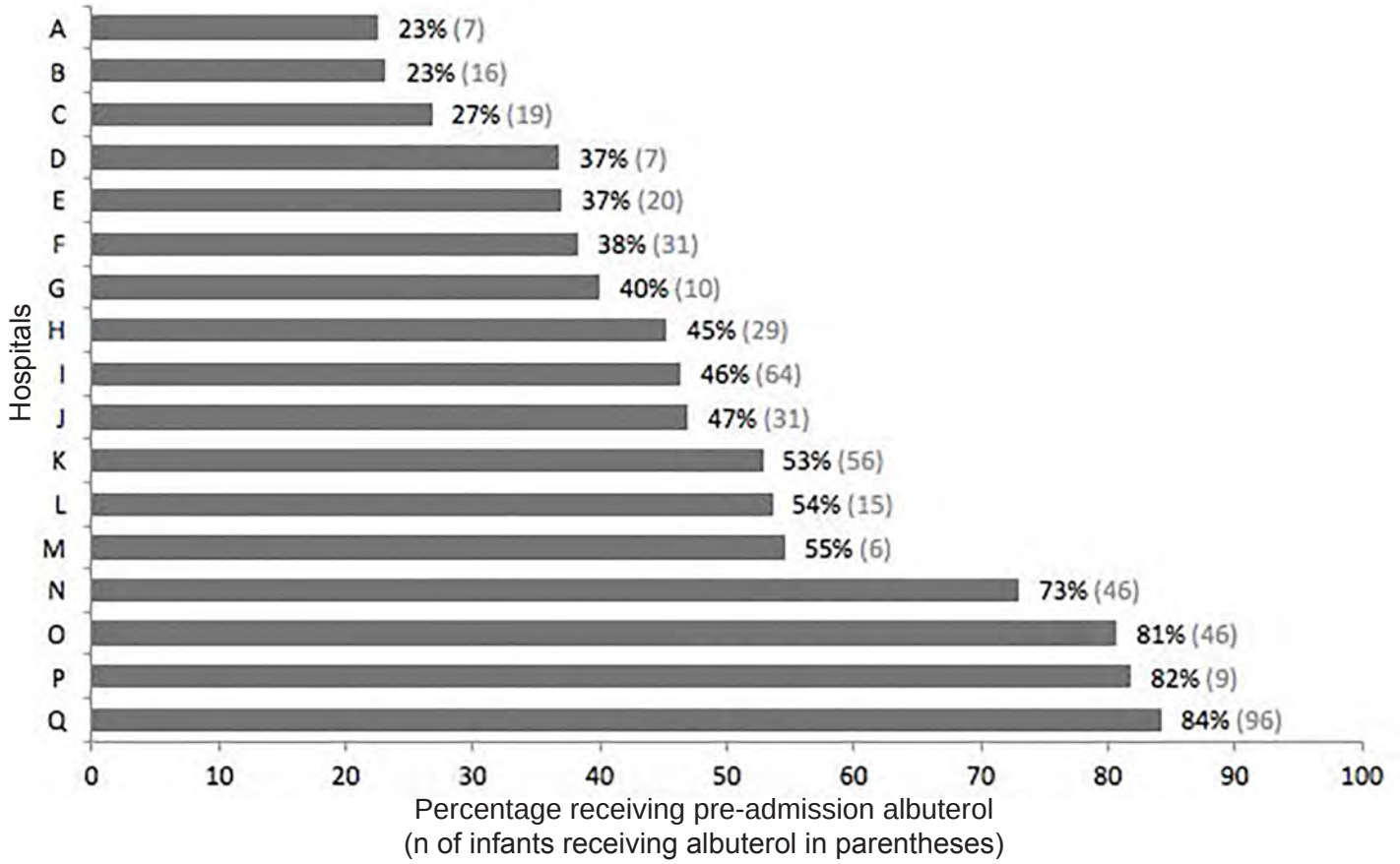

Figure. Pre-admission treatment with inhaled albuterol among infants hospitalized for bronchiolitis, by hospital of enrollment.

applied only to "first-time wheezers."[27]

For evidence against albuterol in infants with recurrent wheeze, the AAP guidelines cite Chavasse and colleagues' 2002 meta-analysis that concluded no benefit was found in the use of short-acting beta-agonists for recurrent wheeze in infants under two years of age. This analysis was also limited by significant heterogeneity, was not specific to bronchiolitis or a clinical setting, and concluded there was overall "conflicting evidence."[28] The evidence cited by the 2014 AAP for eliminating a trial of albuterol in bronchiolitis is still therefore limited to small studies with no standardized outcomes and no clear focus on albuterol or infants less than one year of age.

Notwithstanding this evidence, the AAP guidelines acknowledge that a subgroup of infants may have clinical benefit from the effects of albuterol, but this subgroup was not sufficiently defined at the time of the guidelines' release. The possibility of an unidentified subgroup of responders has been a common refrain in analyses of β_2-agonists for bronchiolitis; a meta-analysis in 1997 noted the "possibility that β_2-agonists are particularly effective therapy for certain subgroups of bronchiolitic patients."[29] Early papers showing benefit from albuterol use in bronchiolitis were considered by the AAP guidelines to be a result, in part, of including older infants (greater than one year of age).[29,30] Thus far, though, attempts to define a subgroup of responders to albuterol have focused more on the clinical setting of bronchiolitis treatment (e.g., a comparison of hospitals or inpatient/outpatient settings) rather than the patient characteristics of those who appear to respond.[11,28] The site of treatment has similarly been the focus of papers examining overall variability in the management of bronchiolitis.[9,14,31]

Our results show that subgroups exist to whom clinicians preferentially give albuterol, enough to cause significant variation in albuterol use even when controlling for hospital-specific variation. The characteristics independently associated with pre-admission albuterol use, including older age, previous bronchodilator use, and presentation with wheeze, resemble those of children whose illness is consistent with recurrent wheeze, a potential precursor of childhood asthma.[32,33] In a recent latent class analysis by our group, a statistical method used on continuous or categorical variables to identify unknown classes, we examined the heterogeneity of 2,500 children (<24 months of age, median age 5.8 months) with bronchiolitis to formally study the issue.[34] Briefly, we identified a distinct cluster ("Profile A") of infants who were older (>6 months), had a history of wheeze, and a higher rate of bronchodilator use. Together with our current results (and previous studies), we believe that there

Table 2. Multivariable predictors of pre-admission albuterol use for bronchiolitis.

Characteristics	OR	95%CI		P-value
Age at enrollment in months				
<2.0 months	1.00	reference		
2.0-5.9 months	2.09	1.45	3.01	<0.001
≥6 months	2.89	1.99	4.19	<0.001
Sex				
Male	1.00	reference		
Female	1.06	0.74	1.52	0.76
Race/ethnicity				
Non-Hispanic white	1.00	reference		
Non-Hispanic black	0.94	0.64	1.37	0.74
Hispanic	1.36	0.51	3.65	0.54
Other	1.21	0.53	2.75	0.65
Insurance				
Private	1.00	reference		
Public	1.12	0.75	1.66	0.57
None	0.63	0.20	2.00	0.44
Parental history of asthma for either or both parents	1.12	0.80	1.59	0.51
Premature birth (≤37 weeks)	0.82	0.56	1.21	0.32
Number of breathing problems prior to admission				
0	1.00	reference		
1	0.88	0.54	1.43	0.60
2	1.76	0.85	3.64	0.13
Previous use of bronchodilator	1.89	1.24	2.90	0.003
Number of days since start of current breathing problem prior to pre-admission				
0-6 days	1.00	reference		
≥7 days	0.66	0.44	1.00	0.049
Fever in 24 hours prior to arrival at hospital	0.75	0.58	0.96	0.02
Stopped breathing in 24 hours prior to ED arrival	0.65	0.41	1.03	0.07
Presence of wheezing (pre-admission chart)				
No	1.00	reference		
Yes	3.94	2.61	5.93	<0.001
Not documented	1.03	0.40	2.61	0.96
Number of pathogens detected*				
0	0.79	0.35	1.78	0.57
1	0.87	0.59	1.28	0.48
≥2	1.00	reference		

OR denotes odds ratio; *CI*, confidence interval; *ED*, emergency department.
*Pathogens tested: RSV types A and B; RV; hMPV, parainfluenza virus types 1, 2, and 3; coronaviruses OC43, 229E, HKU1, and NL63; enterovirus; bocavirus type 1, influenza virus types A and B; adenovirus; *B. pertussis; and M. pneumoniae.*

is a clinical subgroup of infants with bronchiolitis that has been identified now through two different methods: objective statistical analysis and observed clinician choices of therapy.[35,36] Guidelines that restrict the use of albuterol in all bronchiolitis patients without specifically addressing these patient characteristics are not targeting a significant source of the variation that they aim to reduce. Translational work is needed to further refine these patient characteristics.

The AAP guidelines also base their recommendation against albuterol on the lack of an appropriate objective measure to identify a response of bronchiolitis to β_2-agonists. We recognize that an objective measure for assessing short-term response to

bronchodilators in an infant with bronchiolitis is not available for clinical use; however, such tools are available for research purposes and in non-acute settings.[37-40] In addition, objective clinical scores for this purpose have yet to be widely adopted, and have not been shown to change prescribing practices for bronchodilators in bronchiolitis.[41] However, lack of an objective measure serves as only more reason to better understand patterns in clinicians' subjective use of albuterol.[42] Our inability to measure a benefit does not mean it is insignificant.

We suggest that future trials of albuterol for bronchiolitis could be targeted to patients with characteristics consistently identified by clinicans as potential responders, who as a subgroup may have contributed to the clinical benefit shown in earlier generalized trials of albuterol for bronchiolitis.[29,30] Identifying children as possible responders to albuterol would allow for a reduction in variation of the use of albuterol for bronchiolitis, without losing entirely its potential therapeutic benefit. At the same time, future trials would allow this subgroup to be more precisely defined in order to avoid inappropriately labeling children as requiring more intensive treatment.

LIMITATIONS

In our analysis, the factors we evaluated for association with pre-admission albuterol use were predominately limited to those collected during a single intake visit, including a parent interview, and could not account for all possible sources of demographic and clinical variation in pre-admission albuterol use. However, our data were supplemented with medical record reviews for further information pertaining to the pre-admission visit and hospitalization. Another limitation is that we did not collect data on the presence of clinical decision support or local quality improvement efforts, and thus,were unable to address how these may have affected hospital-specific rates of albuterol use. However, the multivariable analysis controlled for the clustering of clinician use of albuterol by hospitals, so these efforts would be accounted for in our primary result. Another limitation is that our study did not include patients who presented with bronchiolitis to the ED or another pre-hospital setting but were not later admitted to the hospital. We did not seek to describe the relationship of albuterol with rates of admission. This could be an area for future study. Finally, our study was not designed to address clinical outcomes of albuterol use, as there is no objective clinical measurement for improvement in the pre-admission setting.

CONCLUSION

This prospective, multicenter, multiyear study of >1,000 infants hospitalized for bronchiolitis showed more than three-fold variation across hospitals in the use of albuterol as a pre-admission treatment from 2011-2014. Several other factors were shown to be associated with albuterol use, including age, presence of wheezing documented in pre-admission chart, and previous use of a bronchodilator. While variation of albuterol use has been reported in previous studies, they have not addressed patient characteristics associated with albuterol use. Given the most recent publication of AAP guidelines recommending against any albuterol use to treat bronchiolitis in infants,[12] defining a possible subgroup of responders is of renewed importance. Factors that were associated with pre-admission albuterol use – based on clinical data, and supported by recent cluster analyses[34] – suggest a promising area for future investigation of the targeted use of pre-admission albuterol among a subset of infants with bronchiolitis.

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Even the Thinnest Salami Contains Some Meat

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In this issue of the journal, Condella *et al* describes apparently vast differences between emergency departments (ED) in the use of albuterol for infants with bronchiolitis who were sufficiently ill as to require admission to the hospital.[1] This study is a secondary analysis of a subset of patients admitted to the hospital or pediatric intensive care unit in the Multicenter Airway Research Collaboration (http://www.emnet-usa.org). The data is relatively old and pre-dates the current American Academy of Pediatrics (AAP) guideline to not even attempt albuterol use in these patients.[2]

At first blush the difference in albuterol use is striking. In some centers as few as 23% of children destined for admission received albuterol; in others, 84% did. Given that the AAP guidelines at the time advised a therapeutic trial of albuterol for bronchiolitis, the obvious question is why was albuterol not tried in everyone?

It is tempting to point to the almost-religious zeal with which some groups oppose albuterol use in these patients. The dogma appears odd given that random controlled trial evidence in fact favors a trial of albuterol in these patients.[3] Meta analyses were crafted that excluded studies which found decreased admissions with albuterol.[4-6] Null analyses with a power as low as 18% have been mischaracterized as evidence to not use albuterol.[6-7] When even these select studies showed that albuterol decreased respiratory distress in infants with bronchiolitis, "relief of respiratory distress" was dismissed as "not patient centered."[2] Perhaps this is the culture to which Condella *et al* refers when trying to explain its findings.

Other reasons may be the natural history of bronchiolitis and the heterogeneity in its diagnosis. The natural history of bronchiolitis is broadly this: inoculation (day #0) with a swift rise in prostanoid production (possibly triggering apnea[8]), followed by cough and runny nose starting on day #3. This is followed on days #3 to #5 by gradual-onset wheezing in the lung bases, which progresses throughout the lungs and from day #5 is accompanied by the development of crackles in the lower lung bases. The disease peaks in severity about day #7 to #9 post-inoculation by which stage crackles heard first become predominant throughout all lung fields before gradually resolving from days #10 to #14. Each of these stages of bronchiolitis invites different treatments, and even different diagnoses. In the upper respiratory tract infection-phase stage, albuterol seems unlikely to help. Later phases may attract diagnostic terms such as viral-induced wheeze, wheezy bronchitis, reactive airway disease and even asthma, rather than bronchiolitis. When a child has wheezing albuterol is more likely to be prescribed, and by the time the child has predominantly crackles the doctor may believe that there is no point trying albuterol.

The inclusion criteria of the parent study do not help. Although Condella *et al* refers to the description of bronchiolitis in the 2004 AAP guidelines, the inclusion criteria of the parent study required that the patient have a "physician diagnosis of bronchiolitis." Some physicians may interpret (in an unfortunately circular logic) a response to albuterol as evidence against bronchiolitis. So, at least some of the difference between EDs' use of albuterol may reflect heterogeneity in diagnosis.

The actual recruitment over a three- to four-year period from some of these sites was very low (range 28 to 139 patients). To a community pediatric emergency physician 28 bronchiolitics sounds more like a single busy shift rather than three to four years of recruitment. With such low numbers from each site there is concern that neither the study patients nor the diagnostic decision-making are representative of infants who attend for bronchiolitis. The authors provide no data to reassure us on this point.

Another reason for the apparent starkness of the differences is the way in which the authors present their data. Condella *et al* uses bar charts of percentages, which do not account for the total number of patients recruited at each site. Here we re-draw Condella *et al's* Figure as a funnel plot to show how such data can be better presented.[9] Over-dispersion observed in funnel plots is commonly seen when unmeasured covariates are not taken into account.[10]

In our clinical experience many children have in addition to a mixture of crackles and wheezes any number of other ill-defined adventitial noises. Unsurprisingly, interrater agreement for auscultatory findings in bronchiolitis is low.[11] These adventitial

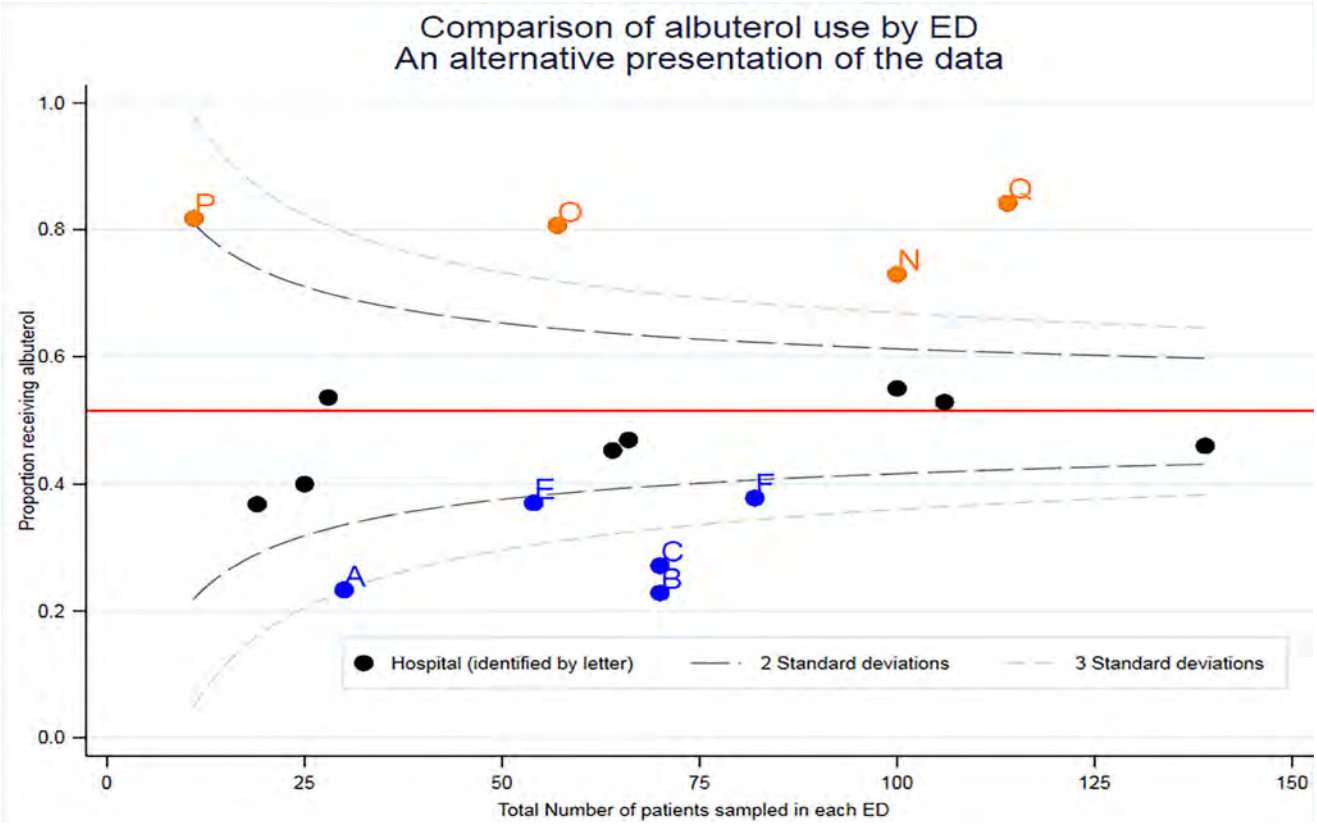

Figure. This funnel plot showing outliers by two and three standard deviations addresses the difficulty of comparing performance when the denominator varies between individual sites. It does not address limitations of the underlying, data-generating mechanism. Data here has been redrawn from Figure 1 in Condella et al. The over-dispersion observed here suggests important unmeasured or unadjusted covariates. *ED,* emergency department.

sounds often improve with albuterol. The accompanying improvement in respiratory distress is often incomplete; even if wheezing resolves, the increased work of breathing often persists. Still, the improvement in respiratory distress is sometimes sufficient to enable safe discharge.

The authors fitted a logistic regression model to explore the relative role of different independent variables that predict the use of albuterol. As might be expected wheezing was associated with more, and duration of illness longer than 7 days with less, albuterol use). Unfortunately, the authors did not take this (analytically straightforward) step further and estimate the probability of a range of typical patients at varying stages of bronchiolitis receiving albuterol at each ED. Plotting these results by ED may have shown the apparent differences to diminish given similar patients. Other quirks in the analysis, such as the reversal of some associations in bivariate and multivariable analysis, remain unaddressed.

Sometimes, as section editors for *WestJEM* we receive manuscripts that have been presented elsewhere prior to reaching our desks. These manuscripts may well have been improved by the input of other reviewers prior to reaching us. However, sometimes we see unwelcome influences and in this manuscript the authors felt the need to state they agree with the AAP guidelines in their abstract's conclusion despite their study not assessing the effect of albuterol. Too often the evidence shows what the most powerful person in the room says it shows. Worse, authors feel the need to genuflect accordingly or remain unpublished. We reviewers and editors are not blameless.

So, what does Condella *et al* offer the practicing emergency physician?

1. An insight into the likely heterogeneity in the diagnosis of bronchiolitis in academic EDs.
2. Evidence of a determination in some academic EDs to not use albuterol in bronchiolitis even when AAP guidelines recommended a therapeutic trial. Presumably convinced of the correctness of their own position (evidence not withstanding) this group felt themselves in no way bound by the AAP guidelines of the time. Community emergency physicians should feel similarly empowered today.
3. (Yet more) evidence of some corners of academia pushing the thinnest of salami papers with the least effort that they can get away with while genuflecting towards power and tenure committees rather than advancing knowledge.

So why publish? First, 1 and 2 are informative for emergency physicians who find the current AAP recommendation to not attempt a therapeutic trial of albuterol at odds with their own experience that albuterol sometimes helps. Second, Condella *et al* demonstrates to future trialists that standardized diagnostic criteria or analysis adjustment based on clinical descriptors of the illness could improve future bronchiolitis research.

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Ruling out Pulmonary Embolism in Patients with High Pretest Probability

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Introduction: The American College of Emergency Physicians guidelines recommend more aggressive workup beyond imaging alone in patients with a high pretest probability (PTP) of pulmonary embolism (PE). However, the ability of multiple tests to safely rule out PE in high PTP patients is not known. We sought to measure the ability of negative computed tomography pulmonary angiography (CTPA) *along with* negative D-dimer to rule out PE in these high-risk patients.

Methods: We analyzed data from a previous prospective observational study conducted in 12 emergency departments (ED). Wells score criteria were entered by providers before final PE testing. PE was diagnosed by imaging on the index ED visit, or within 45 days, demonstrating either PE or deep vein thrombosis (DVT), or if the patient died of PE during the 45-day, follow-up period. Testing threshold was set at 1.8%.

Results: A total of 7,940 patients were enrolled and tested for PE, and 257 had high PTP (Wells >6). Sixteen of these high-risk patients had negative CTPA *and* negative D-dimer, of whom two were positive for PE (12.5% [95% confidence interval {2.2%-40.0%}]). One of these patients had a DVT on CT venogram and the other was diagnosed at follow-up.

Conclusion: Our analysis suggests that in patients with high PTP of PE, neither negative CTPA by itself nor a negative CTPA *plus a* negative D-dimer are sufficient to rule out PE. More aggressive workup strategies may be required for these patients. [West J Emerg Med. 2018;19(3)487-493.]

INTRODUCTION

Pulmonary embolism (PE) is a deadly disease, often with rapid onset and ensuing precipitous decline.[1] It is, therefore, imperative for physicians to be able to safely rule out PE. The complicated nature of the workup has led to numerous publications describing the diagnostic workup of potential PE.[2-11] The American College of Physicians recommends CTPA as the first diagnostic test for patients who have a high pretest probability (PTP) of PE,[9] with D-dimer testing not recommended as a stand-alone test to rule out PE in this

group. This is also the guideline of other societies, including the American College of Radiology,[10] the American Academy of Family Physicians,[12] and websites such as UpToDate.[11] The American College of Emergency Physicians is an exception, having a Level C recommendation to perform two negative tests to rule out PE in high PTP patients.[8] In this study, we sought to validate this guideline by testing the ability of a negative CTPA *with* a negative D-dimer to rule out PE in high-risk patients.

Population Health Research Capsule

What do we already know about this issue?
Pulmonary embolism (PE) is a deadly disease, and in patients with high pretest probability (PTP) of PE, computed tomography pulmonary angiography (CTPA) can often miss PE.

What was the research question?
Is negative CTPA along with a negative D-dimer sufficient to rule out PE in high PTP patients?

What was the major finding of the study?
In patients with high PTP of PE, neither negative CTPA nor negative CTPA plus negative D-dimer is sufficient to rule out PE.

How does this improve population health?
In patients with high PTP for PE, more aggressive workup strategies may be required despite initial negative testing.

METHODS

We used data from a previous prospective, observational study conducted in 12 emergency departments (ED) in the United States from July 1, 2003, until November 30, 2006, using methodology previously described in a report validating the Pulmonary Embolism Rule-out Criteria (the PERC rule).[13] This study was approved by the institutional review boards for the conduct of human subject research at all institutions. Of note, the original study included a New Zealand site; however, given the potential for practice variation between U.S. sites and a single NZ site, we limited our analysis to the U.S. sites. This is consistent with previously published work from this dataset.[14,15]

Patients were enrolled in the ED and included if they had signs or symptoms that the treating physician interpreted as sufficient to warrant testing for PE (at least one of the following: D-dimer blood test, CTPA, or ventilation-perfusion scan) and they indicated willingness to participate by process of informed consent. Patients were excluded if they were already being treated for venous thromboembolic disease (PE or deep venous thrombosis [DVT]) with therapeutic levels of anticoagulation as well as patients with CTPA, ventilation-perfusion scintillation, or duplex Doppler testing performed within the preceding seven days that was diagnostic of PE or DVT. Also excluded were patients with overt circulatory shock or respiratory failure, as well as those with social circumstances that have been highly predictive of loss to follow-up, including homelessness or imprisonment.

All clinical data, including signs, symptoms, and variables (including Wells score criteria), were entered before recording the results of final PE testing while patients were in the ED. Using the standard definitions of negative, Liatest, VIDAS, and MDA D-dimers were considered negative at concentrations of <500 ng/ml, Biopool Minutex at <250 ng/mL, Hemosil at <244 ng/mL, and the advanced D-dimer at <1.6 lg/mL. The outcome of interest was a diagnosis of acute PE during the index ED visit or within 45 days of the patient's ED evaluation. We considered patients to have PE if they were evaluated for possible PE in the ED, and had radiologic confirmation of the diagnosis of either PE or DVT during the index visit or within 45 days of the index visit, or if they died of PE during the 45-day follow-up period. Confirmatory imaging included CTPA or conventional angiography showing a pulmonary arterial or deep venous filling defect interpreted as positive for PE or DVT, high-probability V/Q scan, or positive venous ultrasound consistent with DVT in the proximal or distal vasculature of the upper or lower extremities. All imaging results were based on the dictated report of board-certified attending radiologists not affiliated with (and blinded to) the study. Patients were followed for 45 days using a previously validated, published methodology that included chart review and telephone follow-up.[13,16]

Testing threshold was set at 1.8% based on the Pauker and Kassirer method.[17,18] Proportions are described with confidence intervals (CI) using mid-p exact calculations. We used Microsoft Excel for all calculations.

RESULTS

A total of 7,940 patients were prospectively enrolled in the original study,[13] of whom 257 had Wells score > 6 and thus had high PTP. The table shows baseline characteristics of these patients. The overall rate of PE in these high PTP patients was 37.4% (95% CI [31.5%-43.6%]). Of the 205 high PTP patients who underwent CTPA, four had CTs that were either incomplete or indeterminate. Of the remaining 201 valid CTPAs, 130 were negative for PE. Sixteen of these 130

Table. Characteristics of patients enrolled in 12 emergency departments across the United States presenting with signs or symptoms suggestive of high risk (Wells score > 6) of pulmonary embolism (n=257).

Demographics	% or Mean	95% Confidence Interval	
Age	52.8 [range 17-91]	50.6	54.9
Female	54.9% (141/257)	48.7%	60.9%
White	61.1% (157/257)	55.0%	66.9%
Black	30.4% (78/257)	25.0%	36.2%
Hispanic	6.2% (16/257)	3.7%	9.7%
Asian	0.8% (2/257)	0.1%	2.5%
Other race	1.6% (4/257)	0.5%	3.7%

patients, or 12.3% (95% CI [7.4%-19.5%]), were ultimately positive for PE (Figure 1a.). One of these 16 patients had an intermediate V/Q scan and a proximal clot on extremity Doppler. Seven patients had DVTs found on CT venogram. An additional two had proximal DVTs on extremity Doppler, and one had distal DVT on extremity Doppler. The remaining patients were diagnosed on follow-up.

Eighty-two of the 257 high PTP patients underwent both CTPA and D-dimer (Figure 1b). Sixteen of these patients had negative CTPA *and* negative D-dimer, and two of these 16 (12.5% [95% CI {2.2%-40.0%}]) were positive for PE. One of these patients had DVT on CT venogram, and the other was diagnosed on follow-up.

DISCUSSION

This analysis was undertaken to determine if current guidelines can rule out PE in high PTP patients. Our analysis suggests that neither negative CTPA (by itself) nor negative CTPA *with* negative D-dimer can sufficiently rule out PE in high-risk patients. This is in line with previous research. Multiple studies have shown that CTPAs miss some PE.[19-22] In the landmark PIOPED-II trial, the sensitivity of CTPA was 83%; moreover, in the subset of high-risk patients, 40% of patients with negative CTPA were diagnosed with PE or DVT.[23] Moreover, our analysis suggests that adding a negative D-dimer to a negative CTPA may still be insufficient to rule out PE in high-risk patients.

This appears to be in contrast to literature suggesting that a D-dimer and CTPA algorithm is safe.[5,7] However, studies that evaluated these algorithms included relatively small numbers of high-risk (Wells score > 6) patients, so the apparent safety of the CTPA plus D-dimer strategy may be influenced by the much larger numbers of non-high-risk patients in these studies. When stratifying for high-risk patients, all diagnostic tests have much lower abilities to rule out PE.[3,6,23,24] This is supported by a recent study in which even 64-slice CTPA missed a significant number of PEs in high-risk patients,[25] most of whom were diagnosed by additional imaging within the index visit (with the other few diagnosed during three-month clinical follow-up).[25] Our study shows that in patients with high Wells score, not only is a negative CTPA insufficient to rule out PE, but also that a negative CTPA along with a negative D-dimer still misses a substantial number of PEs.

It is possible that newer CTs with more slices are more sensitive at picking up PEs, and therefore would yield fewer false-negative CTs. However, a Bayesian calculation using meta-analysis data of prevalence of PE in high-probability patients[26] and CTPA sensitivity and specificity[19] also yields an unacceptably high miss rate of 10.4% (95% credible region 6.0%- 15.3%) – similar to our empirical findings of a miss rate of 12.3% (95% CI [7.4%-19.5%]). In other words, to go from a PTP of 37.4% (this prevalence of PE in our cohort was lower than in Ceriani's[26] meta-analysis) to a post-test probability of 1.8%, the negative likelihood ratio (LR[-]) of the test would have to be lower than 0.03. However, a CT sensitivity of 88.9% and specificity of 94.6% (as per the meta-analysis by Hogg et al[19]) yields a LR(-) of only 0.12; other meta-analyses would yield even higher LR(-)s, and therefore make PEs even harder to rule out.[20-22]

Furthermore, a recent study by Moores et al.[25] looked prospectively at outcomes in high-risk patients who underwent 64-slice CTPA. The study found that among patients with high Wells score and negative CTPA, 5.2% had PE or DVT. Therefore, even the newest CT scanners miss an unacceptable amount of PEs in high PTP patients.

It may be that some of these "missed PEs" are subsegmental PEs (SSPE). There is debate as to whether SSPEs need to be treated. On one hand, many SSPEs may not be PEs at all but radiological artifacts,[27] and their clinical significance may be limited.[28] On the other hand, patients with SSPE appear to have similar recurrence rates to those with proximal PEs, and have significantly higher mortality than those without PE.[29] A finding of SSPE may require calculations of risks and benefits regarding anticoagulation, especially in those at increased risk of bleeding.[30,31]

The "test threshold" is meant to balance the benefits of testing (e.g., diagnoses made and treated) with the risks of testing (e.g., for CT, radiation exposure, contrast nephropathy, allergic reactions, false positive results) and to identify patients below which testing is more likely to cause harm than benefit.[17,18] We used a threshold of 1.8%, which is the same threshold calculated by Kline et al.,[18] and similar to the test threshold published by Lessler et al. (1.4%).[32] These thresholds are also similar to the "acceptable" miss rate of pulmonary imaging, determined by the false negative rate of catheter pulmonary angiography. We acknowledge that individual physicians and patients may have their own clinical thresholds for

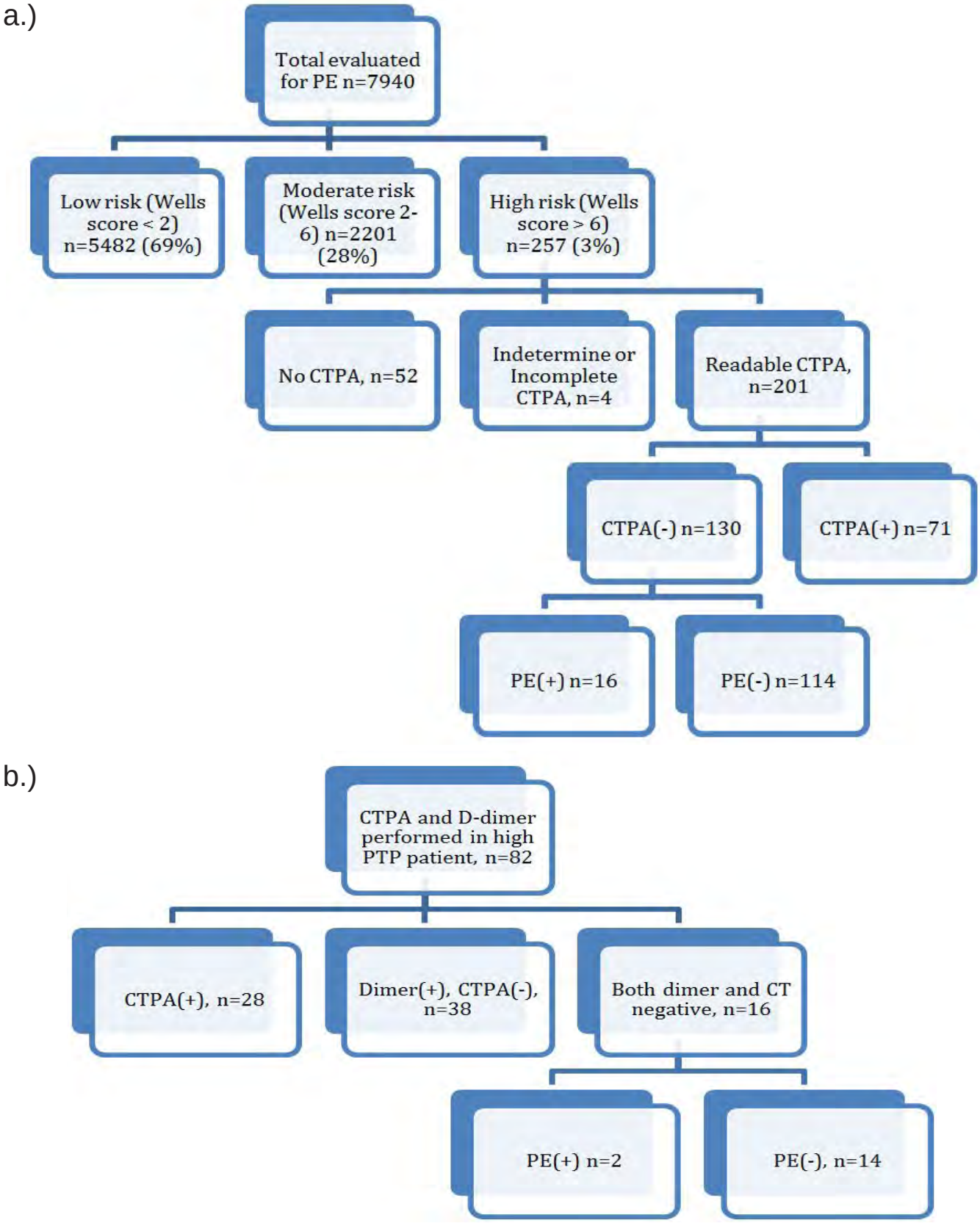

Figure 1. Pathway and outcomes. a)Testing and outcomes of high pretest probability patients. b) Outcomes of high pretest probability patients who had both CTPA and D-dimer
PE, pulmonary embolism; *CTPA*, computed tomography pulmonary angiography; *PTP*, pretest probability.
Note: It is simply a coincidence that the number of patients with negative CTPA who ultimately had PE (n=16) is the same as the number of patients who had both a negative CTPA and negative D-dimer (n=16).

the percentage of PE that are acceptable to miss, and we also acknowledge that the test threshold may vary over time as technology changes and risks of testing (and PE) are recalculated. However, we believe that 1.8% is a reasonable threshold that, at the least, should be reached with diagnostic testing.

LIMITATIONS

The results of this study must be interpreted within the context of its design. Our analysis comes from data from a large, multicenter study, performed in academic and community centers, resulting in a heterogeneous population. The study was observational and noninterventional, such that we believe the results represent the real world, but probably should not be compared or contrasted to studies that purport to follow a rigid study protocol. The diagnostic criterion standard for this study was PE (or DVT) within 45 days of the index visit that was detected by standard care processes. While it is possible that a PE or DVT found during follow-up is truly a *new* thromboembolic event and that negative workup in the ED truly was negative at the time, it is standard in the literature to use diagnosis of PE or DVT during follow-up as the gold standard diagnostic criterion for negative workup in the ED. [3,5,7,19,23,25,29,33-40] The original study did not have the resources to perform radiologic testing to monitor asymptomatic patients for PE or DVT. It remains possible that a few patients had a PE or DVT and went undiagnosed during the follow-up period, and these patients were incorrectly classified as true-negatives.

Since this was a multicenter trial, multiple different D-dimers were used. We feel this strengthens the generalizability of our findings. However, although our data analysis did not suggest this, it is possible that some assays are more prone to false negatives than others.

Despite the fact a large number of patients were enrolled, relatively few patients had a high Wells score. This is consistent with observations from our prior work.[15,33] The relatively small number of patients with Wells score > 6 may be why our empiric data revealed only 16 high-risk patients with negative CTPA *and* negative D-dimer. However, while this particular sample size led to a wide confidence interval, this 95% CI still did not cross the 1.8% threshold at which further workup for PE can be stopped.[18,32,41]

CONCLUSION

Our study suggests that in patients with high pre-test probability for PE, a negative CT should be interpreted with caution, and that even *two* high-sensitivity tests may be insufficient to rule out PE in these high-risk patients. Further studies should evaluate long-term outcomes in high PTP patients – in particular, those who have been "ruled out" by diagnostic testing.

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In the U.S. "Healthcare" Is Now Strictly a Business Term

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In the U.S., healthcare is now strictly a business term. Healthcare organizes doctors and patients into a system where that relationship can be financially exploited and as much money extracted as often as possible by hospitals, clinics, health insurers, the pharmaceutical industry, and medical device manufacturers. If possible, the more that patients resent their doctors, the better it is for the business of healthcare. As long as that dynamic exists, patients and doctors will never align: this would be the ultimate threat to the business of healthcare.

This adversarial patient-doctor relationship is maintained by overworking and under-supporting doctors both with regard to heaping administrative burden/caseloads on them and limiting how much help they can actually offer patients. The patients then encounter a vast number of burned-out doctors whose shining idealism once held in medical school has been slowly drawn out of them.

In primary care, patients feel they are left unheard because doctors spend just 15 minutes with them. Doctors feel as if they don't have time to listen because they only have 15 minutes with their patients. The situation is exacerbated by TV ads that tell doctors and patients the newest pill will fix the patient's problem: the healthcare business only needs the doctor and patient to interact just long enough for the doctor to be the conduit whereby that pill gets prescribed.

We in the emergency department proudly serve as the safety net for patients in need. We see anybody, anywhere, anytime. Along with our colleagues – the hospitalists and on-call specialists – we work tirelessly day and night to help patients. After these interactions, however, the healthcare business offers little by way of support for the patient or the doctor. And then the medical billing mechanism begins to churn. Money is requested by the hospital/clinic billing department on behalf of the doctor from the patient's insurance or the patient directly. This process is so opaque that neither patients nor doctors can understand it, and no one will willingly explain it.

This confusion is created deliberately to obfuscate the way that hospitals, clinics, health insurers, and drug and medical device manufacturers have made billions in the business of healthcare. Publicly traded, for-profit health insurers, for example, make billions per year. As these companies' shares are publicly traded on the New York Stock Exchange, they have a fiduciary (legal) responsibility to make money for their shareholders, not to do what's best for the patient. That seems antithetical to any healthcare system.

Hospitals also siphon billions of dollars from the system, shifting dollars to shareholders to build new hospitals or expand capacity to increase their market share. Meanwhile, patients are sent obscene bills and blame the doctors. It's a beautifully orchestrated scheme in which the U.S. spends more and more on healthcare – more in fact than any other country in the world – and ironically those who gain the least are the patients and the doctors.

What can we do?

I think the first step is awareness that this is happening and getting worse. Awareness is particularly important among medical students and residents. Medical education has long ignored the business of medicine as part of undergraduate/graduate medical education, but that is starting to change. Many medical schools have started rolling out a new curriculum termed Health System Science, which is considered the "third science" along with basic sciences and clinical medicine. A recently released textbook is a good read for medical students, residents and attendings alike (https://www.amazon.com/Health-Systems-Science-Susan-Skochelak/dp/0323461166).

I would also suggest reaching out to the American Medical Association (AMA), your AMA state chapter, or your specialty practice group (American College of Emergency Physicians, for me). Get involved at the state or national level to develop an understanding of the landscape in order to best navigate a way forward. Next, consider getting an MBA. For medical students if your medical school offers a combined

degree, do it. Alternatively, consider taking time off during med school to get an MBA or pursue an MBA after residency. An advanced business degree will provide a level of understanding needed to navigate the financial chaos.

Speak up. Call or write your local congressional Representative and U.S. Senators to voice your concerns. The phone number to the U.S. Capitol switchboard is (202) 224-3121. You can find information on who represents you at this site: https://www.congress.gov/contact-us

Finally, we need to form a coalition of physicians and patients who can advocate for changes that serve our interests. I'm unaware of a strong patient-physician advocacy group at this time that has enough power to oppose the lobbying efforts of the industries noted above. It would be an important next step.

All that being said, I do not mean to equate the business of healthcare with the practice of medicine. To those of us in practice, medicine, both the science and the art, brings us great joy and purpose. We have dedicated our lives to helping others and we are nothing if not resilient. As we move forward, I do not see a simple solution to this problem, nor do I believe there is a particular set of tactics we should pursue that will help us fix this. What I will say is this - as physicians we are the true medical experts and we should not be afraid to speak up on behalf of our patients and ourselves whenever we encounter situations where the business of healthcare is placed above/or is in conflict with the practice of medicine.

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Decreased Nursing Staffing Adversely Affects Emergency Department Throughput Metrics

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Introduction: The effect of nurse staffing on emergency department (ED) efficiency remains a significant area of interest to administrators, physicians, and nurses. We believe that decreased nursing staffing adversely affects key ED throughput metrics.

Methods: We conducted a retrospective observational review of our electronic medical record database from 1/1/2015 to 12/31/2015 at a high-volume, urban public hospital. We report nursing hours, door-to-discharge length of stay (LOS) and door-to-admit LOS, and percentage of patients who left without being seen (LWBS). ED nursing hours per day was examined across quartiles with the effect evaluated using analysis of covariance and controlled for total daily ED volume, hospital occupancy and ED admission rate.

Results: From 1/1/15-12/31/15, 105,887 patients presented to the ED with a range of 336 to 580 nursing hours per day with a median of 464.7. Independent of daily ED volume, hospital occupancy and ED admission rate, days in the lowest quartile of nursing hours experienced a 28.2-minute increase per patient in door-to-discharge LOS compared to days in the highest quartile of nursing hours. Door-to-admit LOS showed no significant change across quartiles. There was also an increase of nine patients per day who left without being seen by a provider in the lowest quartile of nursing hours compared to the highest quartile.

Conclusion: Lower nursing hours contribute to a statistically significant increase in door-to-discharge LOS and number of LWBS patients, independent of daily ED volume, hospital occupancy and ED admission rate. Consideration of the impact of nursing staffing is needed to optimize throughput metrics for our urban, safety-net hospital. [West J Emerg Med. 2018;19(3)496-500.]

INTRODUCTION

Emergency department (ED) efficiency remains a vital aspect of delivering safe, quality care. ED utilization has risen considerably without a corresponding rise in available emergency services.[1,2] To respond to the increased demand, it is imperative to identify factors that contribute to delays in care. Researchers have identified several hospital characteristics associated with worse ED throughput or ED time on ambulance diversion including ED crowding,[3] percentage of ED patients admitted,[4,5,6] number of elective surgical admissions,[5] hospital occupancy,[5,6,7] training level of the treating physician,[3] access to expedited diagnostic testing,[8] socioeconomic status of the surrounding neighborhood,[9] and decreased nurse staffing.[10]

Prior studies identified that increased nurse-to-patient ratios correlate with improved patient outcomes[11,12] and that lower staffing is associated with increased left without being seen (LWBS) rates[13] and increased ED care times.[10] Our urban, tertiary care, safety-net, teaching hospital suffered a nursing shortage during 2015 due to an administrative initiative to decrease costs by limiting nurse overtime hours. Without a concomitant increase in hiring, this change caused significant gaps in ED nurse staffing. These gaps led to unpredictable closures of sections of the ED and increased average nurse-to-patient ratios. Our goal was to evaluate the impact of decreased nurse staffing on ED throughput metrics. We believe decreased nurse staffing adversely affects these metrics.

METHODS

Our hospital is an urban, tertiary care, safety-net hospital with 254 medical/surgical inpatient beds and 80 ED beds. The ED is staffed by full-time, board-certified attending emergency physicians who supervise emergency medicine residents, residents from other specialties, and physician assistants. Hospital-stipulated maximum nurse-to-patient ratios were not changed or exceeded during the study period. Nurses work a mix of 8- and 12-hour shifts. The ED is also staffed by patient care technicians and patient transporters.

We conducted a retrospective observational review using Cerner First Net electronic medical record (EMR) database. All EMRs of 105,887 ED visits from January 1, 2015, to December 31, 2015, were queried after institutional review board approval. We included in the analysis all patients discharged or admitted to the medical/surgical inpatient beds in the analysis regardless of inpatient or observational status. Patients admitted to the intensive care unit or the ED observation unit were excluded as the admission protocol to these units varies significantly from general admission; therefore, we could not accurately capture the length of stay (LOS) of these patients from EMR review. A total of 6,602 patients were excluded.

The unit of measure was a 24-hour period starting at midnight. Daily number of patients admitted, discharged, and LWBS as well as the total daily volume in the ED was recorded. Daily nursing hours were determined from nursing staff records for each shift and summed for each day. We measured door-to-discharge LOS in minutes as the interval from the time of presentation to the ED to when the provider discharged the patient. We captured the time of initial presentation by the time the patient was registered at the front desk. The time of discharge was captured by a physician order for discharge placed in the EMR. Door-to-admit LOS was measured in minutes as the interval from the time of ED presentation to when the nurse placed an electronic order that the patient was ready to be transported to the ward. We defined hospital occupancy as the sum of the number of patients in a hospital bed at midnight and the number of patients discharged in the preceding 24 hours divided by the total number of hospital beds. This method was used previously by Forster,[7] which helps capture the true use of inpatient beds during a 24-hour period.

We evaluated the effect of ED nursing hours on throughput metrics using analysis of covariance and controlled for total daily ED volume, hospital occupancy and admission rate. Daily nursing hours were compared across quartiles as a fixed factor. We used daily door-to-discharge LOS, door-to-admit LOS, and the number of patients who LWBS as the dependent variables in each model. SPSS Univariate GLM procedure was used for all analyses.

RESULTS

The mean number of visits per day was 290 with a range of 129 – 425. Nursing hours ranged from 336 – 580 nursing hours per day with a median of 464.7. The daily mean LOS for discharged patients was 249.8 minutes, and the range was 155 – 389. The daily mean LOS for admitted patients was 441.5 minutes, and the range was 259 – 796. The ED mean admission rate was 17.5% with a range of 10.8% – 23.9%. The daily mean of patients that LWBS was 17.5 and totaled 6,387 with a range of 1 – 55 patients per day. The daily mean hospital occupancy was 98.3%, and the range was 68.5% – 116.3%. The figure depicts the daily mean LOS for discharged and admitted patients as well as nursing hours by date throughout the course of the study.

Outcome variables are summarized in the table. ED door-to-discharge LOS and the number of patients who LWBS were both significantly affected by a decrease in daily nursing hours independent of ED daily volume, hospital occupancy and admission rate. Days in the lowest quartile of nursing hours experienced a 28.2-minute increase per patient in door-to-discharge LOS compared to days in the highest quartile of nursing hours. Across these same quartiles, days in the lowest quartile of nursing hours observed an increase of nine patients that LWBS per day. Both these differences were statistically significant. Door-to-admit LOS was not significantly affected by nursing hours. In the case of door-to-discharge LOS and number of patients that LWBS, while comparing adjacent quartiles did not always lead to statistically significant differences, there was a clear trend in the data across the quartiles that showed correlation.

DISCUSSION

Often, ED throughput metrics are equated to ED performance metrics. Thus, we are constantly seeking to understand the factors that impact our facility's performance. One of those factors in our study was nurse staffing. Suboptimal nurse staffing may impact a number of nursing tasks such as triage, vital signs, phlebotomy, medication administration, procedures, and discharge education. As nursing delays accumulate, this translates into longer wait times, leading to more patients who LWBS. It is likely that

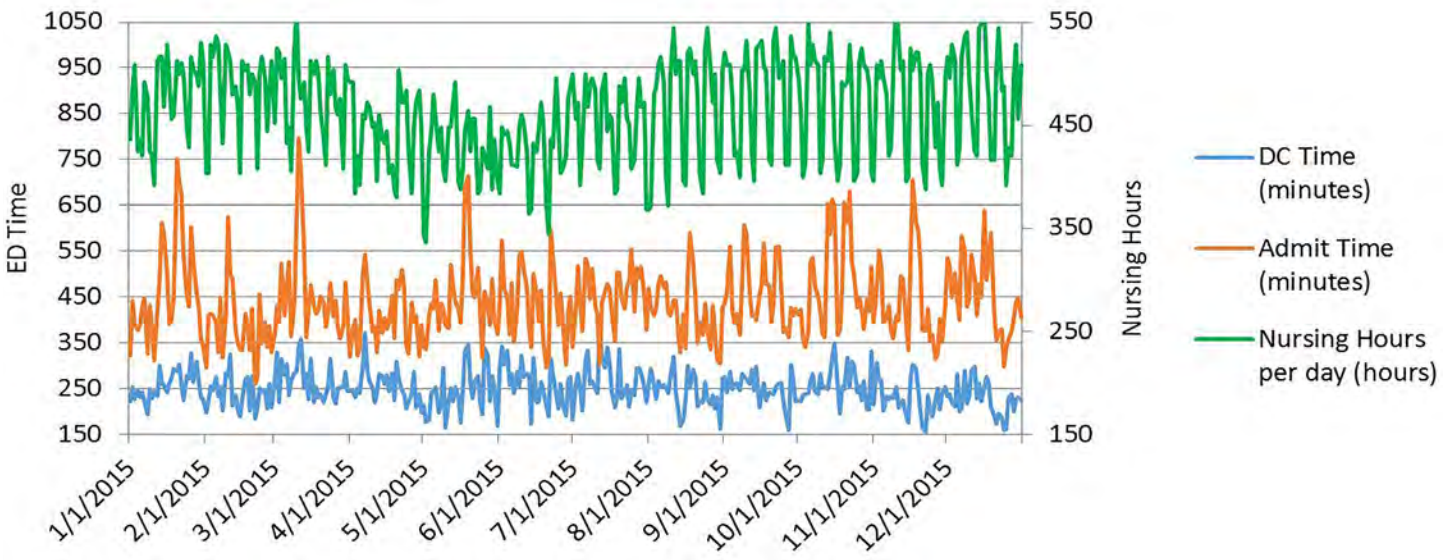

Figure. Daily mean length of stay for discharged and admitted patients as well as daily nursing hours by date. *ED*, emergency department; *DC*, discharge.

nurse staffing levels affect all important steps in a patient's path through the department[13] and has previously been shown to impact patient safety.[11,12] Cost analysis may delineate whether increased nurse staffing drives up front-end costs, but also generates additional revenue through more patient evaluations and decreased LWBS rates. Ultimately, expenses and revenue related to staffing and throughput are likely institutionally specific, but it is an important consideration nonetheless.

Nationwide nursing shortages continue to be an ongoing issue. High nursing turnover, changes to overtime rules and lengthy hiring processes, among other factors, can all contribute to nursing shortages and decreased nursing hours in EDs. Our study further contributes to the body of evidence that decreased nurse staffing directly contributes to the number of patients who LWBS and increased ED LOS, which is also shown to decrease patient satisfaction.[15] Chang showed that organizational characteristics associated with decreased ED LOS included executive leadership involvement, hospital-wide coordinated strategies, data-driven management, and performance accountability.[16] Our study provides additional data that may help providers further engage hospital administration to supply adequate nurse staffing that allows EDs to better achieve performance goals and improve the patient experience.

LIMITATIONS

The authors were not blinded to the hypothesis of this retrospective study during data abstraction; therefore, selection of controls was subject to author bias. The computer-derived data allowed for large data collection, but also contributed to our limitations. It is unknown when discharged patients received final instructions from nurses and hence physically left the ED, as this is not captured in our EMR. We did not address acuity of illness or triage scoring directly, an independent determinant of ED throughput metrics,[14] but rather used the surrogate of ED admission rate. Our analysis only measured data over 24-hour periods. It is possible that certain shifts were affected disproportionately by the decreased nurse staffing.

As a single institution study in an urban, tertiary care, safety-net hospital, our results may not be generalizable to other settings, specifically smaller-volume EDs with smaller nursing staffs. Our hospital spends negligible time on diversion each year so this was not included as a factor, though previous studies[4,5,14] revealed diversion correlates with worsened throughput performance. Lastly, because the statistical method was designed to show correlation rather than causation, other confounding factors may contribute.

CONCLUSION

Decreased nursing hours correlated to an increased ED LOS for discharged patients and increased LWBS rate. This analysis is a pivotal step in identifying and ensuring appropriate nurse staffing to optimize ED quality metrics. Further analysis may illustrate an ideal number of nursing hours per day for maximum benefit, but would likely require breaking down data into specific shifts. Future research may examine the cost impact of increased nursing hours compared to lost revenue from patients who LWBS. Finally, understanding the impact of nurse staffing on patient satisfaction is another area ripe for further study.

Table. Outcome variables.

	Mean ED LOS for discharged patients (n=74,951)	Mean ED LOS for admitted patients (n=18,487)	Mean LWBS per day (n=6,387)
1st Quartile nursing hours (336 – 422)	265.0 Minutes (95% CI [256.4 – 273.6])	454.7 Minutes (95% CI [436.6 – 472.7])	22 Patients (95% CI [20 – 24])
2nd Quartile nursing hours (423 – 472)	257.4 Minutes (95% CI [250.6 – 264.2])	445.6 Minutes (95% CI [431.4 – 459.7])	20 Patients (95% CI [19 – 21])
3rd Quartile nursing hours (473-504)	238.9 Minutes (95% CI [231.6 – 246.2])	429.2 Minutes (95% CI [414.0 – 444.4])	15 Patients (95% CI [13 -16])
4th Quartile nursing hours (505-580)	236.8 Minutes (95% CI [229.0 – 244.5])	436.1 Minutes (95% CI [420.0 – 452.4])	13 Patients (95% CI [12 – 15])

Covariates appearing in the model are evaluated at the following values: Daily ED Volume = 290.3, Hospital Occupancy = 249.7 (98.3%), ED Admission Rate = 17.5%.

ED, emergency department; *LOS*, length of stay; *LWBS*, left without being seen; *CI*, confidence interval.

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Code Help: Can This Unique State Regulatory Intervention Improve Emergency Department Crowding?

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Introduction: Emergency department (ED) crowding adversely affects multiple facets of high-quality care. The Commonwealth of Massachusetts mandates specific, hospital action plans to reduce ED boarding via a mechanism termed "Code Help." Because implementation appears inconsistent even when hospital conditions should have triggered its activation, we hypothesized that compliance with the Code Help policy would be associated with reduction in ED boarding time and total ED length of stay (LOS) for admitted patients, compared to patients seen when the Code Help policy was not followed.

Methods: This was a retrospective analysis of data collected from electronic, patient-care, timestamp events and from a prospective Code Help registry for consecutive adult patients admitted from the ED at a single academic center during a 15-month period. For each patient, we determined whether the concurrent hospital status complied with the Code Help policy or violated it at the time of admission decision. We then compared ED boarding time and overall ED LOS for patients cared for during periods of Code Help policy compliance and during periods of Code Help policy violation, both with reference to patients cared for during normal operations.

Results: Of 89,587 adult patients who presented to the ED during the study period, 24,017 (26.8%) were admitted to an acute care or critical care bed. Boarding time ranged from zero to 67 hours 30 minutes (median 4 hours 31 minutes). Total ED LOS for admitted patients ranged from 11 minutes to 85 hours 25 minutes (median nine hours). Patients admitted during periods of Code Help policy violation experienced significantly longer boarding times (median 20 minutes longer) and total ED LOS (median 46 minutes longer), compared to patients admitted under normal operations. However, patients admitted during Code Help policy compliance did not experience a significant increase in either metric, compared to normal operations.

Conclusion: In this single-center experience, implementation of the Massachusetts Code Help regulation was associated with reduced ED boarding time and ED LOS when the policy was consistently followed, but there were adverse effects on both metrics during violations of the policy. [West J Emerg Med. 2018;19(3)501-509.]

INTRODUCTION

Emergency department (ED) crowding adversely affects at least two of the Institute of Medicine's (IOM) domains of high-quality care: safety and timeliness.[1,2] While the causes of ED crowding are multi-factorial, "output" (flow of admitted patients into inpatient settings) is cited as a leading cause.[3,4] The IOM identifies the phenomenon of holding patients in the ED after the decision to admit (known as boarding) as a public health crisis and has urged hospitals and accrediting bodies to improve inpatient resources and flow to reduce boarding of patients in the ED.[4] Advocates recommend a number of countermeasures to improve the flow of boarded patients, and a common theme among them is the importance of recognizing that the flow of ED patients is a systemic, hospital-wide issue, rather than a problem localized to the ED.[4-6] Sporadic adoption of recommended ED-boarding countermeasures to date has led some authors to suggest that "enhanced regulation" may be required if current strategies fail to reduce boarding.[7,8]

It appears the Commonwealth of Massachusetts's Department of Public Health (DPH) is the first state regulatory body to mandate specific, hospital action plans to reduce ED boarding via its "Code Help" concept.[9] A number of regulatory and state agencies support efforts to reduce ED boarding by permitting inpatient floor boarding or mandating reporting of ED flow data, but none except for the Massachusetts DPH appear to have mandated specific, hospital action plans with pre-defined triggers.[9,10]

In December 2002, as part of a multi-pronged attempt to eliminate ambulance diversion, the DPH sent a letter to Massachusetts hospitals that included a mandate to develop individual hospital "Code Help" policies with "provisions to redeploy hospital staff and resources with a goal of moving all admitted patients out of the ED within 30 minutes [of activation]."[11] When Massachusetts became the first state to ban ambulance diversion,[12] the DPH stipulated that Code Help policies must include escalation to "appropriate emergency management/disaster plans and protocols" should the initial actions not adequately decompress the ED within two hours. Hospitals were required to submit their Code Help plans for review in early 2010, and the DPH's subsequent assessment revealed that many of the plans were inadequate and lacked the specificity required by regulation.[11] In 2015, the DPH re-emphasized the importance of Code Help and insinuated that plans would be reviewed as part of their routine, hospital-survey processes.[11]

Despite the DPH's consistent emphasis on compliance with the Code Help countermeasure, boarding continues to be a critical issue across the Commonwealth,[11] raising questions as to the effectiveness of the Code Help initiative. As a part of process improvement efforts for our institution, one author (MAR) solicited informal feedback from Massachusetts ED directors regarding the application and effectiveness of Code Help at other institutions. Most respondents reported no qualitative improvement in ED flow after creating Code Help policies at their hospitals. Some added that Code Help was inconsistently applied and suggested that this contributed to its lack of effectiveness Martin A. Reznek, (unpublished personal communication).

Anecdotal experience at our institution was similar, and we found adherence to an effective Code Help procedure to be historically difficult and inconsistent. However, as the policy gained broader acceptance from hospital leadership, we saw an opportunity to evaluate whether Code Help is effective when completely implemented and the DPH guidelines followed. We hypothesized that compliance with the Code Help policy would be associated with reduction in ED boarding time and admitted-patient total ED length of stay (LOS), compared to patients seen when the Code Help policy was not followed.

Population Health Research Capsule

What do we already know about this issue?
Emergency department (ED) overcrowding adversely affects quality and patient safety, but countermeasures are limited. Massachusetts mandated hospital action plans ("Code Help"), the impact of which is unknown.

What was the research question?
Does Code Help mitigate adverse effects of overcrowding by reducing boarding time and ED length of when the policy is followed?

What was the major finding of the study?
Code Help implementation is associated with shorter ED boarding time and length of stay when the policy is consistently followed.

How does this improve population health?
If the effects of this single-center experience are replicated more broadly, mandates on hospitals may have potential to decrease patients' exposure to the negative effects of overcrowding.

METHODS

Study Design and Setting

This was a cohort study conducted at a 364-bed urban, academic, tertiary referral center with trauma, stroke, and cardiac programs serving approximately 27,000 adult inpatients annually, with 65,000 annual adult ED visits and a monthly ED adult admission rate of 26-30%. There is a co-

located pediatric center, but it is operationally distinct and includes a separate pediatric ED.

The hospital developed and implemented its Code Help policy in accordance with the DPH mandate and guidelines. The policy includes standardized triggers, activation processes, next steps in the event of failure, and testing and evaluation as outlined by the DPH.[11] In general, three levels of activation were observed: "normal operations;" "Code Help;" and escalation to the hospital emergency operations plan (also known as "disaster plan activation"). The hospital disaster plan required in-person or conference-call response of all hospital managers, use of the Hospital Incident Command System, including a defined incident commander, conducting regularly scheduled briefings, and a continuously operational Emergency Operations Center where resources and decision-makers for the hospital system are located. Table 1 includes relevant text from the Code Help policy.

Measurements and Selection of Participants

We created a prospective Code Help event registry on October 1, 2014, enabling ascertainment of Code Help event timestamps following that date. We retrospectively queried the electronic health record (EHR) for consecutive individual patient visits of all adult ED patients from October 2014 through January 2016. For all admitted patients, we extracted EHR timestamps tracking four patient flow events: ED arrival, ED triage completion, admission decision, and ED departure time (physically moved to an inpatient unit). The electronic inpatient bed request placed by the ED provider following a verbal acceptance of the patient by the admitting team served as a proxy for admission decision.[13] We included patients admitted to either a medical/surgical acute care hospital bed (including telemetry) or critical care bed. Patients admitted to psychiatry, labor and delivery, or directly to a procedural area (operating room or cardiac catheterization lab) were excluded, as the EHR admission timestamp data were known to be unreliable for these patients due to unique admission processes related to those units. We defined boarding patients as those who remained in the ED after the decision to admit and defined boarding time as the interval between the admission-decision time and the departure time from the ED.[10] We defined total ED LOS as the interval between ED arrival time and physical departure time from the ED.[10]

Code Help Exposure Status

We matched each patient visit against our prospectively collected registry of Code Help events, which contained start and stop times for each Code Help event as well as hospital disaster-plan activation time, if applicable. For each patient, we determined the hospital's concurrent Code Help "status" (normal operations, Code Help, or disaster plan) at the time of each of four patient flow events: ED arrival time, ED triage time, admission decision time, and ED departure time.

We then determined whether the concurrent hospital status complied with the Code Help policy or violated the policy at the time of each patient flow event. Any of three possible scenarios constituted a policy violation: (1) the ED operational environment met Code Help activation criteria, but Code Help was not activated; (2) Code Help criteria had been met for greater than two hours without escalation to the hospital disaster plan; or (3) Code Help was re-activated within 24 hours without escalating directly to the hospital disaster plan. We determined the latter two violations by using the Code Help registry timestamps to calculate the elapsed time in the Code Help status and the elapsed time since the last Code Help/disaster event, respectively. Determination of the first violation type (the ED operational environment met criteria for Code help activation but remained in normal operations) required a standardized measure of the state of operations and flow in the ED.

Recognizing inherent limitations of all current quantitative measures of ED crowding, we selected ED occupancy ratio (EDOR), the number of patients currently in the ED divided by the number of licensed ED treatment spaces, as a surrogate for ED resource demand due to its prior use in the literature and relative ease of calculation as an instantaneous measure.[14-22] An EDOR greater than 100%, by definition, would fulfill the Code Help activation criterion of "capacity of the ED exceeds licensed bed capacity" (Table 1).[11] However, our ED routinely operated with staffed, unlicensed "hallway" beds, and the number of these beds varied in response to patient demands and resource availability. As such, an EDOR of 100% would accurately reflect the ED licensed bed capacity but would underestimate our functional ED capacity.

We had no way to determine the exact number of unlicensed, staffed treatment spaces at any given time, so we sought to identify a surrogate EDOR threshold to more accurately reflect our functional ED capacity limit. Our initial analysis suggested that EDOR of 200% corresponded to the 99th percentile for all hours during the study period. Further, we verified that for each hour where EDOR exceeded 200%, there was at least one boarded patient in the ED (minimum 5, median 21, interquartile range [IQR] 9), which fulfilled the second trigger criterion for Code Help (Table 1). We categorized any time during which EDOR exceeded 200%, but neither Code Help nor the disaster plan were active, as being a probable violation of the policy. We validated this approach against an alternative logistic regression model (see Appendix).

Statistical analysis

To assess the effects of compliance and non-compliance with the Code Help policy, we performed univariate comparisons of boarding time and overall ED LOS for patients cared for during periods of Code Help policy compliance and during periods of Code Help policy violation, both with reference to patients cared for during normal operations, using Steel's method, the nonparametric version of Dunnett's test, which controls the error rate for multiple comparisons vs. the control group.[23] We chose to compare each scenario to

Table 1. Text of the Code Help policy.

Triggers for Code Help

Code Help will be activated when the capacity of the ED exceeds licensed bed capacity, there are admitted patients boarding in the ED, and there are no licensed spaces available to see the next patient.

Procedure for activating Code Help

- The ED Flow/Resource RN [Charge Nurse] or ED attending physician will consult ED Nursing Leadership and/or ED Administrator on-call (AOC).
- ED Nursing Leadership will contact the ED AOC (or vice versa) to review the current status of the ED and to determine if any other actions can be taken prior to activation of Code Help to immediately decompress the Emergency Department.
- Should it be determined by the above group that the ED meets Code Help trigger criteria, the ED AOC will activate Code Help by contacting the Care Connection Center [hospital transfer center].
- The Care Connection Center will:
  - Activate Code Help by sending the scripted message to all on the global address listing "Code Help" distribution list. This message will run at initial activation only.
  - Upon receiving Code Help notification, all departments will react according to their standard work for Code Help.

  The Code Help Leadership Team [ED nursing and physician leaders, transfer center staff, bed assignment staff, hospital nursing supervisor] will meet within 30 minutes of activation to review the response effectiveness, additional resources needed, and next steps.

Reassessment, escalation and termination of Code Help

- ED status will be reassessed every hour from Code Help activation by the Code Help Leadership Team. A decision will be made to continue, escalate, or stand down from Code Help status.
- When the burden of admitted patients has eased, the Code Help Leadership Team will come to an agreement on 'Standing Down' from Code Help status.
- If all agree, they will contact the Care Connection Center to announce "Stand Down" of Code Help.
- The Care Connection Center will send 'Standing Down' email/text page to the Code Help distribution list.
- Should ED Capacity exceed licensed beds within 24 hours of Code Help activation, reactivation of Code Help is not considered an adequate response.

Escalation of Code Help

- If Code Help does not eliminate the burden of admitted patients in the ED within two (2) hours of activation, [if Code Help has been activated in the prior 24 hours,] or if the severity of the initial situation warrants it, the Code Help Leadership Team will contact the hospital AOC, COO, CNO, CMO, and President and notify them of ED status and the need to activate the hospital Emergency Operations Plan.
- The Hospital President or Administrator On Call will activate the Hospital Emergency Operations Plan Phase I using the following steps:
  - Notify the Hospital Telecommunication Console operator
  - Declare "Phase 1 of the Emergency Operations Plan is now in effect"
  - The telecomm console will initiate activation of the overhead disaster announcement. They will then conference the caller with Public Safety Console to activate communicator message for "Phase 1 of Emergency Operations Plan activation"
  - Command Centers will be opened and Incident Command will be established.
  - The Command Center will refer to Annex M for roles and responsibilities related to Capacity Emergency Response Plan.
  - Standing down Phase 1 of the Emergency Operations Plan is determined by the incident commander in consultation with the ED AOC, ED Nursing Leadership, ED physician, and Nursing House Supervisor who will review the status of the ED. If the ED is no longer within Code Help criteria the organization will stand down from the Capacity Emergency Response Plan. The notification for "Standing Down" will be made via the same process as the activation.

Testing and after action review

- The Code Help policy will be tested during the months of January and July, unless it has been activated within the previous 6 months.
- An after-action review will be completed and documented for each activation and test. Written notes to be retained by Flow Leadership Committee.

Source: UMass Memorial Medical Center Policy 2246. Reprinted with permission.

a common reference standard (normal operations) because doing so improved the overall error rate compared to pairwise comparisons and allowed us to evaluate the efficacy of Code Help in maintaining patient flow as close to normal operations as possible, despite the crowding and adverse circumstances that triggered Code Help activation. Performing only a direct comparison between policy compliance and policy violation would have ignored the valuable data from the large number of patients seen during normal operations, who could serve as a common control group, and would have dramatically reduced our statistical power to identify a between-group difference because of the reduction in population size.

Using the same technique, we performed a secondary analysis of the same metrics during any Code Help event or disaster activation (regardless of policy compliance), with reference to patients cared for during normal operations. We felt this secondary analysis was important to evaluate the effects of Code Help/disaster itself, even if misapplied or inconsistently followed. We also performed a number of sensitivity analyses to validate our analytic choices (see Appendix). Analyses were conducted using JMP Pro 12 (SAS Institute Inc., Cary, NC). The study was approved by our institutional review board.

RESULTS

Characteristics of Admissions and Code Help Events

Of 89,587 adult patients who presented to the ED during the study period 26,065 (29.1%) were admitted, 24,017 (92.1%) of whom were admitted to either an acute care or critical care bed and included in further analysis. Of the admitted patients, the median age was 64 (IQR 26), and 48% were female. Boarding time ranged from zero to 67 hours 30 minutes (median 4 hours 31 minutes) and was less than two hours for 14.2% of admitted patients. Total ED LOS for admitted patients ranged from 11 minutes to 85 hours 25 minutes (median 9 hours). ED occupancy ratio at the time of decision to admit ranged from 34% to 243% (mean 128%, standard deviation 33) and was stable over the time period of the study.

There were 89 Code Help events recorded in the registry during the study period (every 5.4 days on average), and 23 (26%) progressed to disaster plan activation. The probability of progressing to disaster plan increased over time, while the monthly frequency of Code Help events decreased (Figure). Time from Code Help activation until disaster activation ranged from 57 minutes to 3 hours 25 minutes (median 2 hours 39 minutes), and there were 64 instances of not escalating to the hospital disaster plan, despite meeting the two-hour criteria.

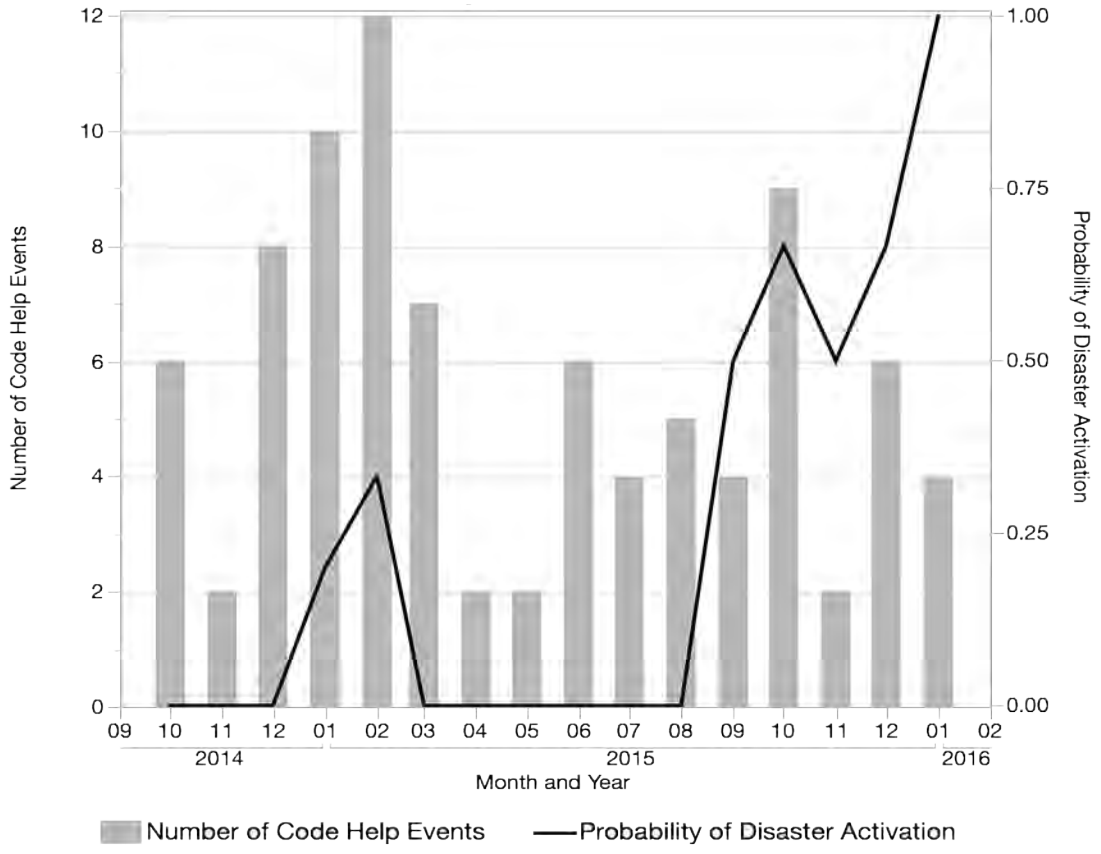

Figure. Code Help trends over time.

Policy Violations

Among all admitted patients, 2,219 (9.2%) had a decision to admit during Code Help, and 492 (2.0%) had a decision to admit during disaster. Among these 2,711 patients, 1,383 (51%) were admitted during a policy violation (1,227 while Code Help had been active greater than two hours, but the disaster plan had not yet been activated, and 156 during a re-activation of Code Help within 24 hours without activating the disaster plan). We identified an additional 94 patients admitted during a presumptive policy violation, where EDOR exceeded 200% but neither Code Help nor the hospital disaster plan were active.

Code Help Effectiveness

Each Code Help event was associated with a mean 17% reduction (95% CI [12%-22%]) in the number of patients boarding at the end of Code Help, compared to the time of activation. However, much of this reduction was accomplished after the first 30 minutes of Code Help, despite the stated policy goal of removing all boarding patients from the ED within 30 minutes. In the first 30 minutes, there was a mean 0% reduction in boarding patients (95% CI [3.4% increase to 0.2% decrease]).

Main Results

When not accounting for policy compliance, median boarding time and total ED LOS were longest during disaster activation and shortest during normal operations (Table 2). However, when accounting for Code Help policy compliance vs. violations of the policy, patients admitted during periods of any type of Code Help policy violation had significantly longer boarding times and total ED LOS, compared to patients admitted under normal operations (Hodges-Lehmann estimate of 25 minutes [95% CI {13-37 minutes} of additional boarding time and 45 minutes [95% CI {26 minutes to 1 hour 5 minutes}] of additional ED LOS). Among patients admitted during periods of Code Help policy compliance, in contrast, we found no significant difference in either metric, compared to normal operations. Table 3 reports the distributions of each metric for each subgroup.

Sensitivity Analyses

Our results were insensitive to the choice of patient flow-event timestamp linkages. Of the four events, we selected decision to admit for the primary analysis because we presumed that Code Help countermeasures were likely to have the greatest

Table 2. Boarding time and total emergency department (ED) length of stay by department status at the time of admission decision.

	Minimum	25th Percentile	Median	75th Percentile	Maximum
			Boarding time (hours:minutes)		
Normal operations (n=21,306)	0:00	2:40	4:31	8:05	67:30
Code Help (n=2,219)	0:02	2:55	4:39	8:41	43:58
Disaster (n=492)	0:23	2:54	4:51	9:14	46:45
			Total ED length of stay (hours:minutes)		
Normal operations (n=21,306)	0:11	6:08	8:57	13:53	85:25
Code Help (n=2,219)	0:49	6:33	9:23	14:30	59:27
Disaster (n=492)	0:55	6:42	9:30	15:39	67:58

Table 3. Boarding time and total emergency department (ED) length of stay by Code Help policy compliance at the time of admission decision.

	Minimum	25th Percentile	Median	75th Percentile	Maximum
			Boarding time (hours:minutes)		
Normal operations (n=21,692)	0:00	2:40	4:30	8:04	67:30
Policy-complaint (n=826)	0:02	2:55	4:36[NS]	7:56	46:45
Any policy violation (n=1,477)	0:03	2:56	4:50[a]	9:15	43:09
			Total ED length of stay (hours:minutes)		
Normal operations (n=21,692)	0:11	6:08	8:56	13:52	85:25
Policy-complaint (n=826)	0:49	6:33	9:14[NS]	13:49	67:58
Any policy violation (n=1,477)	0:57	6:39	9:42[a]	15:05	56:46

[a] $p<0.001$ for difference from normal operations, [NS] $p>0.05$ for difference from normal operations.

potential impact on a patient's flow into the inpatient setting if active at the time of the decision to admit. Lagged effects of Code Help were maintained at 30 and 60 minutes after the end of a Code Help or disaster event, but effects did not persist at 90 minutes or six hours. Our results were substantially unchanged when considering only the second two policy-violation types, discarding the EDOR threshold.

DISCUSSION

Our results suggest that when the Code Help concept is implemented in a manner that complies with DPH requirements and the policy is followed, both ED boarding time and total ED LOS for admitted patients appear to be reduced to durations typical of normal operations, despite increased ED demand. Violations of the Code Help policy appear associated with the loss of those benefits. We observed a 14-minute relative increase in median boarding time and a 28-minute increase in ED LOS among patients admitted during periods of policy violation, compared to those admitted during periods of policy-compliant Code Help or disaster, despite equally adverse ED operational conditions. This difference cumulatively represents approximately 689 patient-hours (28.7 patient-days) of ED capacity during the study period, which would otherwise have been available to care for additional ED patients had the policy been followed.

Our results suggest that compliance with the Code Help policy is pivotal in achieving improved ED flow, rather than simply having the policy in place but not following its guidelines. The DPH's Code Help concept, when implemented correctly and consistently, may reduce ED boarding and crowding and represents an important countermeasure to supplement the relatively limited armamentarium of current strategies.[5,7] It is worth noting, however, that even when the policy is followed Code Help does not appear to achieve its stated objective of removing all boarding patients from the ED within 30 minutes of activation.

While the overall results of this study are encouraging, it is not clear what specific factors within the Code Help policy implemented at our institution led to flow improvements. We believe that its effectiveness lies in the fact that the policy sets clear expectations, has a defined escalation process, requires hospital-wide leadership involvement, and establishes real-time accountability. It mandates action by leaders outside of the ED, who can problem-solve on a system level and engage in real-time, team-based solutions, and it provides a standardized structure for how to do so. At its core, Code Help provides for a hospital-wide response to a hospital-wide patient flow problem, even if the primary manifestation of that problem appears only in the ED.

One shortcoming of the Code help concept is that it focuses on reactive, rather than proactive, responses to crowding. While lessons learned during each Code Help activation may result in incremental process improvements during normal operations, Code Help actions do little to directly smooth flow or increase throughput when the plan is *not* active. Another disadvantage of the Code Help concept is the potential frequency with which the hospital disaster plan must be activated in the event Code Help is ineffective after two hours. When Code Help is routinely activated, the demand for frequent briefings and conference calls may compete with hospital leaders' other duties. This may raise awareness regarding crowding in the short term, but other long-term priorities may be inadvertently adversely affected.

To our knowledge, the DPH Code Help regulation is the first of its kind in the U.S. that mandates specific hospital actions to alleviate ED boarding.[9] The Centers for Medicare and Medicaid Services now requires reporting of ED flow measures, and the Joint Commission requires hospitals to have committees that oversee hospital flow, but neither mandates specific, ED-boarding countermeasures.[24] The DPH Code Help initiative presents a unique opportunity to evaluate whether "enhanced regulation" may reduce ED boarding, as suggested in prior literature.[7] While it remains to be seen if the DPH Code Help regulation will be successful across the Commonwealth over time, the results of this study suggest that it may be effective if hospital policy meets the DPH requirements and is followed consistently.

LIMITATIONS

Given the potential confounders and time-dependent nature of this dataset, we considered a number of analytic approaches and found that each approach, including our final analysis plan, had substantial limitations. ED LOS and boarding time are time-to-event data. Although they do not exhibit censoring (i.e., we have available LOS data for each patient, no matter how long they waited for admission), our observed boarding times do have some similarities to survival data, in that the probability of a given patient remaining in the ED at any point in time is conditional on the patient's presence in the ED during all preceding times since their arrival. Thus, we considered using Cox proportional hazards regression, but our dataset did not seem to fit the assumption that the "hazards" (that is, the probability of a given patient ending their ED LOS in the next minute) are strictly proportional between groups. We also considered a time-series approach, which still did not completely address our limitations. Our simpler approach of comparing group medians and distributions was less powerful, but we felt more assured that our data satisfied the prerequisites of the more conservative Steel test.

Comparisons of group medians, however, are inherently disadvantageous, in part because our method of stratifying patients to policy-compliant and policy-violation groups insinuates that there is a clear delineation between these cohorts. In fact, there is very little discernable difference between a patient admitted 119 minutes into a Code Help event (technically policy-complaint) and a patient admitted at 121 minutes without disaster plan escalation (a policy

violation). Similarly, while the operational environment when the EDOR is 195% is quite similar to that when the EDOR is 205% when Code Help is not active, our approach would trigger a policy violation only for the latter. It is implausible that Code Help would have a differential effect at EDOR 205%, compared to 195%, or 119 minutes, compared to 121 minutes, but our analytical approach assumes that it may.

A related limitation is that detecting failure to activate Code Help when criteria were initially met required a surrogate marker because of the retrospective nature of the investigation. Because ED census exceeding licensed ED bed capacity was a criterion for Code Help activation, EDOR was a natural choice as a marker. Our data demonstrated that there were always admitted patients boarding in the ED when EDOR exceed 102%. However, it was also the case that our usual operations included evaluating and treating patients in staffed but unlicensed hallway spaces, so 100% occupancy is likely an overestimate of functional crowding in our ED. Our threshold of 200% (99th percentile of EDOR) was intended to be conservative and more specific than sensitive. By design, the risk of falsely categorizing a patient as having been admitted during a policy violation was low, but we likely failed to identify some true violations that may have occurred at times when EDOR was between 102% and 200%. This type of violation accounted for only 11% of the patients admitted during any policy violation and probably underestimates actual violations. In our post-hoc sensitivity analysis to consider a comparison of only absolute policy violations (by considering the 94 patients admitted with EDOR >200% to be in the normal operations group), our findings were substantially unchanged.

We also had no mechanism to measure overall hospital demand-capacity mismatch outside of the ED nor insight into the specific decision-making that resulted in Code Help policy violations. Consequently, it is possible that violations were associated with hidden, external factors, such as leaders sensing complete hospital resource saturation and not following the policy due to feelings of futility. Further, a prospective power analysis was not possible given the study design. It is conceivable that any of these factors may have resulted in our failure to detect a difference in outcomes between the policy-compliant and normal operations groups, where one existed in reality (a Type II error). Nevertheless, the magnitude of difference between the policy-compliant and policy-violation groups and the fact that metrics were worse under Code Help when ignoring policy compliance (Table 2) suggest that policy compliance likely has a real differential effect.

Finally, our study reports the experience of a single center, which naturally limits the generalizability of our findings. It is likely that the specific interventions that occur during Code Help/disaster at our institution may not be as effective at other sites because they were designed to fit our local work environment and processes. However, a key strength of the DPH Code Help concept may be that, while it does call for adherence to specific guiding principles, it does not mandate specific tactics. We believe the general principles set forth in the regulations are generalizable to all hospitals, even if they require different implementation tactics. In fact, the failure to customize these specifics to each institution's unique workflow may be partially responsible for the initially slow adoption of the Code Help concept more generally. Based on the DPH's own assessment, Code Help has not been effective Commonwealth-wide,[11] but its analysis suggests this may be due to the fact that many individual hospital policies do not meet DPH requirements. Currently, we are unaware of any penalties levied by the DPH against hospitals that do not comply with the Code Help requirements. Our study may lend credence to the idea that regulators should value actual policy compliance, as opposed to hospitals simply having created a Code Help policy.

CONCLUSION

In our single-center experience, implementation of the DPH Code Help regulation is associated with shorter ED boarding time and ED length of stay when the policy is consistently followed. However, our analytic approach has important limitations that necessitate cautious interpretation of our findings. It remains to be determined whether the regulation will result in improved outcomes more broadly across Massachusetts.

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Acute Pulmonary Embolism in Emergency Department Patients Despite Therapeutic Anticoagulation

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Introduction: Emergency department (ED) patients with acute pulmonary embolism (PE) despite therapeutic anticoagulation at the time of diagnosis are uncommonly encountered and present a diagnostic and management challenge. Their characterization and outcomes are poorly described. We sought to describe the prevalence and characteristics of therapeutically anticoagulated patients among a population of patients with acute PE in a community setting and to describe treatment changes and 30-day outcomes.

Methods: From a large retrospective cohort of adults with acute, objectively-confirmed PE across 21 EDs between 01/2013 and 04/2015, we identified patients who arrived on direct oral or injectable anticoagulants, or warfarin with an initial ED international normalized ratio (INR) value ≥2.0. Patients were excluded from the larger cohort if they had received a diagnosis of venous thromboembolism (VTE) in the prior 30 days. We gathered demographic and clinical variables from electronic health records and structured manual chart review. We report discharge anticoagulation regimens and major 30-day adverse outcomes.

Results: Among 2,996 PE patients, 36 (1.2%) met study criteria. Mean age was 63 years. Eleven patients (31%) had active cancer and 25 (69%) were high risk on the PE Severity Index (Classes III-V), comparable to the larger cohort (p>0.1). Reasons for pre-arrival anticoagulation were VTE treatment or prevention (n=21), and atrial fibrillation or flutter (n=15). All patients arrived on warfarin and one was also on enoxaparin: 32 had a therapeutic INR (2.0-3.0) and four had a supratherapeutic INR (>3.0). Fifteen patients (42%) had at least one subtherapeutic INR (<2.0) in the 14 days preceding their diagnostic visit. Two patients died during hospitalization. Of the 34 ultimately discharged, 22 underwent a change in anticoagulation drug or dosing, 19 of whom received injectables, either to replace or to supplement warfarin. Four patients also received inferior vena cava filters. Thirty-day outcomes included one major hemorrhage and one additional death. No patients experienced recurrent or worsening VTE.

Conclusion: We found a low prevalence of therapeutic anticoagulation at the time of acute PE diagnosis. Most patients with breakthrough PE underwent a change in therapy, though management varied widely. Subtherapeutic anticoagulation levels in the preceding weeks were common and support the importance of anticoagulation adherence. [West J Emerg Med. 2018;19(3)510-516.]

INTRODUCTION

Acute pulmonary embolism (PE) is a common condition and is associated with significant morbidity and mortality.[1] Diagnosis of PE can be difficult, even more so in patients with suggestive signs and symptoms who are already therapeutically anticoagulated at the time of diagnosis. One study suggests that as many as 6.0% of patients diagnosed with acute PE were therapeutically anticoagulated at the time of diagnosis (what we describe as "breakthrough PE").[2] Case reports have described patients presenting with acute venous thromboembolism (VTE) despite therapeutic international normalized ratios (INR) (2.0-3.0).[3,4]

Management of these patients poses an additional challenge as there is little consensus on treatment for breakthrough PE. The American Heart Association 2012 and European Society of Cardiology 2014 guidelines state that inferior vena cava (IVC) filters can be effective for patients with breakthrough VTE despite therapeutic anticoagulation, whereas the American College of Chest Physicians 2016 guideline recommends against IVC filter placement (Grade 1B) and instead recommends a switch from oral anticoagulants to low-molecular-weight heparin (LMWH) for at least one month (Grade 2C).[5-7] To the best of our knowledge, there is little to no evidence to guide these recommendations. Overall, better understanding of clinical characteristics, management, and outcomes of patients with breakthrough PE in a community emergency department (ED) setting is needed to inform management guidelines for these patients.

In a multicenter, retrospective, cohort study of patients with acute, objectively-confirmed PE, we sought to (1) estimate the prevalence of therapeutic anticoagulation at time of ED diagnosis, (2) characterize the patient cohort, (3) describe changes in treatment, and (4) report 30-day major adverse outcomes. We hypothesized that the prevalence of breakthrough PE was low and that it was associated with subtherapeutic anticoagulation in the two weeks preceding diagnosis. The results of this study may help inform the clinical approach to the management of this uncommon condition.

Population Health Research Capsule

What do we already know about this issue?
Some patients develop pulmonary embolism (PE) despite therapeutic anticoagulation. The prevalence, characteristics, and treatment of these patients are not well described.

What was the research question?
What is the prevalence of breakthrough PE and what treatment changes followed the diagnosis?

What was the major finding of the study?
The prevalence of breakthrough PE was low and adjustments to anticoagulation varied widely.

How does this improve population health?
A better understanding of breakthrough PE may aid clinicians in the diagnosis and management of this challenging condition.

METHODS

Setting

Kaiser Permanente (KP) Northern California is a large, integrated healthcare delivery system that provides care to over four million members across 21 medical facilities and multiple clinics and ancillary services. KP members represent approximately 33% of the insured population in areas served and are comparable with respect to age, gender, and race/ethnicity.[8,9] KP Northern California stores patient health records electronically using an Epic-based (Verona, WI) electronic health record (EHR), providing electronically accessible patient-level clinical data within hierarchical databases.[10,11]

In 2015, the 21 study EDs had an annual median census of 56,983 visits (interquartile range [IQR] 37,841-61,005), ranging from 27,977 to 121,494 visits. All emergency care was provided by residency-trained and board-certified/prepared physicians. Computed tomography pulmonary angiography and radiology department services were available 24/7, while formal compression ultrasonography and ventilation perfusion imaging were often unavailable at various hours during the night.

During the study period, no standardized acute PE management departmental policies were in place. All patients were managed at the discretion of the treating physicians. The standard KP Northern California EHR-based discharge electronic orderset for thromboembolism at the time of the study recommended warfarin with enoxaparin bridging and is described in full elsewhere.[12] All post-discharge warfarin was managed by each facility's pharmacy-led, telephone-based anticoagulation service.

Selection of Participants

This retrospective cohort study identified eligible patients from the Management of Acute PuLmonary Embolism (MAPLE) study database. The MAPLE study is an observational, retrospective study of adult patients (age ≥18 years) with acute, objectively-confirmed PE presenting to 21 non-rural community medical centers across KP Northern California from January 2013 to April 2015. Study patients were identified using ICD-9 codes and manual chart

confirmation as described in full elsewhere.[13,14] Consistent with other PE studies, all cases were diagnosed either by computed tomography pulmonary angiogram, ventilation-perfusion scan, or positive extremity compression ultrasound for deep vein thrombosis with concomitant PE symptoms, such as acute onset of dyspnea or chest pain.[15-17] Patients were excluded from the MAPLE study if they had been diagnosed with acute VTE in the prior 30 days or had chronic PE, were designated comfort care status in the ED, were transferred outside the KP system from the ED or left the ED against medical advice, had insignificant PE that was untreated, were younger than 18 years at the time of diagnosis, were known to be pregnant, or were non-health plan members (Figure). This study was approved by the Kaiser Permanente Northern California Institutional Review Board and obtained a waiver of informed consent.

For this study, we identified patients within the MAPLE cohort who arrived in the ED on direct oral anticoagulants (dabigatran, rivaroxaban, apixaban, or edoxaban), injectable anticoagulants (fondaparinux or LMWHs), or warfarin with an initial ED INR value ≥2.0, the lower limit of the therapeutic range (Figure). We screened for anticoagulation use electronically using the patient's active medications list in the EHR, then undertook manual chart review for confirmation. We excluded patients who were found through chart review not to be currently taking anticoagulants. In these cases, the elevated INR was secondary to lab error or hepatic or systemic disease.

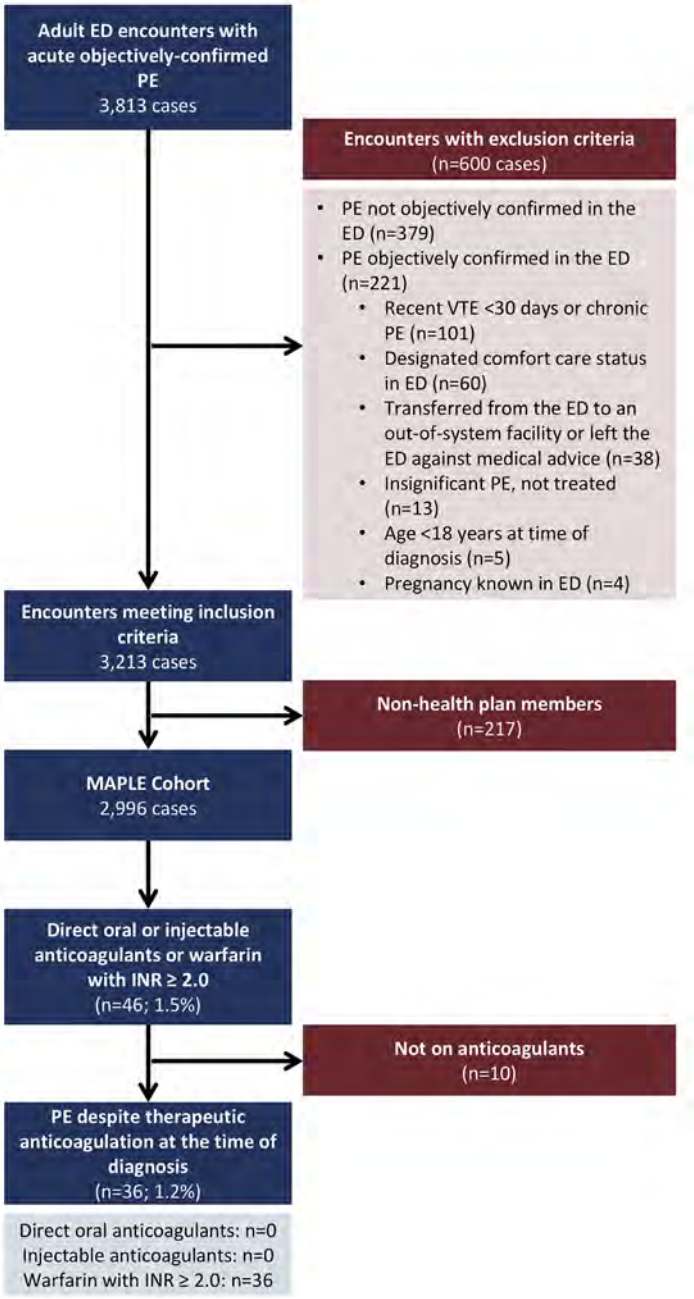

Figure. Cohort assembly of patients with breakthrough pulmonary embolism.
ED, emergency department; *MAPLE*, Management of Acute PuLmonary Embolism; *INR*, international normalized ratio; *PE*, pulmonary embolism.

Data Collection

The two chart abstractors – a practicing emergency physician and a research assistant – received standardized training on data collection methods and use of the electronic data collection tool, which was modified to its final form after pilot testing. The principal investigator (DRV) answered coding questions and adjudicated any differences in chart abstraction. The two abstractors reviewed each case to confirm eligibility and change in post-discharge anticoagulation management. Interrater reliability is reported using a weighted kappa statistic as well as percent agreement.

Using a combination of EHR extraction and structured manual chart review, the abstractors confirmed and collected the following variables: age; gender; indication for anticoagulation (VTE treatment or prophylaxis and atrial fibrillation or flutter); INR measurements in the 14 days preceding the index ED visit; active cancer at the time of index ED visit; PE Severity Index (PESI) score and risk class; and 30-day major adverse outcomes: major hemorrhage, recurrent or worsening VTE, and death.[18,19]

We retrospectively calculated the PESI score and risk class at time of ED disposition using definitions from the initial derivation and validation study by Aujesky et al. and a process described in an earlier MAPLE publication.[13,18] Active cancer was defined as cancer undergoing treatment in the prior 12 months or receiving palliative cancer care at the time of the index ED visit. Non-melanoma skin cancers were excluded. Any INR value <2.0 in the 14 days preceding the index ED visit was considered subtherapeutic.

Outcomes

Our primary outcome was an adjustment in PE treatment for patients discharged from the ED or inpatient units. Changes included alterations in anticoagulation drug or dosing and placement of an IVC filter.

Secondary outcomes included 30-day major adverse events associated with VTE and its treatment: major hemorrhage, new or recurrent VTE, and all-cause mortality. Major hemorrhage, as defined by the International Society on Thrombosis and Haemostasis, included bleeding at high-risk anatomic locations (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome), or overt bleeding with either a reduction of hemoglobin ≥2 g/dL or a transfusion of two or more units of packed red blood cells.[19] Recurrent VTE was defined as a new or expanded abnormality on imaging in a symptomatic patient. Deaths were identified using a healthcare system mortality database that links to the Social Security death master file and the California State Department of Vital Statistics to identify both in-system and out-of-system deaths. We also identified claims for out-of-system medical encounters in order to improve capture of heathcare visits related to our 30-day outcomes.

Statistical Analysis

Means and frequencies are presented using descriptive statistics. We compared active cancer and high-risk designation on the PESI in our cohort to the larger MAPLE cohort using a chi square test with significance level of $p<0.05$. All analyses were conducted using GraphPad Software (La Jolla, CA).

RESULTS

Study Population

Of the 2,996 encounters within the MAPLE cohort, we identified electronically 46 patients as potential study candidates (Figure). After structured manual chart review, 10 were excluded for no current use of anticoagulant medication, leaving 36 patients (1.2%) who met study criteria (Figure). The two investigators agreed on 94% of the post-discharge changes in anticoagulation drug or dosing. The kappa value for the 30-day adverse outcomes ranged from 0.66 to 1.00. The percent agreement for each of the variables ranged from 97.8% to 100%, median 100% (IQR 98.9% to 100%).

Characteristics

The mean age of the cohort was 63 years, and 25 patients (69%) were male. All patients arrived on warfarin and one was also on enoxaparin: 32 had a therapeutic INR (2.0-3.0) and four had a supratherapeutic INR (>3.0). The majority of patients were anticoagulated for VTE treatment and prevention (Table 1). Within 14 days prior to their index ED visit, 16 patients (44%) had one or more INR levels drawn and 15 patients (42%) had at least one subtherapeutic INR (<2.0) measurement with a mean INR of 1.5 (IQR 1.2-1.8), ranging from 1.0 to 1.9. Eleven patients (31%) had active cancer and 25 (69%) had higher risk PESI scores (Classes III-V), rates comparable to the larger cohort ($p>0.1$) (Table 1). Two patients died during hospitalization.

Primary and Secondary Outcomes

Of the 34 patients ultimately discharged, 22 (65%) underwent a change in anticoagulation drug or dosing (Table 2). Twelve patients received no change to their existing warfarin regimen upon discharge, nine of whom had a subtherapeutic INR in the preceding 14 days. Overall, 30-day adverse outcomes included one major hemorrhage and one additional death. Of the three deaths total, two were from lung cancer and one was from bilateral PE. No patients experienced recurrent or worsening VTE.

Patients with Subtherapeutic INR Measurements 14 Days Prior to Presentation

The mean age of the 15 patients with at least one subtherapeutic INR (<2.0) in the 14 days prior to ED presentation was 67 years. Other characteristics and demographics are described in Table 3. Patients with a subtherapeutic INR measurement in the prior 14 days were more likely to be discharged with no treatment change compared to patients without subtherapeutic INR measurements (60% vs. 16%, $p<0.01$).

DISCUSSION

In this retrospective cohort study, we found a low prevalence of breakthrough PE (1.2%; 36/2,996). The majority of patients underwent a change in anticoagulant drug or dosing, with almost half replacing warfarin with injectable anticoagulants, and few (5.9%; 2/34) experienced adverse outcomes in the 30 days following discharge. Many

Table 1. Characteristics of patients with breakthrough pulmonary embolism (N=36).

Characteristics	N	%
Male	25	69
Age (years)		
30-44	8	22
45-64	8	22
>65	20	56
Indications for pre-arrival anticoagulation		
VTE treatment and prevention	21	58
Atrial fibrillation or flutter	13	36
Both	2	6
Active cancer	11	31

VTE, venous thromboembolism.

Table 2. Post-discharge changes in anticoagulation drug or dosing of patients with breakthrough pulmonary embolism (N=34).*

Change in anticoagulation drug or dosing	N	%
None	12	35
Discontinue warfarin (n=15)		
Start or continue enoxaparin	14	41
Start fondaparinux	1	3
Continue warfarin (n=7)		
Start enoxaparin	5	15
Increase warfarin dose	2	6
Inferior vena cava filter placement (n=4)		
Replace warfarin with enoxaparin	2	6
Supplement warfarin with enoxaparin	2	6

* Percentages do not add to 100% because patients who received inferior vena cava filters are included in the "discontinue warfarin" and "continue warfarin" subgroups.

Table 3. Characteristics of patients with breakthrough pulmonary embolism and subtherapeutic international normalized ratios (<2.0) in the 14 days preceding the index emergency department visit (N=15).

Characteristics	N	%
Age (years)		
30-44	3	20
45-64	2	13
>65	10	67
Change in anticoagulation drug or dosing		
None	9	60
Discontinue warfarin (n=4)		
Start enoxaparin	3	20
Continue enoxaparin	1	7
Continue warfarin (n=2)		
Start enoxaparin	1	7
Increase warfarin dose	1	7

patients had at least one subtherapeutic INR measurement in the 14 days prior to index ED visit.

Little research attention has been directed to the study of breakthrough PE. Few studies have characterized the prevalence of this condition. In a retrospective cohort study from a single, tertiary-care center in Australia, Moutzouris et al. identified 56 of 923 patients (6.1%) with acute PE who had had a therapeutic INR at the time of diagnosis.[2] Many dissimilarities between the Australian PE population and our own may account for the difference in prevalence between their study and ours (6.1% vs 1.2%). Notable among these is that the MAPLE cohort excluded patients with a recent VTE diagnosis in the preceding 30 days, thus excluding from the study those patients who may have developed breakthrough PE early in their course of treatment (that is, within the first month).

Potential contributing etiologies of breakthrough VTE include subtherapeutic anticoagulation (often attributed to suboptimal adherence), antiphospholipid syndrome, established myeloproliferative neoplasm, JAK2 V617F mutation in the absence of an established myeloproliferative neoplasm, and cancer.[20-24] In this study, we were able to assess only the predictive risk associated with subtherapeutic anticoagulation and active cancer. The high number of patients with subtherapeutic INR measurements may support prior findings of suboptimal medication adherence as a potential etiology for breakthrough VTE.[20] Prevalence of active cancer in our cohort was comparable to the larger MAPLE cohort, a finding consistent with Moutzouris et al.[2] While we were unable to substantiate prior findings suggesting active cancer as an independent predictor of recurrent PE in anticoagulated patients, our study was not designed, a priori, to test this association and we may have been underpowered to detect such a link.[4] At present, there is insufficient research on breakthrough PE to provide evidence-based guidance for the practicing clinician assessing a therapeutically anticoagulated patient with symptoms suggesting acute PE.

The changes in PE management we observed in this study are consistent with existing guidelines recommending a switch from warfarin to injectable anticoagulants or the placement of IVC filters in patients with breakthrough PE.[5-7] The majority of our patients were discontinued from warfarin and switched to injectable anticoagulants; however, among patients with at least one subtherapeutic INR in the 14 days preceding presentation, the majority received no treatment change, simply a reinforcement of prescribed dosing. The 60% of subtherapeutic patients discharged with no treatment change was significantly higher than the 14% of therapeutic patients whose treatment was unchanged. A history of pre-arrival subtherapeutic INR may guide physicians to attribute breakthrough PE to sub-optimal medication or dietary adherence, or need for long-term dosing adjustment. Although the majority of our patients were discontinued from warfarin, five patients were prescribed dual therapy of enoxaparin and warfarin, a management regimen not studied in the literature or discussed in the guidelines.

Warfarin was the oral anticoagulant of choice for the treatment of acute PE during the study period. It has since been replaced by direct oral anticoagulants as the drugs-of-choice for most patients with PE.[7] Early research suggests that adherence to the newer agents may be similar to adherence to warfarin.[25,26] This implies that missing doses of direct oral anticoagulants may subject patients to the risk of breakthrough PE, just as with missing doses of warfarin. The half-lives of

the direct oral anticoagulants are significantly shorter than that of warfarin (6-17 hours vs. 20-60 hours), suggesting less tolerance for non-adherence.[27] However, missing doses of direct oral anticoagulants may not carry greater risks than missing doses of warfarin. One small study found that only 1% of patients (2/190) developed recurrent VTE in the 30 days following several days without direct anticoagulation.[28] Much larger studies are needed, however, to more precisely define the risk of reduced adherence.

LIMITATIONS

Our study is limited by its retrospective nature and small study size, reducing our ability to identify significant trends within our population. We were also unable to determine the broader prevalence of breakthrough PE in the larger anticoagulated PE population as our study cohort did not include patients whose breakthrough PE went undetected or those with early breakthrough PE. We were not able to collect data on potential predictors of breakthrough PE beyond active cancer diagnosis as testing for antiphospholipid syndrome, established myeloproliferative neoplasm, and JAK2 V617F mutation are not routine in our system. We conducted this study before KP Northern California EDs switched to direct oral anticoagulant use, and thus cannot speak to this new treatment regimen. Finally, although conducted in 21 community hospitals, characteristics and results found in this study may not be generalizable to other practice settings and geographic locations.

CONCLUSION

We found a low prevalence of breakthrough PE, few adverse 30-day outcomes, and frequent and varied changes in treatment among patients with breakthrough PE. Subtherapeutic anticoagulation levels in the preceding weeks were common, supporting the importance of anticoagulation adherence.

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Predictors of Short-Term Outcomes after Syncope: A Systematic Review and Meta-Analysis

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Introduction: We performed a systematic review and meta-analysis to identify predictors of serious clinical outcomes after an acute-care evaluation for syncope.

Methods: We identified studies that assessed for predictors of short-term (≤30 days) serious clinical events after an emergency department (ED) visit for syncope. We performed a MEDLINE search (January 1, 1990 - July 1, 2017) and reviewed reference lists of retrieved articles. The primary outcome was the occurrence of a serious clinical event (composite of mortality, arrhythmia, ischemic or structural heart disease, major bleed, or neurovascular event) within 30 days. We estimated the sensitivity, specificity, and likelihood ratio of findings for the primary outcome. We created summary estimates of association on a variable-by-variable basis using a Bayesian random-effects model.

Results: We reviewed 2,773 unique articles; 17 met inclusion criteria. The clinical findings most predictive of a short-term, serious event were the following: 1) An elevated blood urea nitrogen level (positive likelihood ratio [LR+]: 2.86, 95% confidence interval [CI] [1.15, 5.42]); 2); history of congestive heart failure (LR+: 2.65, 95%CI [1.69, 3.91]); 3) initial low blood pressure in the ED (LR+: 2.62, 95%CI [1.12, 4.9]); 4) history of arrhythmia (LR+: 2.32, 95%CI [1.31, 3.62]); and 5) an abnormal troponin value (LR+: 2.49, 95%CI [1.36, 4.1]). Younger age was associated with lower risk (LR-: 0.44, 95%CI [0.25, 0.68]). An abnormal electrocardiogram was mildly predictive of increased risk (LR+ 1.79, 95%CI [1.14, 2.63]).

Conclusion: We identified specific risk factors that may aid clinical judgment and that should be considered in the development of future risk-prediction tools for serious clinical events after an ED visit for syncope. [West J Emerg Med. 2018;19(3)517–523.]

INTRODUCTION

Background

There are over 1.3 million annual events of syncope (transient loss of consciousness with rapid and spontaneous recovery[1]) in the United States that lead to an emergency department (ED) visit, resulting in 440,000 admissions[2] and $2.4 billion in yearly hospital costs.[3] Syncope may be a harbinger of sudden death, dangerous arrhythmias, or other serious medical conditions (e.g., pulmonary embolism). Evaluation of syncope is challenging as symptoms have resolved by the time patients seek medical evaluation, and fewer than 10% of ED evaluations reveal a serious condition that may explain the episode of syncope.[4] To mitigate the risk of sudden death or other dangerous clinical events, up to 85%[5] of older adults who present with syncope of unclear cause are hospitalized for a diagnostic evaluation.[6,7] However, admission is associated with low diagnostic and therapeutic yield,[8,9] and there is no evidence that current practice patterns improve quality of life or long-term survival.[10]

According to the 2017 American College of Cardiology (ACC) / American Heart Association (AHA) / Heart Rhythm Society (HRS) Syncope Guidelines, accurate risk prediction using the clinical examination (including history taking, physical exam, and a 12-lead electrocardiogram [ECG]) is fundamental to guiding diagnostic and disposition decisions.[1] For ED decision-making, the focus is on predicting the risk of short- term (≤30 days) events that may warrant immediate hospitalization and testing.[11,12] Unfortunately, unstructured physician judgment appears to have poor reliability and accuracy.[13]

Population Health Research Capsule

What do we already know about this issue?
The emergency department evaluation relies on careful history, examination, electrocardiogram, and selective testing to evaluate patients presenting with syncope.

What was the research question?
What are the predictors of serious clinical outcomes after an acute-care evaluation for syncope?

What was the major finding of the study?
The strongest predictors included age, cardiac co-morbidities, hypotension, and abnormal biomarkers.

How does this improve population health?
We identified specific risk factors that may aid in clinical evaluation and risk prediction for patients undergoing ED evaluation for syncope.

Importance

Multiple research groups have proposed objective risk-stratification scores, each with different combinations of predictors.[4, 14-21] However, meta-analyses of published tools suggest equivalent performance compared to unstructured provider judgment.[22, 23] The 2017 ACC/ AHA/ HRS Syncope Guidelines[1] identified several limitations of the existing literature, including small sample sizes that limit the reliability of prediction models.[24] Although the 2017 Guidelines did identify potential predictors of short- and long-term clinical adverse events, diagnostic test characteristics of such factors were not described. Thus, it may not be apparent to front-line clinicians how to weight the presence or absence of high-risk factors identified in the clinical examination. In addition, prior attempts to develop risk scores have not incorporated existing information about potential predictors. A Bayesian approach that includes prior risk-stratification data may potentially result in the development of more reliable and valid risk scores.

Goal of this Investigation

To address this evidence gap, we performed a systematic review and meta-analysis to describe the diagnostic test characteristics of initial history, physical exam, ECG, and selected tests.

METHODS

Study Design

We performed a systematic literature review and meta-analysis that complied with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.[25] This study was exempt from institutional review board review.

Search Strategy and Study Selection

We conducted English-language searches in MEDLINE using a combination of the terms "syncope" and "risk" in any field. We considered papers published between January 1, 1990, and July 1, 2017. We also manually reviewed the reference lists of relevant studies. Titles and abstracts for all articles were screened by one of the authors (BCS). The full text of potentially eligible studies was reviewed by the entire study team.

Inclusion criteria included the following: 1) Patients presenting to an ED after a syncope event; 2) serious, short-term (≤30 days) clinical outcomes (such as death, arrhythmia, structural/ ischemic cardiac events, neurovascular events, major bleeding) were reported[12]; and 3) data sufficient for potential predictors stratified by the presence of adverse outcomes. For univariate data, this meant either (a) counts of the number of patients with a given characteristic (e.g., abnormal ECG) that did have an adverse event and the number of patients with the characteristic that did not have adverse events, along with the total number of patients with and without adverse events (i.e., contingency table counts for adverse outcomes by the presence of the characteristic), or (b) odds ratios and confidence intervals. For multivariate data, we required output from a multiple logistic regression model in (a) coefficient estimates and standard errors, or (b) odd ratios (OR) and confidence intervals (CI). All the papers that we included intended to either identify predictors of adverse events after syncope or validate existing risk-stratification methods.

We excluded studies that included non-ED referral populations (e.g., arrhythmia clinic, falls and syncope unit) or that were conditioned on prior testing (e.g. electrophysiology or tilt-table test) or pre-existing co-morbidities (e.g., prior cardiac arrest, cardiomyopathy). Because the focus of this review was to aid short-term decision-making relevant in the ED, we excluded studies that only had data on long-term (>30 days) outcomes. We excluded studies that had implausible results (defined as OR >20).

For each included article, we evaluated for potential bias with a modified version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) Criteria,[26] a meta-analytic system devised specifically for diagnostic studies. Two members of the study team (TAG, BCS) independently reviewed the methodological quality of included studies, and disagreements were settled through consensus.

Information Extraction

Papers provided varying degrees of covariate information, and the method of extraction varied with the type of information: direct, for papers that provided exact counts for contingency tables; direct after rounding, for papers that provided percentages instead of counts; and extrapolated, for papers that provided ORs and 95% CIs (see Appendix A for detailed description of methodology). We analyzed all variables for which at least two papers provided information.

Statistical Analysis

We calculated sensitivity, specificity, and likelihood ratio positive (LR+) and negative (LR-) for predictor variables. We did not assess diagnostic performance of specific risk scores, as two meta-analyses have previously addressed this issue.[22,23] A Bayesian random effects model was used for meta-analyses. The Bayesian approach allows for direct probability statements to be made about quantities of interest; for example, the probability that the positive likelihood ratio for a given variable is above some diagnostic threshold. Additionally, all parameter uncertainty is accounted for automatically in each analysis (see Appendix A for detailed description). Positive and negative likelihood ratios were deemed statistically significant if the 95% posterior interval did not contain 1.0. All analyses were implemented in the R statistical package.[27]

We numerically assessed the level of heterogeneity of effect sizes via the mean posterior standard deviation of random effects on the log-odds ratio scale. Smaller (larger) values indicate less (more) heterogeneity. Values very close to zero would suggest a fixed-effects model (i.e., no variation in the effect size across papers), while values above 2.5 would signal a problem with the data or the model. We visually assessed heterogeneity with L'Abbé plots.[28] The L'Abbé plot shows the event rate for those with a given covariate against those without the covariate for each paper that provided exact count data, where each circle represents a paper. Circle sizes are proportional to the square root of the sample size. Points above the line represent a higher event rate for those with the covariate than those without, and an OR or LR greater than one. Points clustered near the line suggest little or no covariate effect.

RESULTS

Initial Medline and manual screening identified 2,773 potentially eligible studies, and we identified seven additional studies through citation reviews. Seventeen articles met our inclusion criteria and were included in the systematic review (Appendix B [eTable 1]; Appendix C [eFigure 1]).[4,15,16,18,20,21,29-39] Definitions for serious clinical outcomes, abnormal ECG findings, and binary thresholds for continuous variables (such as age, vital signs, and biomarker tests) varied across papers; these are summarized in Appendix B [eTables 1-3]. Risk for bias is described in Appendix B [eTable 4]. We identified 32 predictors for which there were sufficient data for analysis. Visual representation of effect size heterogeneity is presented in Appendix C [eFigure 2]. There were 12 predictors with a significant LR+, and 12 predictors with a significant LR-. In this section, we highlight findings of LR+>2.0 and LR-<0.5 as the strongest predictors of short-term outcomes identified in this meta-analysis.

Pretest Probability of Serious Outcomes

Rates of serious outcomes after an ED evaluation syncope ranged from 1.2-36.2% (interquartile range 6.7-16.9%). There was heterogeneity in the definition of serious outcomes across studies (Appendix B [eTable 1]) and whether patients with serious outcomes identified during the index ED visit were excluded from analysis (Appendix B [eTable 4]).

Patient Characteristics and Co-morbidities (Table 1)

Pre-existing co-morbidities predictive of short-term outcomes included a history of congestive heart failure (LR+ 2.65, 95%CI [1.69, 3.91]) and prior arrhythmias (LR+ 2.32, 95%CI [1.31.-3.62]). Younger age was variably defined (e.g., less than 58-75; see Appendix B [eTable 2]) and was associated with lower risk of outcomes (LR- 0.44, 95%CI [0.25, 0.68]). Other patient characteristics, including gender, race and prior history of syncope were weakly predictive of short-term outcomes.

Symptoms (Table 2)

A complaint of dyspnea was predictive (LR+ 2.29, 95%CI [1.31, 3.65]). Other symptoms, including traumatic injury after syncope, palpitations, position, effort, chest pain, and absence of prodromes, had non-significant LR+ and LR-.

Physical Exam (Table 3)

Hypotension was variably defined (e.g., systolic blood pressure less than 80-90; see Appendix B [eTable 2]) but identified as a strong predictor (LR+2.62, 95%CI [1.12, 4.90]). Presence of cardiac murmur, rapid respiratory rate, and low oxygen-saturation level were not predictive.

Tests (Table 4)

We identified multiple biomarkers predictive of short-term risk; thresholds used to dichotomize test values are presented in Appendix B [eTable 2]. Predictors of increased risk include

Table 1. Test characteristics for demographics and co-morbidities.

Variable	Papers	Patients	LR+ (95% CI)	LR- (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	Posterior SD
CHF	8	40279	2.65 (1.67, 3.94)	0.73 (0.54, 0.89)	0.23 (0.17, 0.29)	0.85 (0.77, 0.92)	0.740
Arrhythmia	5	39773	2.30 (1.29, 3.60)	0.72 (0.48, 0.94)	0.14 (0.10, 0.20)	0.81 (0.70, 0.90)	0.777
Heart disease	8	44074	1.82 (1.26, 2.51)	0.73 (0.54, 0.91)	0.14 (0.10, 0.19)	0.75 (0.64, 0.84)	0.716
Older age	8	28624	1.80 (1.39, 2.36)	0.44 (0.25, 0.68)	0.11 (0.08, 0.15)	0.58 (0.43, 0.72)	0.778
Pacemaker	3	38207	1.58 (0.62, 2.96)	0.89 (0.62, 1.09)	0.11 (0.06, 0.17)	0.83 (0.70, 0.92)	0.840
Diabetes	5	39773	1.38 (0.80, 2.12)	0.88 (0.64, 1.07)	0.09 (0.06, 0.13)	0.75 (0.62, 0.86)	0.736
Male gender	9	44481	1.35 (1.07, 1.70)	0.72 (0.51, 0.94)	0.09 (0.07, 0.12)	0.55 (0.40, 0.69)	0.666
Cerebrovascular	2	36000	1.34 (0.55, 2.43)	0.87 (0.47, 1.20)	0.06 (0.03, 0.10)	0.70 (0.52, 0.86)	0.843
Arrhythmic medication	2	977	1.30 (0.37, 2.84)	0.94 (0.56, 1.25)	0.16 (0.08, 0.27)	0.77 (0.60, 0.90)	0.940
Hypertension	4	39103	1.28 (0.83, 1.76)	0.77 (0.44, 1.15)	0.08 (0.05, 0.12)	0.54 (0.37, 0.69)	0.801
Seizure	2	36014	1.01 (0.27, 2.29)	1.00 (0.68, 1.25)	0.05 (0.03, 0.09)	0.79 (0.62, 0.91)	0.897
Hispanic	2	3061	0.97 (0.35, 1.94)	1.02 (0.64, 1.36)	0.08 (0.04, 0.13)	0.70 (0.51, 0.85)	0.853
Stroke	2	3268	0.81 (0.24, 1.78)	1.08 (0.73, 1.40)	0.06 (0.03, 0.10)	0.73 (0.54, 0.87)	0.886
Previous syncope	4	3908	0.73 (0.30, 1.39)	1.09 (0.88, 1.30)	0.08 (0.05, 0.12)	0.76 (0.60, 0.88)	0.807
Nonwhite Race	3	38391	0.67 (0.30, 1.18)	1.24 (0.87, 1.64)	0.04 (0.02, 0.06)	0.59 (0.41, 0.76)	0.791

CHF, congestive heart failure; *CI*, confidence interval, *SD*, standard deviation; Posterior SD is the SD of random effects.

Table 2. Test characteristics for symptoms.

Variable	Papers	Patients	LR+ (95% CI)	LR- (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	Posterior SD
Dyspnea	6	4772	2.29 (1.31, 3.65)	0.78 (0.57, 0.94)	0.25 (0.18, 0.33)	0.85 (0.75, 0.92)	0.765
Trauma	2	3254	1.68 (0.70, 3.00)	0.76 (0.38, 1.12)	0.11 (0.06, 0.18)	0.72 (0.54, 0.87)	0.850
Palpitations	4	1713	1.51 (0.59, 3.02)	0.91 (0.66, 1.09)	0.18 (0.11, 0.27)	0.84 (0.72, 0.92)	0.900
Supine	2	915	1.42 (0.55, 2.66)	0.82 (0.36, 1.29)	0.17 (0.09, 0.28)	0.66 (0.45, 0.83)	0.987
Effort	3	1420	1.36 (0.51, 2.64)	0.91 (0.59, 1.17)	0.14 (0.08, 0.22)	0.78 (0.62, 0.89)	0.887
Chest Pain	3	3561	1.18 (0.45, 2.30)	0.96 (0.66, 1.20)	0.12 (0.07, 0.19)	0.77 (0.62, 0.89)	0.886
No Prodromes	7	8980	1.10 (0.72, 1.51)	0.93 (0.65, 1.21)	0.09 (0.06, 0.13)	0.58 (0.43, 0.72)	0.810

CI, confidence interval, *SD*, standard deviation; Posterior SD is the SD of random effects.

Table 3. Test characteristics for physical findings.

Variable	Papers	Patients	LR+ (95% CI)	LR- (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	Posterior SD
Hypotension	5	4540	2.62 (1.12, 4.90)	0.82 (0.59, 0.98)	0.25 (0.17, 0.35)	0.89 (0.82, 0.95)	0.936
Respiratory Rate	2	4714	2.26 (0.83, 4.44)	0.74 (0.38, 1.04)	0.15 (0.08, 0.24)	0.81 (0.66, 0.92)	0.869
Murmur	4	3792	1.86 (0.84, 3.47)	0.83 (0.55, 1.04)	0.20 (0.13, 0.30)	0.82 (0.70, 0.91)	0.873
Oxygen	3	1660	1.49 (0.77, 2.46)	0.79 (0.45, 1.12)	0.15 (0.09, 0.22)	0.68 (0.49, 0.84)	0.807

CI, confidence interval; *SD*, standard deviation; Posterior SD is the SD of random effects.

elevated blood urea nitrogen (LR+ 2.86, 95%CI [1.15, 5.42]), troponin (LR+ 2.49, 95%CI [1.36, 4.10]), B-type natriuretic peptide (LR+ 2.19, 95%CI [1.14, 4.00]), and hematocrit (LR+ 2.14, 95%CI [1.21, 3.43]). A low B-type natriuretic peptide level was associated with reduced risk (LR- 0.45, 95%CI [0.15, 0.91]). The presence or absence of ECG abnormalities (Appendix B [eTable 3]) was modestly predictive (LR+ 1.79, 95%CI [1.14, 2.63]; LR- 0.6, 95%CI [0.33, 0.92]).

Table 4. Test characteristics for biomarkers and electrocardiogram

Variable	Papers	Patients	LR+ (95% CI)	LR- (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	Posterior SD
Urea	2	4535	2.86 (1.15, 5.42)	0.57 (0.23, 0.96)	0.20 (0.10, 0.31)	0.79 (0.63, 0.91)	0.946
Troponin	3	6952	2.49 (1.36, 4.10)	0.54 (0.26, 0.87)	0.19 (0.11, 0.27)	0.75 (0.59, 0.87)	0.857
Creatinine	2	4535	2.43 (0.96, 4.59)	0.65 (0.29, 1.01)	0.16 (0.08, 0.26)	0.78 (0.62, 0.90)	0.913
BNP	2	663	2.19 (1.14, 4.00)	0.45 (0.15, 0.91)	0.35 (0.20, 0.50)	0.65 (0.41, 0.84)	0.877
Hematocrit	8	9354	2.14 (1.21, 3.43)	0.85 (0.67, 0.97)	0.19 (0.14, 0.26)	0.88 (0.80, 0.93)	0.799
ECG	7	5114	1.79 (1.14, 2.63)	0.60 (0.33, 0.92)	0.20 (0.13, 0.28)	0.65 (0.51, 0.78)	1.083

BNP, b-type natriuretic peptide; *ECG,* electrocardiogram; *CI*, confidence interval, *SD*, standard deviation; Posterior SD is the SD of random effects.

DISCUSSION

In this systematic review of ED patients presenting with syncope, we identified 17 articles that contained short-term prognostic information about patient characteristics, symptoms, physical exam findings, and objective testing. We identified several predictors of short-term serious outcomes. The strongest predictors of increased risk were elevated blood urea nitrogen level, a prior history of congestive heart failure, hypotension in the ED, a history of arrhythmia, and an abnormal troponin value. Younger age was the strongest predictor of lower risk. Prognostic factors had modest specificity and poor sensitivity, and likelihood ratios suggest that no single factor is sufficient to classify patients at high risk for short-term serious events. In the absence of effective risk scores, our findings can be used to supplement clinical judgment to guide management of ED patients without an obvious cause of syncope. Our results can also inform the development of more accurate and robust risk-prediction tools. For example, these data can inform "prior" estimates of association in novel risk score development using a Bayesian framework.

Higher risk patient characteristics are mostly concordant with the 2017 AHA Guidelines, including older age, male gender, and prior cardiac co-morbidities such as heart failure, arrhythmias, and coronary artery disease. We did not find an increased event rate associated with previous episodes of syncope. A prior population-based study did suggest increased 30-day mortality associated with prior syncope[40]; however, this report was excluded from our results due to inability to extract data amenable to meta-analysis.

Despite conventional clinical teaching,[41] we found that most symptoms were poor predictors. Dyspnea was the only factor that had significant positive and negative likelihood ratios. The absence or presence of other symptoms, including palpitations, syncope while supine, chest pain, and lack of prodromes, did not significantly alter risk. It is possible that patients had poor or inaccurate recall of the circumstances associated with syncope, which would limit the discriminating value of symptoms.

Low blood pressure was the only physical exam factor predictive of risk. Although the auscultation of cardiac murmur is suggestive of structural heart disease,[42] this finding was not predictive of short-term serious events. A potential explanation may be poor inter-rater reliability of cardiac auscultation.[16,43]

Initial ECG testing is a Class I recommendation in the 2017 AHA Guidelines.[1] We found that the ECG has modest discriminating value, consistent with a prior study that reported a <3% diagnostic yield.[44] Troponin and B-type natriuretic peptide may be objective indicators of cardiac dysfunction, and they appear to be predictive of serious short-term risk after syncope. Low hematocrit may be associated with anemia and other chronic diseases that confer risk after syncope. Finally, our meta-analysis suggests that blood urea nitrogen is associated with short-term serious events. The biological mechanism for this observation is not clear, although patients with renal dysfunction may be at higher risks for arrhythmias, bleeding, or death.[45,46]

Our study builds on a prior meta-analysis of predictors of adverse outcomes in syncope.[47] D'Ascenzo identified eight variables associated with serious outcomes (OR>5) including palpitations, exertional syncope, heart disease, bleeding, supine syncope, absence of prodromes, increasing age, and trauma related to syncope. Our meta-analysis builds on this prior effort by doing the following: focusing on studies of short-term outcomes that would be relevant to emergency physicians; including recently published studies; excluding improbable results (e.g., D'Ascenzo reported an OR=65 for palpitations); analyzing a broad set of potential predictors; and reporting test characteristics that are relevant to clinicians, such as likelihood ratio, sensitivity, and specificity. Discrepancies in the reported findings between the two studies are likely due to these methodological differences.

LIMITATIONS

First, risk prediction studies of ED patient with syncope are characterized by heterogeneity in outcomes.[24] The majority of investigations used composite outcomes of a broad range of serious clinical conditions, which reflects clinical reality facing the ED provider – syncope can be related to a wide range of dangerous conditions that may not be apparent on initial evaluation. Although the precise outcomes definitions varied by

study, there was substantial overlap in included conditions. For example, all studies included death and arrhythmia, and most studies included such conditions including acute myocardial infarction, pulmonary embolus, and significant hemorrhage.

Second, there was heterogeneity in predictor measurement. For example, binary cutoffs for continuous variables and the definition for "abnormal" ECG results differed across studies. However, we found strong consistency in direction of effect for ECG abnormalities and most continuous variables (e.g., blood pressure, serum tests). Measurement heterogeneity would likely result in a conservative bias toward a null finding.

Third, most of the studies did not exclude patients with outcomes identified during the ED evaluation. The majority of serious clinical conditions are identified during the initial ED evaluation for syncope,[4] and failure to exclude such patients biases risk prediction toward "obvious" events. There is also the potential for incorporation bias, where a test result is used to define the outcome (e.g., an ECG that documents a clinically significant arrhythmia). We attempted to mitigate incorporation bias by excluding studies with implausibly high associations.

Finally, we performed a meta-analysis on univariate predictors of outcomes, and it is likely that these factors are not independent of each other. This limitation underscores the importance of developing risk scores that account for the correlations among potential predictors.

CONCLUSION

We identified specific risk predictors of short-term clinical events after an ED evaluation for syncope. Individual risk factors, symptoms, exam findings, and test results in isolation are modestly predictive of risk. These findings should be used to supplement clinical judgment and inform the development of novel risk scores.

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Isolated Hand Palsy in National Institutes of Health Stroke Scale (NIHSS): Is It Useful?

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Stroke is the third cause of death in industrialized countries,[1] and the main cause of neurological disability in the world.[1] This has led to the need to significantly evaluate the effectiveness of an intervention both at the individual patient level as well as in clinical trials. The meaning of stroke-survivor recovery should be described by more sophisticated measures than are required by simple dichotomous end points, i.e., mortality or stroke recurrence.

The National Institutes of Health Stroke Scale (NIHSS) is a 42-point impairment scale that could be administered reliably by a variety of clinicians in a relatively short time to reveal neurological symptoms and signs in patients with stroke in a standardized manner.[2,3,4] The NIHSS provides an ordinal, nonlinear measure of acute stroke-related impairments by assigning numerical values to various aspects of neurological function.[2,3] This scale is used to quickly evaluate the stroke severity before and after each treatment.[2,3,4] The NIHSS takes about six minutes to perform, with no need for additional equipment, and is easily executable after training in how to use it.[3,5]

NIHSS scores are reliable across observers, as shown when used both by neurology-trained and non-neurologist raters. The potential to perform a neurological exam with a reliable method suitable for nonspecialists is an important strength of the NIHSS. NIHSS reliability and validity has also been demonstrated for remote assessment via telemedicine.[2] The NIHSS also has predictive validity. In fact, the initial NIHSS score is a robust predictor of in-hospital complication and outcome at three months.[3,4,5] The validity of NIHSS derives from correlations with objective measures of stroke severity, such as size of infarct on imaging. [3,5]

Developed in the early 1980s, the NIHSS is used in acute-stroke studies, particularly in early trials regarding thrombolytic and neuroprotectant treatments.[5] The NIHSS was developed through a robust consensus approach, taking the most informative measures from existent stroke-examination scales (Toronto Stroke Scale, Oxbury Initial Severity Scale, and Cincinnati Stroke Scale) and creating a composite scale that was further reviewed by a panel of stroke researchers and then amended. Further items were added to ensure the assessment was as comprehensive as possible. It has been used as a primary endpoint during trials with thrombolytic agents and patients with acute stroke.

The NIHSS is composed of the following elements: level of consciousness, horizontal eye movements, visual field test, facial palsy, motor arm, motor leg, limb ataxia, sensory abilities, language, dysarthria, and extinction and inattention (attention to surrounding environment). The score extends from 0 (normal neurological examination) to 42 (unresponsiveness coma). A score of 10 or higher is more probably related to a large-artery occlusion.[2,3] The score has a good correlation with anterior circulation stroke but underestimates clinical severity in posterior circulation stroke.[5] It is well recognized that while an individual can score 0 on the NIHSS, he might have an ischemic stroke, in particular in the posterior circulation area.[3]

Although some items related to the anterior-circulation infarction in NIHSS can be scored, other elements such as isolated hand/fingers palsy receive no score. Isolated hand/fingers palsy is not included in the NIHSS because it is a rare type of stroke. This non-inclusion could represent a weakness of the NIHSS because this type of palsy is a disabling clinical condition. Because the NIHSS is an impairment scale, it can provide only limited information about individual stroke survival. For example, an NIHSS score of 1 is considered an "excellent" outcome from stroke; a hemianopia would score NIHSS 1,

but for the individual this may not seem an "excellent" result because this symptom precludes driving and may cause loss of employment. However, isolated hand palsy in patients with cortical lesions has been rarely reported,[6] probably because this isolated nerve palsy is misdiagnosed as peripheral nerve lesions. The incidence of acute stroke with isolated hand paresis is not known, but it seems to constitute between 0.83% to 1.5 % of all ischemic strokes.[7]

Previous studies have shown that a paralysis of hand and fingers without sensory deficit is due to the cortical infarction of the precentral dial knob.[6] Anatomically, the precentral knob is a knob-like segment of the precentral gyrus projecting to the middle genu of the central sulcus, which is known as a reliable landmark for the motor hand area.[8] Moreover, the medial and lateral portions of the precentral knob are responsible for the ulnar and radial side of the fingers,[6,8] and it is consistent with the classical description of motor somatotopy in Penfield's homunculus.[9] Embolic mechanisms were more often associated with small cortical infarction associated with isolated hand/fingers palsy.[6] Clinicians must consider that patients with isolated hand palsy may have an alternative explanation, including a history of pain suggesting vasculitis, waking from sleep with the deficit (compression), fall (trauma), and shoulder (neuralgic amyotrophy) or neck pain with radicular symptoms. In the absence of these findings, the patient should be aggressively treated for acute ischemic stroke.

An ischemic stroke in patients without large cerebral-vessel occlusion or peripheral occlusions on intra-arterial digital subtraction arteriography have a low NIHSS score and a favorable outcome to thrombolytic treatment.[10] However, the use of diffusion-weighted magnetic resonance imaging could help clinicians diagnose ischemic stroke, including cerebral small ischemic lesions.[4] The delayed diagnosis of acute stroke or absence of thrombolytic therapy may induce the involvement of corticofugal tracts on arm and hand recovery with consequent disability.[11] One might question, however, whether the absence of this item for isolated hand palsy in NIHSS might underestimate the effect of thrombolytic therapy. There are no data about the benefit of thrombolytic therapy in this type of stroke, even though it has been reported that intravenous thrombolytic therapy is more effective in embolic stroke (i.e., isolated hand/fingers palsy) compared to atherothrombotic stroke.[11]

Hence, we suggest the inclusion of this finding to improve the sensitivity of NIHSS for anterior circulation stroke. If the NIHSS were to be expanded by adding this item for isolated hand palsy, it could have an impact on clinical and therapeutic trials, as well as on outcomes of anterior strokes. This could also be useful to maintain a high index of suspicion for acute stroke, particularly of anterior circulation, in the presence of NIHSS score = 0. We suggest adding one category to the existing item 7 of the NIHSS (Table). When neurological examination, particularly in patients with vascular risk factors, reveals an acute, isolated hand palsy without sensory deficit, we can use this modified NIHSS to diagnose a cortical brain lesion.

In conclusion, patients with isolated hand palsy do not receive an evaluation score. Thus, further studies are needed to consider this important central sign in the current NIHSS score, and open the possibility of adequate and aggressive treatment.

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Table. National Institute of Health Stroke Scale (NIHSS) item 7 (current) and suggested modification to item 7.

Item 7, NIHSS current	Item 7, NIHSS modified
0 = No drift; limb holds 90 (or 45) degrees for full 10 seconds	0 = No drift; limb holds 90 (or 45) degrees for full 10 seconds
1 = Drift; limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support.	1 = Drift; limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support.
2 = Some effort against gravity; limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity.	2 = Some effort against gravity; limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity.
3 = No effort against gravity; limb falls.	3 = No effort against gravity; limb falls.
	3= isolated hand palsy
4 = No movement.	4 = No movement.

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Altered Mental Status: Current Evidence-based Recommendations for Prehospital Care

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Introduction: In the United States emergency medical services (EMS) protocols vary widely across jurisdictions. We sought to develop evidence-based recommendations for the prehospital evaluation and treatment of a patient with an acute change in mental status and to compare these recommendations against the current protocols used by the 33 EMS agencies in the State of California.

Methods: We performed a literature review of the current evidence in the prehospital treatment of a patient with altered mental status (AMS) and augmented this review with guidelines from various national and international societies to create our evidence-based recommendations. We then compared the AMS protocols of each of the 33 EMS agencies for consistency with these recommendations. The specific protocol components that we analyzed were patient assessment, point-of-care tests, supplemental oxygen, use of standardized scoring, evaluating for causes of AMS, blood glucose evaluation, toxicological treatment, and pediatric evaluation and management.

Results: Protocols across 33 EMS agencies in California varied widely. All protocols call for a blood glucose check, 21 (64%) suggest treating adults at <60mg/dL, and half allow for the use of dextrose 10%. All the protocols recommend naloxone for signs of opioid overdose, but only 13 (39%) give specific parameters. Half the agencies (52%) recommend considering other toxicological causes of AMS, often by using the mnemonic AEIOU TIPS. Eight (24%) recommend a 12-lead electrocardiogram; others simply suggest cardiac monitoring. Fourteen (42%) advise supplemental oxygen as needed; only seven (21%) give specific parameters. In terms of considering various etiologies of AMS, 25 (76%) give instructions to consider trauma, 20 (61%) to consider stroke, and 18 (55%) to consider seizure. Twenty-three (70%) of the agencies have separate pediatric AMS protocols; others include pediatric considerations within the adult protocol.

Conclusion: Protocols for patients with AMS vary widely across the State of California. The evidence-based recommendations that we present for the prehospital diagnosis and treatment of this condition may be useful for EMS medical directors tasked with creating and revising these protocols. [West J Emerg Med. 2018;19(3)527-541.]

INTRODUCTION

Altered mental status (AMS) represents a broad spectrum of disease processes, making treatment modalities equally broad and varied. If the cause for AMS is found, the prehospital care providers will then transition to that more-specific protocol. However, emergency medical service (EMS) providers have limited time to evaluate these undifferentiated patients. Therefore, guidelines for assessment and initial treatment prior to arriving at an emergency department (ED) are essential. The prevalence of AMS in the prehospital care setting is not well known given the limited research in this area. One California county found 27% of all EMS patients had an abnormal Glasgow Coma Scale (GCS).[1] ED data report AMS at a prevalence between 1-10% of visits.[2-4] Prehospital protocols and treatment recommendations for AMS vary widely across the U.S.[5] We provide a summary of available evidence for prehospital assessment and treatment of patients with undifferentiated AMS and additionally evaluate consistency across California protocols.

METHODS

The State of California divides the EMS system into 33 local EMS agencies (LEMSAs). One set of governmental medical control policies regulates EMS response in each county-wide or region-wide system. Medical directors of those agencies, along with other interested EMS medical directors within the state, make up the EMS Medical Directors Association of California (EMDAC). EMDAC supports and guides the various agencies and makes recommendations to the California EMS Authority about policy, legislation and scope of practice. In an effort to improve the quality of EMS care in our state, EMDAC has endeavored to create evidence-based recommendations for EMS protocols.[2,3] These recommendations are intended to assist medical directors of the LEMSAs to develop high-quality, evidence-based protocols.

A subcommittee of EMDAC developed this manuscript and chose by consensus the elements that should be included in any protocol for a patient found to have AMS by EMS personnel. The subcommittee then created a narrative review of the existing evidence for prehospital treatment of a patient with AMS. Clinical questions regarding those interventions were developed in the PICO (population, intervention, control and outcome) format. In answering these questions, our population consisted of those patients in the prehospital setting with undifferentiated AMS, not those with clear causes for their AMS.

We relied heavily on recommendations made by various organizations that have performed systematic reviews and meta-analyses regarding treatment interventions. We supplemented the recommendations from those organizations with additional literature searches through PubMed from 1966 to 2017 for each question. The initial literature review of PubMed searched for the term "Prehospital and Altered Mental Status." That yielded 42 articles, only five of which were published in English and pertinent to the topics identified by the EMDAC subcommittee (Figure). This search was supplemented with additional PubMed searches for each clinical question. See Appendix table for additional search terms.

We assigned levels of evidence (LOE) and graded our recommendations based on the American College of Emergency Physicians (ACEP) process of creating clinical policies,[4] with slight modification, such as the EMDAC committee members performed literature search and assigned classes of evidence to diagnostic, therapeutic and prognostic questions, instead of a professional librarian or methodologist. This committee of EMDAC reviewed studies and assigned LOE based on the study design, including features such as data collection methods, randomization, blinding, outcome measures and generalizability.

LOE I consisted of randomized controlled trials, prospective cohort studies, meta-analysis of randomized trials or prospective studies or clinical guidelines/comprehensive review. LOE II consisted of nonrandomized trials and retrospective studies. LOE III consisted of case series, case reports, and expert consensus. After assigning LOE to the studies, we translated those to clinical grades of recommendations using the following standards:

Level A Recommendations

- Prehospital recommendations with a strong degree of certainty based on one or more LOE I studies or multiple LOE II studies.

Level B Recommendations

- Prehospital recommendations with a moderate degree of certainty based on one or more LOE II studies or multiple LOE III studies.

Level C Recommendations

- Prehospital recommendations based on only poor quality or minimal LOE III studies or based on consensus.

No Recommendation

- No recommendation was given in those cases where only preliminary data or no published evidence exists and we had no expert consensus.
- We also withheld recommendation when studies, no matter their LOE, showed conflicting data.

After answering the clinical question and providing recommendations for diagnostic and treatment interventions, we reviewed each current AMS protocol from the 33 agencies for consistency with the recommendations. The clinical protocols were reviewed during the months of November 2016 and July 2017.

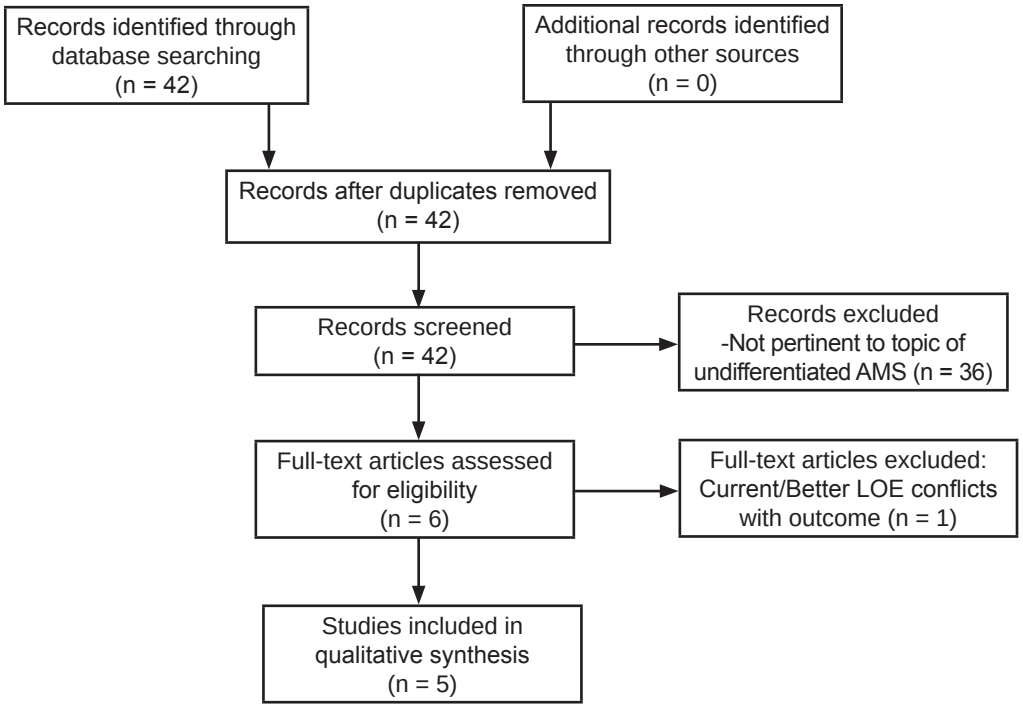

Figure. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) diagram based on initial PubMed search term "Prehospital and Altered Mental Status".
AMS, altered mental status.

Patient Assessment

Clinical Question

What patient and scene assessment should be performed by EMS for patients with AMS?

Summary of Current Evidence

Patients with an abnormal GCS are more likely to have a history of the condition known to be associated with their confused state, especially alcohol use disorder/hepatic encephalopathy, diabetes, illicit substance use, stroke/transient ischemic attack (TIA) and seizure.[1] This is particularly true if they have had a history of transient AMS in the past.[5] Obtaining the patient's history of present illness and past medical history often leads to identifying the cause of AMS.[6,7]

EMS providers have a unique opportunity to obtain pertinent history from family and bystanders who have knowledge of the patient's underlying medical conditions and access to materials found in the home. Often, if the history does not clarify the cause for AMS, the physical examination and environment will provide the needed clues.[2,8] If evidence as to the etiology of their AMS is found during scene assessment, these findings should be relayed to receiving ED personnel.

Given that neurologic causes (seizures, TIA/stroke), toxicologic causes, hypoglycemia and infection are the most common reasons for AMS, it would be prudent to check for signs of these pathologies. A full examination focusing on neurological and traumatic findings is important to evaluate for the subtle stroke, seizure, or traumatic brain injury.[1,5,6,8–10]

If the history and physical examination do not immediately elucidate the cause of AMS, the acronym AEIOU TIPS (Alcohol, Epilepsy/Electrolytes, Insulin/Inborn Errors of Metabolism, Overdose/Oxygen, Uremia, Trauma, Infection, Psychiatric/Poisoning, Stroke/Subarachnoid Hemorrhage (SAH)/Shock) can be used to consider a broader differential.[11]

Current Prehospital Treatment Recommendation

Level A Recommendation

- In a patient with AMS, obtain history of present illness, past medical history and cause for past episodes of AMS from patient or caregiver.
- A thorough physical examination is needed on all patients with AMS.

Level B Recommendation

- EMS should examine the scene for any evidence as to the cause of AMS (e.g., toxins) and communicate this finding to receiving personnel

Level C Recommendation

- To evaluate for the etiology of AMS, consider using the acronym AEIOU TIPS to provide a differential.

Clinical Question

What point-of-care tests should EMS perform on patients with AMS?

Summary of Current Evidence

Apart from a study in Finland,[8] most research on causes of AMS focused on patients seen in the ED, rather than in the prehospital setting. However, from this information, we can deduce the possible causes of AMS in the prehospital setting, as many of these patients are brought to the ED by EMS, and can infer probable point-of-care tests that would be helpful. In this review, we define point-of-care tests as bedside testing, or diagnostic testing at the time of patient assessment.

In several studies, patients with an abnormal GCS were found to be more likely to have a history of conditions known to be associated with their current altered state, the most common of those being neurologic, toxicologic, diabetic-related, and infection.[5,6,8,9] Hypoglycemia is one of the most common causes of AMS in adult patients in the prehospital setting; thus, rapid glucose testing is recommended for patients with AMS.[8,10] Upon literature review, other point-of-care tests that have been evaluated for the use of evaluating AMS were 12-lead electrocardiogram (ECG), pulse oxygen (O_2)-oximetry, pulse carbon monoxide (CO) oximetry, and end-tidal carbon dioxide detection ($ETCO_2$).

Several studies demonstrated cardiac etiologies of AMS in the general population were infrequent, suggesting that a routine 12-lead ECG would not be helpful.[1,5–9,12] However, if a dysrhythmia was noted on the cardiac monitor, obtaining a 12-lead ECG was useful to clarify the rhythm.[9] In populations aged 65 years and older, there is a higher prevalence of cardiac causes of AMS, such as myocardial infarction (MI), complete heart block. [5,6] This suggests that for the elderly population with AMS there may be a benefit in obtaining a 12-lead ECG. Lastly, if an overdose is suspected with medications known to cause cardiac toxicity, such as antipsychotics, sodium channel blockers (tricyclic antidepressants ([TCAs]), diphenhydramine, beta-blockers (BB) and calcium channel blockers (CCB), consider obtaining a 12-lead ECG.[13–15]

Another cause of AMS is hypoxia, especially in the elderly population, which can be evaluated with pulse oximetry and may be considered the fifth vital sign.[16,17] A similar point-of-care test is the pulse CO-oximeter. When looking at studies that compared Rad 57 (a type of pulse CO-oximeter) to the gold standard blood test, the evidence was conflicting, with wide ranges of precision and accuracy found.[18–20] Since CO poisoning is not a common cause of AMS and since pulse CO-oximeter's clinical accuracy remains unclear, we do not currently recommend evaluating for CO poisoning in the undifferentiated AMS patient.

Hypercapnia is a well-known cause of AMS. It is commonly observed with exacerbation of chronic obstructive pulmonary disease (COPD) and status asthmaticus, but may also be associated with pulmonary edema, neuromuscular respiratory failure, central hypoventilation, aspiration, and obesity hypoventilation syndrome.[21,22] To evaluate hypercapnea in the field, $ETCO_2$ is available. However, some researchers demonstrated a strong correlation between the gold standard $PaCO_2$ and $ETCO_2$[23] while others have only demonstrated a correlation in the healthy state.[24,25] It is our opinion that the causes of high and low $ETCO_2$ measurements appear to be too numerous and complex to apply in the field for undifferentiated AMS at this time. However, extremes of measurement such as a high measurement >80mmHg would usually indicate high $PaCO_2$.[22] This would be a change in how $ETCO_2$ is used in the prehospital setting since currently it is measured in those receiving positive pressure ventilation.[24,26,27]

Of note, breathalyzers, urine drug screens and lactate might be useful in some systems, but no prehospital studies on the use of these tests to evaluate patients for AMS were found during this literature review and they are not currently allowable for field use by paramedics in California.

Current Prehospital Treatment Recommendation

Level A Recommendation

- Place all patients with AMS on a cardiac monitor.
- Obtain pulse oximetry on all patients with AMS.
- Check blood glucose on every patient with AMS.
- Consider evaluating for a cardiac cause of AMS in the patient 65 years or older with a history of present illness or past medical history that suggests cardiac etiology.

Level B Recommendation

- Consider obtaining a 12-lead ECG on patients with AMS if they have a history of possible ingestion/overdose/intoxication, have an abnormal rhythm strip.

Level C Recommendation

- Not given

General treatment for AMS

Clinical Question

What treatment is recommended in the prehospital setting when no cause of AMS has been identified?

Summary of Current Evidence

Most of the literature on AMS in the field and ED focuses on identifying the etiology. Once the cause is identified, the provider will implement the treatment pathways based on that assessment. Therefore, upon literature review, no evidence was found for a universal treatment that is appropriate for every patient with AMS.

The empiric treatment of AMS with a "coma cocktail" has largely been abandoned. This cocktail included one or more of the following medications: dextrose, naloxone, thiamine, and flumazenil. These medications are not without risk, so a more focused approach to treatment is required.[28,29]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Not given

Level B Recommendation

- Not given

Level C Recommendation

- The empiric treatment of undifferentiated AMS with a "coma cocktail" should not be used.

Supplemental Oxygen

Clinical Question

Should patients with AMS in the prehospital setting be treated with supplemental oxygen?

Summary of Current Evidence

Hypoxia can be detrimental to patients; even in healthy volunteers with <90% readings on pulse oximetry, the middle cerebral artery dilates.[30] Hypoxia should be treated in a stepwise manner, with a goal of maintaining oxygen saturation ≥94%.[31,32] Care should be taken to prevent hyperoxia because this can also be detrimental. In healthy volunteers, providing 100% oxygen for 10-15 minutes was associated with a 20-30% decrease in cerebral blood flow.[33]

Specific complaints and diagnoses that have historically led to the administration of empiric oxygen can result in worse outcomes when hyperoxia occurs. These include MI, dyspnea in COPD, and stroke. Hyperoxia may increase MI size, impair cardiac performance, and worsen heart failure.[34–36] In COPD patients, hyperoxia can lead to hypercapnia, thus providing supplemental oxygen to keep saturations between 88% and 92% is recommended.[37] Hyperoxia decreases cerebral blood flow from vasoconstriction and can increase ischemia in stroke and can decrease survival.[38] In the setting of trauma, especially with traumatic brain injury, patients with significant hyperoxia (PaO_2 >487) did worse.[39,40]

The surviving sepsis campaign guidelines also recommend that peripheral oxygen saturation be maintained between 88% and 95% in septic patients with adult respiratory distress syndrome, and advocate the avoidance of hyperoxia.[41] In general, hyperoxia seems to impair oxygen delivery to patients during sepsis.[42]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Provide supplemental oxygen to maintain O_2 saturation ≥94%, unless COPD is present, then maintain a saturation of 88%-92%.
- Prevent hyperoxia in patients with MI, heart failure, stroke or COPD exacerbation.

Level B Recommendation

- Not given

Level C Recommendation

- Not given

Use of a Standardized System or Score to Measure Level of Consciousness

Clinical Question

Is a standardized scoring system characterizing level of consciousness useful in the treatment of AMS in the prehospital setting?

Summary of Current Evidence

The GCS is the most widely used prehospital coma assessment tool. The GCS was originally developed to assess the head-injured patient, but has been adopted more broadly over the years to describe level of consciousness in patients with AMS of many etiologies, with subsequent studies suggesting that the GCS is valid in patients who are altered from toxicologic causes.[43,44] Numerous studies have shown significant variability in inter-rater reliability for these scores, even among experienced physicians[45–47] as well as more broadly across healthcare teams and inexperienced users.[48–50] One study showed only moderate agreement between GCS determined in the prehospital setting and in the ED.[51] The GCS is heavily weighted towards the motor score; therefore, low motor scores due to inability to cooperate may be misleading when predicting patient outcome particularly in patients with AMS.[52]

More recently, the Full Outline of UnResponsiveness (FOUR) score has been developed as an alternative to the GCS,[53] with several studies showing this to be valid in both adults[54–56] and children,[52] while providing some additional prognostic information about brain stem injury. Most studies do not show a significant difference in inter-rater reliability between GCS and FOUR scoring systems.[54,56,57]

Another score that is used frequently in the prehospital setting is AVPU (awake, verbal stimuli, painful stimuli, and unresponsive/unconscious). This was introduced as a tool for rapid assessment of trauma patients as part of the Advanced Trauma Life Support course,[58] with good correlation to GCS.[59]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Not given

Level B Recommendation

- Choose a standardized scoring system, such as GCS or FOUR scale to assess level of consciousness in the prehospital setting for patients with AMS.
- The AVPU score can be used for rapid assessment of alertness, since it correlates well with GCS.

Level C Recommendation

- Not given

Evaluate for Seizure

Clinical Question

Are patients with AMS in the prehospital setting having a seizure or are they in postictal phase?

Summary of Current Evidence

Numerous studies demonstrate that seizures are one of the most common causes of AMS. [1,6,8–10,60] When a patient exhibits obvious seizures, a seizure protocol will be implemented by paramedics instead of an AMS protocol. It is more challenging to identify prolonged postictal states, non-convulsive status epilepticus (NCSE) and partial seizures, which are all seen more frequently in elderly and pediatric populations.[5,10]

Most studies that examine seizures in the emergency setting do not indicate if the seizure was obvious, difficult to identify, or later identified to be NCSE. However, a study in 2014 by Zehtabchi assessed rates of NCSE confirmed with EEG and found undifferentiated altered patients had a 5% chance of being in NCSE.[61] NCSE can present with discrete and subtle muscle twitching of face or limbs, increased tone, automatisms, clonic jerks, eye deviations/twitching, repetitive behaviors or prolonged postictal phase.[62,63]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Not given

Level B Recommendation

- Consider treating for non-convulsive or subclinical seizures with history of previous episodes or prolonged postictal state, focal muscle twitching, automatisms, clonic jerks, eye deviations or repetitive behaviors.

Level C Recommendation

- Not given

Evaluate for Trauma

Clinical Question

What factors make traumatic brain injury the likely cause for AMS in the prehospital setting?

Summary of Current Evidence

Most studies excluded obvious trauma while evaluating patients with AMS. Some patients with AMS were found to have occult traumatic brain injury (TBI). Otherwise occult trauma was not found to be a major cause of AMS.[5,7,8] If intoxication is present, especially from alcohol, the evaluation is more challenging and less accurate. Due to alcohol use, these patients as well as elderly patients and those on anticoagulation or antiplatelet therapy are at higher risk for occult TBI, especially intracranial hemorrhage.[64–67]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Not given

Level B Recommendation

- Consider TBI in patients with undifferentiated AMS, especially in the setting of intoxication, anticoagulation or antiplatelet therapy and in the elderly.

Level C Recommendation

- Not given

Treatment of Hypoglycemia

Clinical Question:

When and how should EMS providers treat hypoglycemia in patients with AMS?

Summary of Current Evidence

There is significant variation in how hypoglycemia is treated. About 12% of hypoglycemic patients present with AMS.[68] Many EMS systems and EDs are switching from using dextrose 50% (D50) to dextrose 10% (D10). Seventy percent of agencies in the U.S. as of 2016 only allowed D50 for the treatment of hypoglycemia in adults, 8% only D10, and 22% either D10 or D50 with a trend toward increasing use of D10.[69] This transition to D10 use is occurring for several reasons, including less extravasation risk, less acute hyperglycemia, less rebound hypoglycemia, and shortages of D50. D10 is less expensive and can be used in every age group. Many studies have demonstrated the feasibility, safety, and efficacy of using D10 instead of D50, with no increased time to resolution of symptoms and no significant differences in on-scene times.[70,71] In comparing glucagon intramuscular (IM) to dextrose intravenous (IV), median time to full orientation for glucagon was 10-30 minutes, compared with 1-10 minutes for dextrose.[72,73]

The median blood glucose level threshold for treatment of hypoglycemia was 60mg/dL for patients of all ages.[69] It is the committee's opinion to treat hypoglycemia at 60 mg/dL in an adult. However, if clinically indicated hypoglycemia may be treated at higher levels in diabetic patients. The most frequently specified initial dose of glucose was 25gm of glucose for adults and 0.5 g/kg for pediatric patients.[69]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Not given

Level B Recommendation

- In patients with AMS and hypoglycemia treat with oral glucose if indicated, or if venous access is

available administer IV dextrose; IM glucagon is a second line agent.
- The preferred medication for treatment of AMS due to hypoglycemia is D10; if not available, D25 or D50 may be substituted.

Level C Recommendation
- Not given

Evaluate for Toxicologic Causes of AMS
Clinical Question

How should patients in the prehospital setting be evaluated and treated for toxicologic causes of AMS?

Summary of Current Evidence

Toxicologic causes of AMS are common and result from a large number of toxins. The result is often a marked reduction in GCS.[9] However, in patients >65 years old, toxicologic causes of AMS are less frequent.[5] A history of depression, medication use, or illicit substance ingestion, especially alcohol, are important risk factors for a toxicologic cause of AMS. Almost 50% of alcohol-intoxicated patients who present to the ED arrive by ambulance and have higher blood alcohol levels and lower GCS scores than those arriving via private means.[64]

Drugs like methylenedioxymethamphetamine (MDMA), gamma-hydroxybutyrate (GHB), and synthetic cannabinoids are gaining popularity, especially by persons visiting clubs and festivals. Of those patients who seek medical help after GHB, most are altered, some with severely depressed GCS ≤9. Hallucinations, hypotension, bradycardia/tachycardia and hypo/hyperthermia are commonly found. Cooling measures, IV fluids, and symptomatic support including benzodiazepines are treatments that may be indicated for agitated delirium or seizures in this setting.[74,75]

If sodium channel blocker overdose is suspected (e.g., following diphenhydramine or TCA ingestions), sodium bicarbonate may be given. For calcium channel blocker (CCB) and beta blocker (BB) overdoses, calcium gluconate/chloride and glucagon are appropriate. These interventions have been demonstrated to be safe in the ED,[76,77] but have not been studied in the prehospital setting.

Current Prehospital Treatment Recommendation
Level A Recommendation
- Not given

Level B Recommendation
- If an amphetamine or another sympathomimetic is ingested, treat symptomatically with cooling, IV fluids and benzodiazepines as needed.
- If a sodium channel blocker ingestion/overdose is suspected in an altered patient, consider sodium bicarbonate administration.
- If a CCB or BB ingestion/overdose is suspected in an altered patient, consider giving calcium and/or glucagon.

Level C Recommendation
- Not given

Naloxone for Opioid Overdose
Clinical Question

When should naloxone be administered in the prehospital setting in patients with AMS?

Summary of Current Evidence

Treating patients with AMS empirically with naloxone is of no benefit unless there is evidence of opioid ingestion with respiratory depression. However, if there is concern for opioid overdose, naloxone has proven to be relatively safe. Naloxone has been found to be associated with a small but consistent rate of complications like seizures, arrhythmias, and severe agitation.[78–81]

Most of the criteria that studies examined when considering opioid overdose were respiratory rate ≤12, pinpoint pupils, and presence of drug paraphernalia, with AMS. These were found to be highly sensitive in predicting a response to naloxone. Miotic pupils outperformed respiratory rate as the best single criterion, with 91% sensitivity.[82–84]

To protect EMS personnel, several studies compared various routes of naloxone administration. IV, IM and intranasal (IN) administration of naloxone all result in reversal of opioid-overdose symptoms.[85] IN naloxone is statistically as effective as IV and IM naloxone, causes improvement and withdrawal effects almost as rapidly as IV, but requires rescue doses more often.[86–89] IN naloxone was shown to be faster, easier to administer and perceived as safer in those trained.[90] This evidence suggests that IN is the preferred route, with IV and IM as alternative routes.

Current Prehospital Treatment Recommendation
Level A Recommendation
- Administer naloxone IN for AMS patients with evidence of hypoventilation, (i.e., respiratory rate ≤12), pinpoint pupils, presence of drug paraphernalia, and AMS.

Level B Recommendation
- Do not empirically administer naloxone without a clinical suspicion of opioid ingestion/overdose.
- Alternative routes for naloxone administration are IM or IV routes.

Level C Recommendation
- Not given

Pediatric Altered Mental Status

Clinical Question

How are the causes of pediatric AMS different from those of an adult?

Summary of Current Evidence

The recommendations listed previously for adults apply for children as well, except for the recommendation to obtain a 12-lead ECG. Cardiac causes of AMS are exceedingly rare in children, so a 12-lead ECG is unlikely to be useful unless a dysrhythmia is suspected or evident on a rhythm strip. Studies did reveal that seizures, shock (e.g., sepsis), apparent life-threatening event (ALTE), now called brief resolved unexplained events (BRUE), hypoglycemia, and electrolyte abnormalities are common causes for pediatric AMS.[10,91]

Hypoglycemia can be seen in children for the same reasons as in adults, but pediatric patients are also at higher risk of hypoglycemia from toxic ingestions (e.g., ethanol), dehydration and sepsis.[10] While the blood glucose level that requires treatment of hypoglycemia in children is variable, many EMS systems have used < 60 mg/dL universally for all patients.

TBI is another cause of AMS in children, especially non-accidental trauma.[10,91,92] Although strokes are not usually considered a common pediatric cause of AMS, they do occur and their presentations are delayed because the diagnosis of stroke in children is often unrecognized.[93]

ED chart reviews identified common pediatric toxicologic emergencies causing AMS that require resuscitation including ingestion of ethanol, clonidine and acetaminophen. Other toxins more rarely causing AMS in children include CCB, BB and TCA.[76,77,91,94]

Current Prehospital Treatment Recommendation

Level A Recommendation

- Consider toxicologic causes as history and physical examination dictate and treat with naloxone if opioid ingestion is suspected in the setting of respiratory depression.

Level B Recommendation

- Place all pediatric patients with AMS on a cardiac monitor.
- Obtain pulse oximetry on all pediatric patients with AMS.

Level C Recommendation

- Check blood glucose on every pediatric patient with AMS and treat symptomatic hypoglycemia at values less than 60 mg/dL.

RESULTS

We reviewed protocols from all 33 EMS agencies within California for consistency with the recommendations made by EMDAC for prehospital AMS management (Tables 1-3). Of the 33 LEMSAs, 30 (91%) have specific AMS protocols, often named "Altered Level of Consciousness."

Point-of-Care Tests

All LEMSAs recommend evaluation of blood glucose as part of their AMS protocols. Twenty-seven percent recommend obtaining a 12-lead ECG for adult patients with AMS, while other LEMSAs only recommend placing the patient on a cardiac monitor.

General Treatment of AMS

No LEMSA suggests empiric treatment of AMS with dextrose, glucose, glucagon or naloxone without evidence of hypoglycemia or concern for opioid overdose.

Supplemental Oxygen

The most common recommendation is providing supplemental oxygen (48% of LEMSAs) as needed. Only seven (21%) agencies provide parameters for oxygen supplementation. Three (9%) recommend general high-flow oxygen for all patients, and seven (21%) do not mention supplemental oxygen in the protocol itself.

Use of a Standardized System or Score to Measure Level of Consciousness

Thirteen (39%) of the LEMSAs mention GCS in their protocols, often guiding the prehospital care provider to use the AMS protocol when the GCS <15.

Evaluation for Seizure

Nineteen (58%) of the LEMSAs suggest evaluating for seizure as a cause of AMS. Many of these systems use the acronym AEIOU TIPS to allow for this consideration.

Evaluation for Trauma

The majority of LEMSAs (79%) recommend evaluating the patient with AMS for signs of trauma.

Evaluation for Hypoglycemia

The majority of LEMSAs (67%) suggest treating at <60mg/dL, the other levels recommended for treatment are <70, <75, and <80 mg/dL. More than half the agencies (64%) use D10 to treat symptomatic hypoglycemia while the remainder use D50. There is a trend away from D50 at this time. The most common suggested first dose of dextrose for adults is 25gm (73%), though there is a trend toward smaller initial doses.

Evaluation for Toxicologic causes of AMS

Seventeen (52%) of the LEMSAs suggest evaluating for toxicologic causes of AMS, often by scene assessment and history from bystanders.

Table 1. Treatment of hypoglycemia in adults and pediatrics.

LEMSA	Dextrose used	Level treated (mg/dL)	Dextrose dose (gm)	PED D10		PED D25		PED D50		Glucagon	
	For adult	For adult	For adult: 1st,2nd	D10 age	D10 dose (gm/kg)	D25 age	D25 dose (gm/kg)	D50 age	D50 dose (gm/kg)	Adult (mg)	Pediatrics
Alameda	D10	<60	10,15	All	0.2 <30 sec, 0.5	NA	NA	NA	NA	1 IM	0.1mg/kg IM
Central California	D50	<80	25,25	NA	NA	<2yo	0.5	>2yo	0.5	1 IN, IM	Per Broselow Tape
Coastal Valleys	D50/D10	<60-80	15,10	All	0.2 neonate, 0.5	NA	NA	NA	NA	1 IM	1mg IM
Contra Costa	D10	<60	10,15	All	0.5	NA	NA	NA	NA	1 IM	0.5, 1mg >24 kg IM
El Dorado	D10	<60	10,10	All	0.2<1mo, 0.5	NA	NA	NA	NA	1 IM,IN	0.1mg/kg IM,IN
Inland Counties EMS	D10	<60	25	All	0.5	NA	NA	NA	NA	1 IM,IN,SC	0.025mg/kg IM,IN
Imperial	D50	<60	25	NA	NA	0-2yo	0.5	>3yo	0.5	1 IM	0.05mg/kg IM
Kern	D10	<60	25,25	All	0.5	NA	NA	NA	NA	1 IM,IN	0.5mg, 1mg >8yo IM,IN
Los Angeles	D10	<60	12.5,12.5	All	0.5	NA	NA	NA	NA	1 IM	0.5mg, 1mg >1yo
Marin	D10	<60	12.5,12.5	All	0.2 neonate, 0.5	NA	NA	NA	NA	1 IM	0.3mg/kg IM
Merced	D50	<75	25,25	neonate	0.3	neonate-2yo	0.5	>2yo	0.5	1 IM	1mg IM
Monterey	D50	<70	25,25	neonate	0.2	>neonate	0.5	NA	NA	1 IM	0.5mg, 1mg >20kg IM
Mountain Valley	D50	<60	25,25	NA	NA	0-2yo	0.5	>2yo	0.5	1 IM	0.05mg/kg IM
Napa	D10	<60	25,5 q 5min	All	0.5	NA	NA	NA	NA	1 IM	1mg IM
North Coast	D50	<80	25	neonate	0.5-1	>neonate	1-2	NA	NA	1 IM	1mg IM
Northern California	D50	<75	25,25	neonate	0.5	>neonate	0.5	NA	NA	1 IM	1mg IM
Orange	D10	<60	25	neonate	0.5	neonate-1yo	0	>2yo	0.5	1 IM	0.5mg IM
Riverside	D50/10	<80	25	neonate	0.5	neonate-13kg	0.5	>14kg	0.5	1 IM	0.5mg, 1mg >14kg IM
Sacramento	D50/D10	<60	25,25	NA	NA	All	0.5	NA	NA	1 IM	0.5mg IM
San Benito	D10	<70	25,25	All	0.5	NA	NA	NA	NA	1 IM	0.5mg, 1mg >20kg IM
San Diego	D50	<60	25	All	1	All	0.5	NA	NA	1 IM	0.05mg/kg IM
San Francisco	D50	<60	25,25	<1mo	0.2	>1mo	0.5	NA	NA	1 IM	0.5mg, 1mg>20 kg

LEMSA, Local EMS Agency; *PED*, Pediatric; *D10*, Dextrose 10%; *D25*, Dextrose 25%; *D50*, Dextrose 50%; *NA*, not applicable; *IM*, intramuscular; *IN*, intranasal; *SC*, subcutaneous; *yo*, year old; *mo*, months.

Table 1. Continued.

LEMSA	Dextrose used	Level treated (mg/dL)	Dextrose dose (gm)	PED D10		PED D25		PED D50		Glucagon	
	For adult	For adult	For adult: 1st,2nd	D10 age	D10 dose (gm/kg)	D25 age	D25 dose (gm/kg)	D50 age	D50 dose (gm/kg)	Adult (mg)	Pediatrics
San Joaquin	D50/D10	<60	25,25	neonate	0.3	NA	NA	>neonate	0.25, 0.5 >2yo	NA	NA
San Luis Obispo	D50	<60	25	NA	NA	All	0.5	NA	NA	1 IM	0.1mg/kg IM
San Mateo	D50/10	<80	25,50/10,15	All	0.5	NA	NA	NA	NA	1 IM	0.5mg, 1mg >18kg
Santa Barbara	D10	<60	25,25	All	0.5	NA	NA	NA	NA	1 IM	0.1mg/kg IM
Santa Clara	D10	<80	10,20	All	0.3	NA	NA	NA	NA	1 IM	0.5, 1mg>6yo
Santa Cruz	D10	<70	25,25	All	0.5	NA	NA	NA	NA	1 IM	0.5mg, 1 mg>20kg
Sierra-Sacramento Valley	D50	<60	25	All	0.5	NA	NA	NA	NA	1 IM	0.5mg, 1mg>24kg
Solano	D50	<60	25,25	neonate	0.3	neonate-1yo	0.5	>2yo	0.5	1 IM	1mg IM
Tuolumne	D10	<75	25-50	All	0.5	NA	NA	NA	NA	1 IM	0.05mg/kg IM,IN
Ventura	D50/D10	<60	12.5,12.5/10,15	All	0.5	<2yo	0.5	>2yo	0.5	1 IM	0.1mg/kg IM
Yolo	D10	<60	25	All	0.5	NA	NA	NA	NA	1 IM	0.5mg IM,IN

LEMSA, Local EMS Agency; *PED*, Pediatric; *D10*, Dextrose 10%; *D25*, Dextrose 25%; *D50*, Dextrose 50%; *NA*, not applicable; *IM*, intramuscular; *IN*, intranasal; *SC*, subcutaneous; *yo*, year old; *mo*, months.

Table 2. Naloxone criteria and suggested dose.

	Trigger		Dose	
LEMSA	Adult	Pediatrics	Adult (mg)	Pediatrics
Alameda	RR<8	RR<12	1-2 IV,IM,IN	0.1mg/kg IV,IM
Central California	RR<8	NA	1 IV,IM, 2 IN	0.1mg/kg IV,IM,IN
Coastal Valleys	NA	NA	1-2 IV,IM,IN	0.1mg/kg IV,IM,IN
Contra Costa	RR<8	NA	1-2 IV,IM,IN	0.1mg/kg IV,IM
El Dorado	NA	NA	0.5-2 IV,IM,IN,ET	0.1mg/kg IV,IM,IN
Inland Counties EMS	NA	NA	0.5-10 IV,IM,IN	0.1mg/kg, 0.5-10mg >8yo IV,IM,IN
Imperial	RR <12	NA	0.5-2 IV,IM,IN	0.1mg/kg IV,IM
Kern	NA	NA	0.4-2 IV,IM,IN	0.1mg/kg,2mg >5yo IV,IM,IN
Los Angeles	NA	NA	0.8-4 IV,IM,IN	0.1mg/kg IV,IM,IN
Marin	NA	NA	0.4-2 IV,IM,IN	0.1mg/kg IV,IM,IN
Merced	NA	NA	1-2 IV,IM	2mg IV, IM, ET
Monterey	RR<10	RR<10	2 IV,IM,IN	0.1mg/kg IV,IM,IN
Mountain Valley	RR<10, SBP <90	NA	2 IV,IM,IN	0.1mg/kg IV, IM, IN
Napa	NA	NA	2 IV,IM,IN	0.4-2mg IV,IM,IN
North Coast	NA	NA	0.4-2 IV,IM,IN	0.01mg/kg IV, IM, IN
Northern California	NA	NA	0.4-6 IV,SQ,IM,IN	0.1mg/kg IV,IM,IN
Orange	RR<12	RR<12	0.4-2 IV, IM, IN	0.1mg/kg IV,IM,IN
Riverside	NA	NA	2 IV,IM,IN	0.1mg/kg IV,IM,IN
Sacramento	RR<16	NA	1-6 IV,IM,IN	0.1mg/kg IV,IM,IN
San Benito	NA	NA	0.5-2 IV,IM,IN	0.01mg/kg IV,IM,IN
San Diego	<12	NA	2 IV,IM,IN	0.1mg/kg IV,IM,IN
San Francisco	NA	NA	0.4-2 IV,IM,IN	0.1mg/kg IV,IM,IN
San Joaquin	NA	NA	1-2 IV,IM,IN	0.1mg/kg IV,IM,IN
San Luis Obispo	RR<94%, ETCO2>45	NA	0.4-2 IV,IM,SL	0.4-2mg IV,IM,IN
San Mateo	NA	NA	1-2 IV,IM	0.1mg/kg IV,IM
Santa Barbara	<12	<12	0.4-2 IV,IM,IN	0.1mg/kg IV,IM,IN
Santa Clara	NA	NA	1-2 IV,IM	0.1mg/kg IV,IM
Santa Cruz	NA	NA	0.5-2 IV,IM,IN	0.01mg/kg IV,IM,IN
Sierra-Sacramento Valley	<12	Inadequte RR	1-2 IV,IM,IN	0.1mg/kg IV,IM,IN
Solano	<8	NA	0.5-2 IV,IM,IN	0.5-2mg IV,IM
Tuolumne	NA	NA	0.4-2 IV,IM,IN	0.1mg/kg IV,IM
Ventura	<12	<12	0.4-2 IV,IM	0.1mg/kg IV,IM
Yolo	NA	NA	2 IV,IM,IN	0.1mg/kg IV,IM

LEMSA, Local EMS Agency; *RR,* respiratory rate; *SBP*, systolic blood pressure; *IV*, intravenous, *NA*, not applicable; *IM*, intramuscular; *IN*, intranasal; *ET,* endotracheal tube; *yo*, year old; *mo*, months.

Naloxone for Opioid Overdose

Forty-two percent of the LEMSAs provide specific parameters for naloxone administration, whereas 19 (58%) advise naloxone administration if opioid overdose is likely. Of agencies that recommend specific parameters, most provide a respiratory rate below which naloxone should be administered, the most common being ≤12 breaths per minute. In terms of the route of naloxone administration, 28 agencies (85%) allow IV, IM, or IN.

Pediatric Altered Mental Status

Twenty-four (73%) of the LEMSAs have a different protocol for pediatric AMS than for adults. Of the 30% that do not provide a separate document, 21% provide pediatric recommendations in parallel to those for adults on the same document. One agency simply refers to the pediatric drug card.

CONCLUSION

A wide range of disease processes can cause AMS. Because of the rapid treatment needed for many of these causes, prompt identification is important. Though few studies address specific assessment and treatment recommendations for AMS in the prehospital setting, we

Table 3. Evaluating patients for various etiologies of altered mental status (AMS).

LEMSA	Separate PEDS protocol	EKG	Supplemental O_2	Use of GCS	Assess for trauma	Assess for stroke	Assess for seizure	Assess for TOX except narcotics	How to consider differential
Alameda	Y	Y	<94%	N	Y	Y	Y	Y	AEIOU TIPS
Central California	N-same doc	N	High flow	N	Y	Y	Y	Y	AEIOU TIPS
Coastal Valleys	Y	Y	NA	Y	Y	Y	Y	Y	AEIOU TIPS
Contra Costa	N-same doc	Y	<94%	Y	Y	Y	Y	Y	AEIOU TIPS
El Dorado	Y	N	PRN	N	Y	N	Y	Y	List
Inland Counties EMS	Y	N	PRN	N	Y	N	Y	Y	List
Imperial	No-PEDS drug guide	N	<94%	N	Y	Y	Y	N	List
Kern	N-same doc	N	PRN	N	Y	N	Y	Y	List
Los Angeles	N-same doc	Y	PRN	N	Y	N	N	N	List
Marin	Y	N	NA	Y	Y	Y	Y	Y	AEIOU TIPS
Merced	Y	N	High flow	Y	Y	N	N	N	List
Monterey	Y	N	NA	N	N	N	N	N	No AMS protocol
Mountain Valley	Y	N	PRN	Y	N	N	N	N	NA
Napa	Y	Y	PRN	Y	Y	Y	Y	Y	No AMS protocol, AEIOU TIPS
North Coast	N-same doc	N	High flow	Y	N	Y	N	Y	List
Northern California	Y	N	<92%	Y	Y	Y	Y	N	List
Orange	Y	N	<95%	N	N	Y	N	N	List
Riverside	N	N	NA	N	Y	Y	Y	Y	AEIOU TIPS
Sacramento	Y	N	<94%	Y	Y	Y	Y	Y	AEIOU TIPS
San Benito	Y	N	NA	N	Y	N	N	N	List
San Diego	Y	Y	<94%	N	Y	Y	Y	N	List
San Francisco	Y	N	PRN	N	Y	N	N	N	List
San Joaquin	Y	N	NA	Y	Y	Y	N	Y	List
San Luis Obispo	Y	N	PRN	N	Y	Y	Y	Y	AEIOU TIPS
San Mateo	Y	N	PRN	N	Y	Y	Y	N	List
Santa Barbara	N-same doc	N	PRN	N	N	Y	N	N	List
Santa Clara	Y	Y	PRN	N	Y	Y	Y	Y	List
Santa Cruz	Y	N	NA	N	Y	N	N	N	List
Sierra-Sacramento Valley	Y	N	PRN	Y	N	N	N	N	List
Solano	N	N	PRN	N	Y	Y	N	N	List
Tuolumne	Y	Y	PRN	Y	N	N	N	N	List
Ventura	N-same doc	N	PRN	N	Y	Y	Y	Y	AEIOU TIPS
Yolo	Y	Y	PRN	Y	Y	Y	Y	Y	AEIOU TIPS

LEMSA, Local EMS Agency; *PEDS*, Pediatrics; *EKG*, electrocardiogram; *GCS*, Glasgow Coma Scale; *TOX*, toxicology; *Y*, yes; *N*, no; *AEIOU TIPS*, Alcohol, Epilepsy/Electrolytes, Insulin, Overdose/Oxygen, Uremia, Trauma, Infection, Psychiatric, Stroke/Subarachnoid Hemorrhage (SAH)/Shock; *doc*, document; *NA*, not applicable; *PRN*, as needed.

have ED studies that can be extrapolated for use prehospital, although not ideal. The evidence-based recommendations presented in this paper will inform EMS medical directors and guide creation of protocols for identifying and treating patients presenting with undifferentiated AMS in the prehospital setting.

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Emergency Physicians at War

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Operation Enduring Freedom (OEF-A) in Afghanistan and Operation Iraqi Freedom (OIF) represent the first major, sustained wars in which emergency physicians (EPs) fully participated as an integrated part of the military's health system. EPs proved invaluable in the deployments, and they frequently used the full spectrum of trauma and medical care skills. The roles EPs served expanded over the years of the conflicts and demonstrated the unique skill set of emergency medicine (EM) training. EPs supported elite special operations units, served in medical command positions, and developed and staffed flying intensive care units. EPs have brought their combat experience home to civilian practice. This narrative review summarizes the history, contributions, and lessons learned by EPs during OEF-A/OIF and describes changes to daily clinical practice of EM derived from the combat environment. [West J Emerg Med. 2018;19(3)542-547.]

INTRODUCTION

Operation Enduring Freedom in Afghanistan (OEF-A) and Operation Iraqi Freedom (OIF) in Iraq, were the first major, sustained conflicts that involved formally trained emergency physicians (EPs) treating larger numbers of war-wounded. OEF-A began in October 2001 and officially completed in December 2014, although U.S. troops remain in Afghanistan as part of Operation Freedom's Sentinel.[1] Between 2001 and 2017, there were 2,400 U.S. military fatalities[2] and 20,048 U.S. military considered wounded in action.[3] Operation Iraqi Freedom began in March 2003 and transitioned in September 2010 to Operation New Dawn through 2011.[4] U.S. troops remain in Iraq at this time. Between 2003 and 2017, 4,520 U.S. military fatalities occurred[5] and 31,956 were wounded in OIF.[6] These numbers do not include civilian contractors and local citizens who were patients routinely cared for during the conflicts.

EPs worked in all settings during the conflicts from point-of-injury to transport to tertiary care. The roles of EPs were more limited at the beginning of the conflicts and expanded to ultimately include direct emergency care, unique missions, and leadership. EPs are now the most frequently deployed medical specialists by percentage in the U.S. Army and U.S. Air Force (USAF) and the second most in the U.S. Navy.[7] EPs' ability to prioritize emergency conditions, thrive in chaotic and resource-constrained environments, and remain cognitively and clinically flexible proved valuable in combat.

This article shares the story of military EPs by highlighting the indispensable roles they played throughout these recent combat operations.

MILITARY EMERGENCY PHYSICIANS

The military environment of EPs is complex. Each year changes occur rapidly in combat training requirements, retention, tasking for combat deployments, as well as in the policies of the different military branches. For example, in the USAF for the past three years, there have been approximately 34 EPs trained each year. On average, 20 of those 34 have trained each year at military programs and 14 have trained at civilian programs (a process called "civilian deferment"). EPs who train either in a military program or civilian deferment owe a time commitment to the military. Often, military physicians do not stay past the years owed. Many military EPs choose to return to civilian

practice after their initial time commitment is complete, rather than remain in the military for a career of 20 years or more, There is variability in the length of deployments in the different services. For instance, an Army deployment could be 12 months depending upon the circumstances, while an Air Force deployment is typically six months. The frequency of deployment is also variable by service and circumstance, but was often one time period deployed, followed by two time periods at home, often followed by deployment again.[7] The Navy and Marines similarly have provided strategies for deployment to allow dwell times at home to improve wellness and combat readiness.

The variation in U.S.-based clinical environments is difficult to compare to the diverse experiences EPs confronted during OEF-A/OIF. The following review explores several unique environments and job positions that EPs faced: medical planning, levels (echelons) of care with dramatically varied capabilities, special operations units, and critical care air transport teams.

Population Health Research Capsule

What do we already know about this issue?
Many are aware that emergency physicians (EPs) were deployed to Iraq (OIF) and Afghanistan (OEF-A), but many do not know of all their roles and contributions, nor of the impact on civilian practice.

What was the research question?
This paper reviews the roles of EPs in battle zones and how civilian practice has been affected as a result.

What was the major finding of the study?
The recent conflicts were a major utilization of EPs in war, and civilian practice has been affected.

How does this improve population health?
This narrative review summarizes the history, contributions, and lessons learned by EPs during OIF and OEF, and describes changes to civilian practice derived from the combat environment.

Roles in Deployment

Settings for deployment and levels of care

The military divides its medical assets into "roles" based on capabilities, and EPs served to some degree in each of these levels (or echelons) of care. Some understanding of the levels of care is important to understand the roles of EPs during OEF-A and OIF. Initially, the injured casualty (self care), fellow soldiers, and medics provide point-of-injury (POI) care. Role 1 facilities, which are attached to small military units, provide emergency first aid, triage, and non-surgical resuscitative care. Role 1 facilities are staffed by one or two physicians or physician assistants and augmented by medics. Role 2 facilities expand this initial capability with additional services, such as dental and limited laboratory capability, and can be combined with a team that provides stabilizing surgical capabilities.[8] Role 3 facilities are the most robust facilities in a combat zone, and function like trauma centers. Role 3 facilities have subspecialty medical and surgical capability, but do not have all the resources of a U.S.-based Level I trauma center. Role 4 and 5 facilities are outside the combat zone and have progressively more capability as it relates to staff, specialists, services (for example, dialysis).[8]

EPs worked at all levels of care during OEF-A/OIF, and played a robust role in providing en route care as casualties transitioned between these levels. EPs and EMS-subspecialty trained physicians provided medical direction and implemented prehospital education programs that impacted battlefield survival. In addition to serving in all the levels of care above, EPs served in many other unique environments including medical engagement missions with local communities, humanitarian assistance work, advisors to foreign medical systems, and liaison roles with allied governments, among other roles.

Clinical Leaders

EPs performed combat support planning at a variety of levels in OEF-A/OIF. EPs served in high-level leadership roles for combat medical units, such as medical group commanders, as well as in military staff and advisory positions. As EPs advanced to military leadership roles, they assisted with the strategic planning of the military's entire medical support system. While difficult to quantify, EPs significantly impacted military medical preparation, evacuation platforms, and hospital commands during OEF-A/OIF in a way never previously experienced in U.S military history.

EPs have contributed to the Committee on Tactical Combat Casualty Care (CoTCCC) that developed, promulgated, and refined the Tactical Combat Casualty Care (TCCC) guidelines.[9] TCCC directs medical care within the unique limitations of a resource-constrained, hostile environment. EPs were themselves educators and trainers for many levels of providers, to include the training of frontline medics. EPs also conducted research that led to improvements in combat casualty care and improved outcomes.

Special Operations

EPs served with a variety of special operations units. EPs regularly provided medical care in austere locations during high-risk operations conducted by elite fighting units. National security classification prevents us from knowing the full impact

of EPs' involvement in these missions. However, special operations units routinely request EPs for their diverse skill set and "can do" mindset in challenging circumstances. Even when EPs did not directly participate in combat missions, they supported special operations units through medical planning and training far-forward medics who provide direct patient care.

Critical Care Air Transport (CCATT)

Critical Care Air Transport Teams (CCATT), conceived by the USAF in the 1990s and first used in large-scale operations during OEF-A/OIF, allow safe and rapid movement of critically injured and ill patients.[10] CCATT teams consist of a critical care-qualified physician, a critical care nurse, and a respiratory therapist with an equipment package designed to support three ventilator-dependent patients. CCCAT in particular were involved in intra-theater transport as well as transports of greater length. Common transports of greater length included Iraq or Afghanistan to U.S. airbases/hospitals in Germany. After further procedures or interventions, the patients would then be transported to the U.S. from Germany.

EPs contribute approximately 40% of deployed CCATT requirements and have filled key CCATT leadership and instructor roles.[11] Physicians are prepared for deployment with two courses focused on providing critical care at altitude, the austere environment of an aircraft, and equipment familiarization. EPs deployed as CCATT physicians faced a challenging case mix with approximately two-thirds of patients having poly-trauma injuries and the remainder with complex medical diagnoses. Among trauma patients, 60% had Injury Severity Scores > 15 and over a quarter had a score > 25. EPs provided complex critical care interventions to these patients, including mechanical ventilation (80%), blood product administration (9%), intracranial pressure monitoring (13%) and vasopressor use (15%).[12]

Various studies commented on the absence of serious problems during transport, such as flights not diverting due to unstable patients and exceptionally few deaths during flight or in the 24-hour time period after flight.[12,13] The mean time from battlefield injury to aircraft launch for the U.S. military hospital in Germany was 28 hours, and 93% of all CCATT patients arrived in Europe within 72 hours of injury. Most patients arrived in the U.S. a few days later. By comparison, it took an average of 45 days to move patients from the battlefield to the U.S. during the Vietnam War.[14]

Analysts credit this rapid transport of critically ill casualties, unprecedented in prior wars, with a marked reduction in mortality.[15] A 10-year review of Joint Theater Trauma Registry (JTTR) data demonstrated an en route mortality of less than 0.02%, and an overall 30-day mortality of 2.1%.[16] Building on these OEF-A/OIF successes, CCATT teams have played roles in civilian disaster response including Hurricane Katrina and the 2010 Haiti earthquake, and analysts recommended increasing their use in the future.[17]

Roles of Reservists

The conflicts of OEF-A and OIF relied on the National Guard and Reserves to a remarkable degree, to include physician roles. The impact of such deployments led to many EPs being deployed in active duty roles, to include frequent participation in all roles previously described in OEF-A and OIF. The actual numbers of EPs deployed from the National Guard and Reserves is not provided here, but we believe that such EPs provided a great deal of support and their impact should be recognized.

Unique Patients

EPs treated complex, severely injured poly-trauma patients during OEF-A/OIF. The complexity of injuries of a single patient was notable as the advent of powerful improvised explosive devices (IED) wrought remarkable injury patterns to individuals in vehicles. Dismounted IED injuries were frequently experienced at the height of OEF-A and commonly resulted in amputations. EPs' contributions to the military medicine team helped more than 97% of injured casualties who reached combat hospitals survive.[18] Despite a recognition throughout the military that EPs offered a unique contributions and skill set, a review of the literature reveals that few articles highlighted the unique contributions and skill set of EPs.[19,20] Through recognition of the unique patients in the combat environment and how EPs are uniquely suited to treat them, this provides further evidence for contributions of EPs during conflict.

EPs' role in trauma care certainly deserves emphasis. However, as seen in previous wars, more soldiers during OEF-A/OIF suffered from disease and non-battle injuries (DNBI) than from battlefield injuries.[21] The ability of an EP to manage such diverse disease conditions from toxic ingestions, environmental exposures, infectious diseases (the rare and the common), psychiatric conditions, obstetric and gynecologic emergencies, and pediatric conditions was repeatedly voiced by command to be invaluable in the deployed settings of Afghanistan and Iraq. EPs' patients included U.S. soldiers, sailors, airmen, Marines, members of the Coast Guard, allied military members, U.S. federal and contract workers, local national civilians, opposing military members and prisoners of war, third-country national civilians (often contractors hired to work at U.S. bases), and children, among others. EPs' unique training and experience prepared them to treat the full spectrum of patients, diseases, and injuries encountered in OEF-A/OIF.

Mass Casualty (MASCAL) Events

Mass casualty (MASCAL) events occurred frequently during OEF-A/OIF, loosely defined by volume of patient numbers and patient requirements that were beyond the normally used resources. Military EPs planned, participated and led during MASCAL events throughout both war theaters. The authors personally responded to multiple MASCALs during their deployments. One author participated in a 45-patient MASCAL, the majority of whom were children, from a suicide bomber in a

local park. This presented unique challenges for a military facility equipped to treat adults. Another author responded to multiple MASCALs during a 24-hour long patient surge that resulted in a facility equipped with 10 beds and two EPs treating 60 seriously injured patients. Lessons from these experiences have been applied in the U.S. During the 2009 Fort Hood shooting, combat-experienced EPs contributed to positive outcomes for 30 patients with life-threatening injuries who presented to the base's small military community hospital.[22] Specific lessons learned in combat that contributed to the positive outcomes included having an appropriate MASCAL plan, rapid and appropriate adjustments to the plan, positive interactions between physicians, expectation of a second wave, and having a calm approach in a chaotic scenario.

Knowledge and Skill Translation

EPs returned with combat medical-care experience and skills that were immediately applied and have been disseminating throughout the civilian system. The knowledge and skill translation demonstrates how the combat experiences of EPs has impacted medical care in the non-combat environment and how healthcare is delivered to provide best practices in the domestic world of clinical practice. This was highlighted by Kellermann and Peleg after the Boston bombing as it related to the treatment of bombing victims when they wrote, "Although most health care providers in the United States have never treated a bombing victim, lessons learned by military surgeons, emergency physicians, and nurses in Iraq and Afghanistan are progressively percolating through the trauma care community."[23] One example of practice or approach change brought by war includes hemorrhage control, after it was recognized as an important cause of death in the combat environment.[24] The importance of hemorrhage control advanced the use of tourniquets in the civilian setting. Tourniquet use has been highlighted in such examples as laypersons being employed for tourniquet application[25] and the national "Stop the Bleed" campaign.[26] As many providers used hemostatic dressings in the combat setting, they were quick to look for applicable opportunities in the civilian setting. The resuscitation practice of increasing platelets and plasma ratios with packed red blood cells (1:1:1 or 1:1:2) was used in the theater of war and was supported for use in the civilian setting by Holcombe et al.[27] The use of intraosseous devices was further advanced by many of us who used them frequently in the theater of war.[28,29] Advances in cricothyroidotomy techniques and devices were promulgated as a result of the combat environment.[30] Of note, many military providers had experience using medications for pain that were used in novel ways and studied during OEF-A/OIF. The synergy of military studies and civilian studies led to the study of such things as intranasal ketamine and ketamine for pain.[31,32]

Future of Military Emergency Physicians

In the immediate time frame, deployments continue with anticipated benefit to the broadening experience of EPs, the advance of emergency medicine, and the knowledge transfer that will occur when EPs bring back lessons learned to the civilian practice environment. This knowledge transfer occurs through publications, educational opportunities between the military and civilian communities and by EPs transitioning out of the military and beginning civilian practice.[33] An example of civilian trainings directly resulting from the military experience include the TCCC training now used by the National Association of Emergency Medical Technicians. Another example includes the Medical Emergency Response Teams (MERT) borrowed from the military that is now used in civilian training programs.

As to EPs in the military, there is no evidence to expect that the reliance on EPs or the expanded roles will diminish anytime soon. Uniformed Services University (USU) and the military graduate medical education (GME) system continue to train providers with the unique perspectives of military and combat medicine. Combat medicine continues to grow as a unique area of research and training with heavy overlap between EMS and disaster medicine. The role of EPs is expected to continue to grow in the military in the role of leaders/planners. The military has EP contributors and leaders in research in such organizations as the Institute of Surgical Research, Joint Trauma System, and the En Route Care Research Center.

LIMITATIONS

Multiple attempts were made to obtain specific data that would support some of the assertions made. For instance, we went to great lengths in our attempt to find specific data on such things as the numbers of EPs in leadership roles and EPs deployed within a specific branch of service, given role, or specialty. However, the authors were unable to obtain such data, which limits the strength of the conclusions. The limitations of ill-defined data also limited our discussion on topics such as the expanding role of EPs in combat. Every attempt was made to not overstate or describe activities that were not well known to those EPs who participated in OEF-A and OIF. Through mentioning specific branches of service, there is no intention to minimize the contributions of any other branch of service.

CONCLUSION

OEF-A and OIF were the first major combat operations with robust EP participation. EPs' unique skill sets served casualties well in combat's highly varied environments: from the point-of-injury to flying ICUs. During the past 15 years, EPs led military medical units, participated in medical planning and engagement, became one of the military's most deployed specialties, and provided invaluable battlefield trauma and medical care for one of the first times at this level in U.S. military history. Through research, civilian trainings based on the military experience (i.e., TCCC), and through daily clinical practice, the lessons learned in combat by EPs now shape the civilian practice environment.[33]

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Peritoneal Dialysis in Austere Environments: An Emergent Approach to Renal Failure Management

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Peritoneal dialysis (PD) is a means of renal replacement therapy (RRT) that can be performed in remote settings with limited resources, including regions that lack electrical power. PD is a mainstay of end-stage renal disease (ESRD) therapy worldwide, and the ease of initiation and maintenance has enabled it to flourish in both resource-limited and resource-abundant settings. In natural disaster scenarios, military conflicts, and other austere areas, PD may be the only available life-saving measure for acute kidney injury (AKI) or ESRD. PD in austere environments is not without challenges, including catheter placement, availability of dialysate, and medical complications related to the procedure itself. However, when hemodialysis is unavailable, PD can be performed using generally available medical supplies including sterile tubing and intravenous fluids. Amidst the ever-increasing global burden of ESRD and AKI, the ability to perform PD is essential for many medical facilities. [West J Emerg Med. 2018;19(3)548–556.]

INTRODUCTION

Peritoneal therapies historically focused on the removal of accumulated fluids.[1] In 1923 Dr. Georg Ganter, emboldened by animal studies, performed peritoneal dialysis (PD) on an anuric patient, which temporarily improved the patient's mentation.[2] This proof of concept spurred decades of further research, culminating in the successful treatment of acute renal failure via peritoneal lavage by Seligman, Frank and Fine in 1946.[1]

Subsequently, the production of malleable dialysis tubing and standardized dialysate improved patient outcomes. Mortality rates for acute renal failure treated by PD dropped below 50%, and acceptable treatment durations grew from days to months.[1] These advancements were applied to casualties of the Korean War and Vietnam War, who had significantly better recovery from acute kidney injury (AKI) compared to their World War II counterparts.[3] The goal of eliminating repeated abdominal wall punctures and continually improving patient outcomes culminated in the Tenckhoff catheter, which was introduced in 1968.[1] This tunneled device used the latest in materials, reduced complications, and allowed safe PD therapy for extended periods, creating the foundation for modern-day therapy.[1]

Currently used by an estimated 196,000 patients worldwide, PD is heralded for its ease of initiation, conservation of resources, and efficacy.[4] Accordingly, PD may be a reasonable alternative to hemodialysis (HD) for AKI even when both are available.[5,6] During disaster responses and in resource-limited settings, including Turkey in 1999 and Haiti in 2010 following devastating earthquakes, improvised PD has been performed successfully using general medical resources.[7,8,9,10] Likewise, without adequate supplies or equipment to sustain HD in the aftermath of Hurricane Katrina in 2005 and in India in 2010, PD was rapidly and safely initiated by trained professionals, including emergency physicians (EP), to manage renal disease.[9,11,12] These successes have been re-demonstrated by international programs, including those in Brazil and India, and the Saving Young Lives Program in sub-Saharan Africa and Southeast Asia, which provide vital PD care in low-

resource settings.[5,13,14,15] Similarly, PD has been vital to the care of chronic and acute renal injury patients alike during contemporary military operations in Iraq and Afghanistan, as well as during the 2014 Syrian humanitarian crisis.[7,8,16] From emergent initiation following natural disasters to routine use in non-austere settings, PD has become a keystone in managing renal insufficiency worldwide; its use is aided by the International Society for Peritoneal Dialysis (ISPD) Guidelines, which promote safe and effective therapy.[17]

INDICATIONS FOR PERITONEAL DIALYSIS IN AUSTERE SETTINGS

Acute Kidney Injury

General indications for dialysis are the same in austere and non-austere settings. An example renal replacement therapy (RRT) protocol for AKI management highlights the impact of electrolyte and metabolic data, if available, on deciding to initiate therapy (Table 1). Common indications for PD in austere settings include severe acidosis, hyperkalemia, and uremia.

Rhabdomyolysis with myoglobinuric AKI is a common indication for urgent PD therapy, particularly following crush injuries that occur, for example, during earthquakes.[18] The initial treatment includes correcting electrolyte abnormalities and maintaining renal tubular flow with volume resuscitation, with a goal urine output of 3 mL/kg/hr.[19] Delays in care can result in anuric AKI with life-threatening acidosis, multi-organ failure and hyperkalemia, and may prompt emergent PD prior to transport for HD.

Shock is an important cause of acute tubular necrosis and life-threatening AKI.[7,8,20] Despite aggressive resuscitation, these patients are at high risk of progressive AKI and subsequent severe acidosis and hyperkalemia. Evacuation may not be feasible prior to the development of life-threatening indications for dialysis, necessitating immediate management. For neonatal and pediatric AKI, including from diarrheal illness and sepsis, PD is the preferred therapy.[12]

Hypervolemia and toxin clearance in isolation may also require urgent-start PD. Using high dextrose dialysate, volume can be removed. There is significant variability in toxin clearance via dialysis, with large or extensively plasma protein-bound molecules more difficult to clear. However, PD has been used alone or as a bridge to HD for potentially lethal exposures amenable to dialysis treatment, though PD would be expected to be less effective than conventional HD.[21,22]

During War or Natural Disaster

Patients requiring PD in austere settings include those previously undergoing chronic PD or HD therapy, and those newly meeting dialysis criteria. Consideration of timeline to HD access and of clinical data, including severity of illness, patient volume status, and electrolyte profile, may dictate the immediate or eventual initiation of PD.

Contraindications

Relative contraindications to PD initiation include recent abdominal surgery, diaphragmatic injury, overlying soft tissue infection, and known peritoneal adhesions.[23] Additionally, patients with severe respiratory failure may not tolerate intraperitoneal fluid.

ESTABLISHING ACCESS FOR PERITONEAL DIALYSIS

Catheter Options

Two primary types of PD catheters are commonly used: rigid and flexible. Flexible catheters are preferred when available.[15] If PD is anticipated, dedicated catheters may be ordered and made available (Figure 1). However, improvised catheters may be the mainstay of PD therapy in austere settings. The Tenckhoff continues to be the gold standard in flexible catheters, based on its higher dialysate flow rates, and fenestrations that make it less prone to obstruction.[25] Available in single- and double-cuffed designs, the latter is preferred for

Table 1. Indications for emergent renal replacement therapy.[24]

Disturbance	More urgent	Less urgent	Non-urgent
Acid-base	Metabolic acidosis; pH < 7.2	pH 7.2-7.3	pH > 7.3
Electrolytes	K > 6.5 or EKG changes	K 6.0 - 6.5	K < 6.0
Ingestion	Toxin		
Overloaded	Massive anasarca hypoxemic respiratory failure: fiO_2 > 0.7 urine output < 100mL/24hrs	2-3+ Peripheral edema hypoxemia : fiO_2 0.5-0.7 urine output 100-500mL/24hrs	< 1 Peripheral edema urine output > 500mL/24hrs
Urea	Uremic symptoms altered mental status	BUN 60-130	BUN < 60

K, Potassium; *FiO_2*, fraction of inspired oxygen; *BUN*, blood urea nitrogen.
Electrolyte derangements, metabolic factors, and patient characteristics must be taken into account when considering the initiation of peritoneal dialysis. The presence of any 'More Urgent,' or three or more 'Less Urgent' features should prompt consideration of peritoneal dialysis.

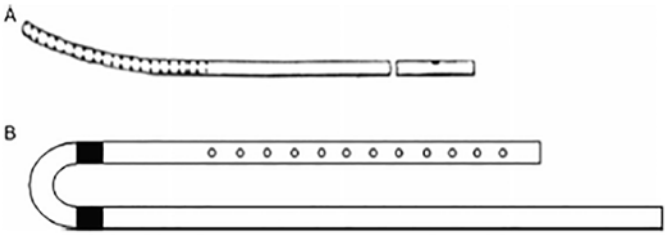

Figure 1. Dedicated peritoneal dialysis catheters are commercially available in rigid (A) or flexible (B) configurations, and typically measure 9.5 French diameter and approximately 37 centimeters in length (Reprinted from Abraham, G et al, A review of acute and chronic peritoneal dialysis in developing countries, Clinical Kidney journal, 2015, Volume 8, Issue 3, Pages 310-317, by permission of Oxford University Press).[15]

its additional anchor point in the preperitoneal space, added barrier to infection, and improved overall patient satisfaction.[4,7,26] Though more expensive than rigid catheters, and requiring a tunneled insertion, the flexible catheter is associated with lower rates of complication.[7]

Rigid catheters are inserted using a sharp, removable trocar in a non-tunneled fashion, which allows for quicker placement.[25] However, they are also prone to higher rates of complication, including dialysate leakage, and increased occurrence of bowel or bladder perforation upon insertion.[25] While a feasible option, especially for short-term management, the flexible Tenckhoff catheter is preferred. In austere settings, dedicated PD catheters will often be unavailable, and any sterilized medical tubing can be used. Alternative materials, such as nasogastric tubes, suprapubic catheters, pediatric chest tubes and central venous catheters have been effective for initiating PD in resource-limited environments.[27] Clinical data including anticipated duration of therapy, availability of supplies, and patient body habitus may dictate catheter selection.

Catheter Placement

The most experienced provider should place the catheter using best available resources, and if available, consultation should always be sought. General surgeons, interventional radiologists, and nephrologists commonly place PD catheters, but EPs and other procedurally experienced physicians can place PD catheters in austere and non-austere settings alike.[3,8] Percutaneous catheter insertion is standard in austere settings, with catheters placed blindly or under ultrasound or radiographic guidance. Percutaneous placement does not require specialized surgical equipment or general anesthesia.[28] General sterile technique and analgesia are necessary, with moderate sedation also encouraged. Pre-procedural intravenous (IV) antibiotics, such as vancomycin are recommended to decrease the risk of peritonitis.[15,29]

Catheter type dictates the optimal approach. If an improvised flexible catheter is being used, the placement requires a midline incision 2 cm below the umbilicus, blunt dissection to the linea alba, puncture through the linea alba with a rigid catheter, infusion of a small volume of dialysate, insertion of a guidewire through the initial catheter, and dilation using Seldinger technique to the final catheter.[28] For rigid catheters, placement includes anesthetizing the point of insertion immediately lateral to the umbilicus, and advancing the device with the aid of a pointed trocar, directed caudal toward the iliac fossa.[17]

When using a dedicated PD catheter, with the patient in a supine position, the upper border of the distal catheter coil should be aligned with the superior border of the pubic symphysis (Figure 2).[28,30] This position correlates with the boundary of the true pelvis, and helps limit catheter tip migration. The catheter should be oriented cephalad, approximately 3 cm lateral of midline, and the deep- and superficial-cuff points should be marked on the anterior abdominal wall.[28] A small skin incision is made at the deep-cuff point, and blunt dissection is completed down to the abdominal

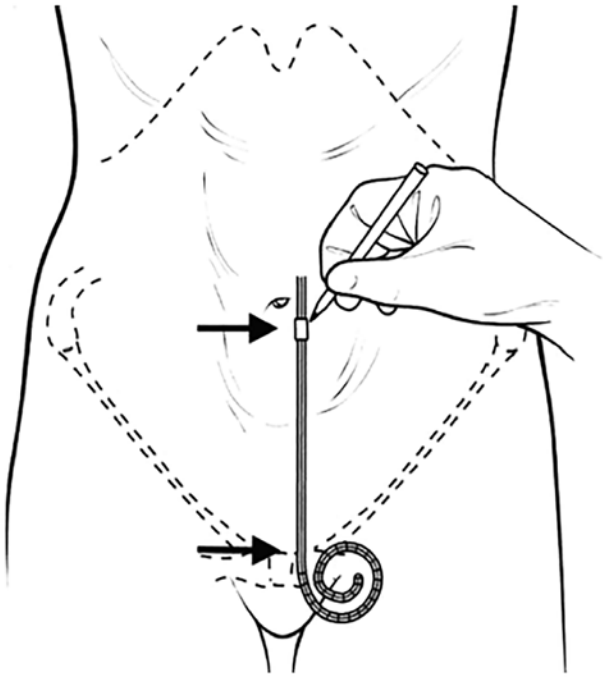

Figure 2. In the supine patient, prior to surgical placement, the upper border of the distal catheter coil should be aligned with the superior border of the pubic symphysis, and the corresponding cuff insertion sites marked (with a handheld marker as shown). This technique helps limit catheter tip migration by positioning the device at the inlet of the true pelvis (Reprinted from Kidney International, Volume 70, Crabtree, JH, Selected best demonstrated practices in peritoneal dialysis access, Pages S27-S37, 2006 with permission from Elsevier).[28,30]

rectus sheath. Using Seldinger technique, a guidewire followed by dilator and peel-away sheath are advanced into the peritoneal cavity. The catheter is then advanced through the sheath, which is gradually peeled away. The catheter's free end is then tunneled via blunt dissection to the superficial-cuff point, where it exits the subcutaneous tissue and is available for use, following closure of the skin incisions.[28]

When available, this technique may be assisted by fluoroscopic or ultrasound guidance for real-time, intraoperative monitoring.[31] In a small, prospective study of ultrasound-guided percutaneous catheter placement, providers demonstrated comparable success rates to the surgical technique, without any immediate procedure-related complications.[31,32] Continued investigation into alternative techniques for PD catheter placement has improved outcomes, while limiting the use of certain costly, prohibitive materials.[33]

Open or laparoscopic surgical placement allows direct visualization of catheter tip placement, and enables adhesiolysis and omentopexy to reduce the likelihood of catheter tip obstruction or impaction.[28] Following insertion of the catheter at the previously marked, deep-cuff point, a subcutaneous tunnel is created toward the superficial-cuff point, the catheter is secured, and operative sites closed. While no studies have demonstrated a significant difference between surgical and percutaneous placement with respect to complications and survival at one year, each modality should be vetted against available resources and personnel.[34]

Patients with Indwelling PD Catheters

PD catheter connectors are not universal. In patients with established catheters, use of their indwelling device may require a specific adaptor. If an adaptor is unavailable and an improvised adaptor cannot be constructed, the decision must be made to either modify (and possibly compromise) the existing catheter or to place a second, improvised catheter.

DIALYSATE

Dialysate is a solution of water, electrolytes and osmotic agents, formulated to aid in the clearance of metabolic waste while stabilizing acid-base or electrolyte derangements.[35] Commercially available solutions, such as Physioneal®, Dianeal® and Nutrineal® by Baxter, are prepared under stringent aseptic standards, but might not be universally available.[36] Accordingly, dialysate may be prepared from IV fluids and tailored to the clinical indication (see Tables).[5,37] Peritoneal dialysate typically contains sodium (131-134 mmol/L), chloride (95-105 mmol/L), bicarbonate plus lactate (35-41 mmol/L), dextrose (1.5, 2.5, or 4.25%), and zero potassium. Dialysate can be mixed using normal saline with additives including sodium bicarbonate and dextrose with water, but produces a notably sodium-rich solution.[38]

Lactated Ringer's solution (LR) has a similar electrolyte profile to commercial dialysate but contains 4 mEq/L of potassium. Accordingly, the addition of an osmotic agent, such as 50 mL of 50% dextrose (D50) per liter LR, will yield a potassium-containing dialysate solution ready for use.[3] For the hypervolemic patient, volume removal may be further augmented by adjusting dialysate osmolality via the addition of dextrose. For example, dextrose concentrations increase 1% by adding 20mL of D50 per liter, targeting the 1.5-4.25% dextrose concentration found in most commercial dialysates.[38] Through frequent electrolyte monitoring of the effluent and serum, the dialysate can be adjusted, e.g., by adding potassium to dialysate at serum potassium concentrations less than 4 mmol/L.[34] Of note, when prepared from individual components, special considerations should be made to ensure sterile technique. With each addition to the dialysate prescription, the risk of iatrogenic infection increases, which represents a modifiable risk to patient safety and outcomes.[39,40] Additionally, antibiotics including aminoglycosides, cephalosporins and vancomycin can be added to each PD

Table 2. Improvised peritoneal dialysis recipe.[13] Depending on circumstances and available resources, dialysate of varying dextrose concentrations may be emergently prepared to correct patient metabolic and electrolyte derangements.

	1.45% Dextrose	1.45% Dextrose	1.7% Dextrose	2.5% Dextrose
Plasmalyte B (mL)	1000			
Lactated ringers (mL)		1000		
0.45% saline (mL)			1000	
0.9% saline (mL)				1000
3% NaCl (mL)			60	
5% Dextrose water (mL)				1000
50% Dextrose (mL)	30	30	40	
8.4% $NaHCO_3$ (mEq)			40	100

NaCl, sodium chloride; *$NaHCO_3$*, sodium bicarbonate; *mEq*, milliequivalent.
Plasmalyte B: Na+ 130, K+ 4, Ca_2+ 0, Mg 1.5, Cl- 110, HCO3 – 27, pH 7.4, Osmolarity 273.

Table 3. Examples of acute peritoneal dialysis in austere environments[8,27,65,66] Worldwide, there are a variety of indications for initiation of emergent peritoneal dialysis, which may be accomplished with dedicated or improvised dialysate solutions and catheters.

Location	Indication	Dialysate	Dialysis catheter	Outcome
Ghana	Anuria; urosepsis	Improvised	12fr thoracic trocar catheter	Full recovery
Nigeria	AKI; HUS	Improvised	14fr NG tube	Recovery
Tanzania	AKI; malnutrition	Improvised	Suprapubic catheter	Full recovery
Afghanistan/Iraq	Acidosis; hyperkalemia	Improvised	Abdominal drain	Full recovery
Afghanistan/Iraq	Acidosis; hyperkalemia	1.5% dianeal	Abdominal drain	Lost to follow-up
Afghanistan/Iraq	Acidosis; fluid overload	Improvised	Pediatric chest drain	Full recovery
Afghanistan/Iraq	Fluid overload	4.25% dianeal	Abdominal drain	Death

AKI, acute kidney injury; *HUS*, hemolytic uremic syndrome; *NG*, nasogastric.

exchange for prophylaxis or treatment. To prevent PD catheter obstruction, heparin can be added to each liter of dialysate, with a typical dose of 500 units per liter.[38]

DIALYSIS PROCESS

Urgent-Start Peritoneal Dialysis

Following placement of the indwelling catheter, PD may be accomplished by several means. PD is either an automated or non-automated process. The abdominal cavity is filled with a prescribed volume of dialysate; the solution is allowed to dwell for a period of time, during which the peritoneum functions as an exchange barrier for fluids and solutes before the dialysate is drained. For non-automated PD, the most common technique includes attaching a three-way stopcock to the improvised catheter, infusing 1-2 L of dialysate in an adult, with dwell times of 2-4 hours, four times per day.[39] In pediatric cases, 10-20 mL/kg of dialysate is appropriate, with total exchange times of 60-90 minutes, incorporating 30-40 minutes of dwell time.[17,41,42] Drainage may be performed by gravity or aspiration of the dialysate. Case reports from military providers in Iraq and Afghanistan suggest small volume dwells of 500-1,000mL for 2-4 hours are also reasonable, with subsequent optimization based on volume status (e.g. altering dialysate dextrose).[7,42] Dialysate volume usage for adult AKI may range from 4-70 liters per day, depending on modality and targets of therapy.[6,8,39] Frequency and duration of therapy can be tailored to clinical circumstances, in consultation with ISPD Guidelines and a nephrologist, if available.[17]

While less frequently used in developed countries, continuous ambulatory PD is the primary method in 59% of the nearly 160,000 PD patients worldwide.[4] Furthermore, successful initiation of non-automated PD is well-documented in regions with limited medical infrastructure. Military physicians have successfully implemented non-automated PD in austere, deployed settings for critically ill patients, while reports from post-earthquake Haiti and Turkey have highlighted similar benefits in low-resource environments.[7,8,10,18]

Automated peritoneal dialysis (APD) refers to the electricity-dependent mechanical infusion and drainage of dialysate, and has limited utility in austere environments based on its use of large dialysate volumes and the requirement of a dependable energy source.

Throughout PD therapy, electrolytes, especially potassium, should be measured frequently. Daily electrocardiograms are also recommended, and may serve as an alternative for hyperkalemia screening if laboratory testing is unavailable.[17] The adequacy of PD is best assessed by the absence of hypertension, edema, and electrolyte and acid-base abnormalities.[37] Other markers of adequacy, such as weekly kT/V of urea where k is the clearance per unit time of urea, T = time and V = volume of distribution of urea, have been adapted for PD prescriptions, targeting kT/V >2.1 in AKI or >1.7 in ESRD.[6,34,39]

As above, the prescription required to achieve adequate PD is not precisely defined. Patient characteristics, including total surface area and peritoneal transport kinetics, should be considered when adjusting this regimen, though this is seldom known in austere settings. Of note, some patients have intrinsically high rates of diffusive peritoneal transport, and may benefit from shortened dwell times at increased frequency to promote clearance and limit excessive resorption of dialysate.[17] Thus, sometimes the non-intuitive intervention of shortening dwell times may be required to increase volume removal and dialysis efficacy. PD prescriptions should be optimized based on available resources, subject matter experts, and the ISPD Guidelines.

COMPLICATIONS

Advancements in PD catheter materials and placement technique ensure a safety profile comparable to other common invasive procedures. Complications from PD are classified as "early" and "late," and correspond to the first days following placement, or thereafter.[43] Comprehensive reviews of complications are essential but beyond the scope of this paper.[44,45,46,47]

During catheter placement, significant injury is a rare but important potential complication. Significant hemorrhage is often confined to the skin or subcutaneous tissue; it is mitigated by blunt dissection during catheter placement, and the provider's procedural experience.[43] Similarly, bowel or bladder injury, especially during rigid catheter placement, may be limited or rapidly identified by the use of ultrasonography or radiography.[48] Post-operative vital sign abnormalities or progressive abdominal pain in the awake patient should raise concern for viscus injury.

Intraperitoneal and exit-site infections, while limited by sterile technique, may present with local erythema and discharge at the operative site. While uncomplicated cases may be managed with oral antibiotics, surgical debridement and hardware removal should be considered for complicated cases.[43]

Peritonitis remains the most common late complication in PD, with varying incidences up to 0.24 episodes per patient per year.[45] While infection risks are minimized by pre-procedural prophylactic antibiotics, often with vancomycin or cephalosporins, signs of peritonitis should be promptly investigated and treated with two weeks or more of antibiotics.[43,49] During antibiotic therapy, prophylactic oral nystatin or fluconazole should be considered to reduce the risk of concomitant fungal peritonitis.[49] In hemodynamically stable patients, dialysis therapy should be continued while treatment is administered through the peritoneal catheter.[43] In cases of fungal peritonitis, lack of improvement following five days of antibiotic therapy, or relapsing/refractory peritonitis, removal of the device is strongly recommended.[43]

Dialysate leakage is a frequent complication of this procedure, and is often related to initiating therapy soon after catheter placement, or using a large dialysate volume.[43] Leakage may be minimized by allowing 10-14 days for tract healing following surgery, which will generally not be feasible for austere urgent-start PD. Of note, certain placement centers have had excellent success with urgent-start PD in the non-ambulatory setting, with leakage rates as low as 2% within the first month.[42,50] This complication is often managed conservatively with reduced dialysis frequency or volume, and rarely with repeated surgical intervention.[51]

Hydrothorax is an uncommon early and late complication of peritoneal catheter placement, though it may cause dyspnea and respiratory insufficiency in PD patients, requiring thoracentesis or thoracostomy.[52] Small-volume PD exchanges may be helpful to minimize the accumulation of the hydrothorax, though surgical intervention via pleurodesis or thoracotomy with diaphragm repair may be indicated, if available.[44]

Finally, catheter tip migration can occur following placement and result in obstructed dialysate drainage and discomfort. If the catheter is improperly placed or secured, the device's inherent shape-memory may displace the catheter tip as it reverts back to its native configuration.[51,53] Migration into the omentum increases the risk of local trauma from mechanical irritation or forceful attempts at flushing the catheter.[43,54] Depending on the technique for catheter placement and provider comfort, prophylactic omentectomy or omentopexy may reduce this complication**.**

OUTCOMES

PD is a life-saving therapy in austere and non-austere settings for both AKI and ESRD, but data regarding long-term outcomes are limited. A review of published literature by Chionh et al. did not identify a significant difference in outcomes between PD and extracorporeal blood purification for AKI.[6] Patients have regained renal function with long-term survival after urgent-start PD, when used as either primary therapy or bridging therapy to HD or renal transplant. Some patients will improve, with or without renal insufficiency, whereas others will require lifetime RRT or die.[7] The underlying cause often dictates prognosis of acute renal failure patients, but optimizing outcomes may require early dialysis in the austere setting. A small, prospective study demonstrated no increased incidence of early complications with immediate initiation of PD, and therapy should not be delayed for the acutely ill.[43] If transport to higher level of care of HD is unavailable, PD using available resources may be required.

Incident, or abrupt-start, PD patients have a nearly 87% one-year survival rate overall.[55] Furthermore, there is no significant difference in mortality between continuous ambulatory PD (CAPD) and APD for incident patients immediately following initiation, and the 11.3% survival rate at 10 years for CAPD patients is likely confounded by underlying patient co-morbidities.[48,56,57] A recent trial comparing PD with HD in the management of severe acute tubular necrosis showed comparable metabolic control, mortality rates and renal recovery rates, and supports PD as an effective, alternative form of RRT.[58] While the high volumes of dialysate and automated cyclers would likely be prohibitive in austere settings, PD has been proven beneficial in the critically ill.[14] Finally, the safety and efficacy of PD has successfully expanded its use to austere and resource-limited regions by certain international organizations combatting AKI and ESRD. Such groups, including the Saving Young Lives Project, bring essential supplies, training and support to medical teams serving sub-Saharan Africa and Southeast Asia.[13,59] Through infrastructure development, the survivability and total recovery from AKI in these regions has improved, while also empowering the local medical community to continue effective, safe dialysis practices.

Regardless of the etiology for acute or chronic renal insufficiency, preservation of residual renal function is a fundamental goal of RRT. Patients with continued renal function demonstrate a significant reduction in the relative risk of death, proportional to their glomerular filtration rate (GFR).[56] While further investigation is warranted, several observational studies have shown a more rapid decline in

native GFR with APD compared to continuous non-automated PD.[60] In case reports detailing the use of non-automated PD for acute renal failure in patients without prior kidney disease, several patients had no long-term clinically significant impairment on renal function, compared to 23% renal recovery rate with high-dose automated PD.[7,55] By helping preserve renal function, PD may limit the severity of acute renal insufficiency and improve outcomes in select patients.

Peritonitis continues to be a major contributor to PD failure, with annual incidence as high as 1.66 per patient at some programs.[40] This is significantly influenced by duration of therapy, underlying patient comorbidities, and psychosocial demographics.[60] Continued development of standardized practices, in conjunction with ISPD Guidelines, may minimize the incidence of treatment failure. Mortality rates for ESRD patients undergoing PD continue to decline worldwide.[61] For ESRD patients managed chronically on PD in the U.S., there has been notable progress in the reduction of adjusted mortality rates, despite the aforementioned 10-year survival rate. Improved techniques in catheter placement and management contributed to the decline in overall mortality rate for PD patients by 25% between 2004 and 2014, to fewer deaths per 1,000 patient-years than their matched HD counterparts.[62,63] This progress supports PD as a feasible alternative to HD therapy, and is gradually being replicated internationally.

For example, Sudan initiated a government-sponsored CAPD program for ESRD patients in 2005, and in a mere 20-month span established a treatment network capable of meeting accepted standards for efficacy and peritonitis rates.[64] Such programs demonstrate the feasibility of CAPD in resource-limited regions, and will hopefully promote continued international use of this treatment modality. As a means to manage ESRD or treat acute renal failure in austere settings, PD is an option with demonstrated efficacy in diverse settings throughout the world.

CONCLUSION

Peritoneal dialysis is a time-tested therapy for managing acute renal failure and ESRD. Despite significant improvements in alternative renal replacement therapies, PD remains an affordable, easy-to-initiate, and effective treatment option for patients with impaired kidney function.[67] For physicians practicing in austere or low-resource settings, PD should be considered a mainstay of renal failure therapy. In consultation with local and international organizations, subject matter experts, and ISPD Guidelines, PD is an essential and life-saving therapy.

Future research should focus on optimizing the safety and efficacy of improvised PD using readily available medical equipment. Additionally, further investigation could be directed toward establishing improvised hemodialysis. To better understand and use PD in austere settings, outcomes analysis from such applications must continue whenever possible.

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The Opioid Crisis in America: Too much, too little, too late

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TOO MUCH

There is widespread awareness of one component of today's opioid crisis in America – the overuse of opioid medications. With overdose deaths reaching epidemic levels, some U.S. states have issued emergency declarations to bring legal authorities to bear for this unprecedented situation. Following a 2015 fall in life expectancy for the first time in decades, the Centers for Disease Control and Prevention identified opioid overdoses as a major contributor to this increase in population mortality. On October 26, 2017, the President of the United States declared the opioid epidemic to be a "national public health emergency";[1] the declaration was renewed on January 24, 2018.

Prescription opioids have been a major contributor to addiction and overdose deaths. While in the not-too- distant past, physicians were trained to treat pain aggressively, and even to consider pain to be a fifth vital sign that must be immediately addressed, strong caution is now advised when prescribing opioids. Comprehensive mitigation strategies have been enacted, including a requirement to check databases of prior opioid prescriptions before dispensing new pain medications.

As the emergency medical services (EMS) medical director for a large county with a population of approximately 3.3 million residents spread over more than 4,000 square miles, I have joined others in the implementation of various strategies to prevent opioid overdose deaths. This includes developing policies and protocols to authorize and train law enforcement and emergency medical technician first responders, in addition to higher-trained personnel such as paramedics, to administer naloxone to patients with hypoventilation after opioid use. But naloxone is a short-lived emergency intervention, not a complete solution to a long-term problem.

TOO LITTLE, TOO LATE: ANOTHER OPIOID CRISIS

Despite the abundance of opioids in our communities, particularly when compared with other countries, there are patients who legitimately need treatment of their pain and are in danger of not receiving it. Pain should be treated as early as possible to halt its escalation. This is especially true in emergency settings, including treatment by paramedics in the prehospital environment.

Today we are experiencing a national shortage of critical life-saving medications and drugs needed immediately to mitigate suffering.[2] This "too little" gap has been exacerbated by the recent hurricane event in Puerto Rico – a very important source of medical drug and device manufacturing, which has markedly diminished on account of destruction wrought by the storm, and the glacial pace of recovery and restoration. Should there be a national effort to restore pharma production in the U.S. territory of Puerto Rico? Or an effort to rebuild elsewhere? Or should we expand our efforts to purchase medications from other countries?

This emergency drug shortage crisis – including opioids – has led to challenges in reliable and consistent access to important medications in our nation's emergency departments and hospitals as well as the prehospital setting. If not addressed more consistently nationwide, could this escalate to the point where we regularly lack the resources to treat pain and other time-sensitive conditions in an emergency situation?

As an EMS medical director, part of my job is to authorize destruction of expired opioids in the prehospital setting. This requirement is tragic, especially when science tells us that these drugs are effective long after their official expiration dates and prehospital agencies are severely challenged by lack of timely access to these suffering-reducing medications. While it is possible to apply for "shelf life extension" and "emergency use authorization" for these expired products,[3] obtaining authorization is generally not feasible or timely due to the current complex regulatory framework for use of expired drugs. Thus, once the expiration date arrives, it is "too late."

Important initiatives such as Executive Order 13588, Reducing Prescription Drug Shortages, signed by President Obama on October 31, 2011, and Title X of the Food and Drug Administration Safety and Innovation Act of 2012, signed into law on July 7, 2012, have increased industry notification requirements for impending shortages, but more is needed. An evidence-based, federal extension of authorization

for use of expired medications for a reasonable period of time during a period of national shortages might be one option for addressing this emerging new twist on the "too little, too late" national opioid shortage.

NATIONAL CALL TO ACTION

Critical drug shortages have been addressed in the past, for example, by the Association of State and Territorial Health Officials (ASTHO) in 2012,[4] with supporting evidence from an Institute of Medicine report entitled "Crisis Standards of Care–A Systems Framework for Catastrophic Disaster Response."[5] Yet, this important suite of suggested solutions has not been implemented to any large degree and, in fact, seems to have been dwarfed by the current attention focusing on opioid overdoses.

At the time of publication of the ASTHO document, it was estimated that nearly 40% of the short-supply drugs contributed negatively to emergency care delivery. The report described a menu of strategies to address resource shortfalls, including techniques for conservation, substitution, and adaptation. It further suggested the potential to tap into existing federal and state emergency stockpiles . . . but the reality is that regulatory authority is generally lacking for this action.

We must rekindle our national efforts to address this other manifestation of the current opioid crisis, that is, the one of "too little, too late." These emergency drug shortages require critical attention and acknowledgment. Certainly it is essential to limit opioid use when unnecessary as well as to explore non-opioid alternatives for pain treatment. This could include techniques as simple as using ice packs and splinting, as novel as emergency acupuncture, or usage of other less-commonly employed analgesics in the emergency setting such as ketamine, intravenous acetaminophen or ketorolac, and nitrous oxide. The bottom line, however, is that there is a legitimate need for opioids, when properly prescribed.

The emergency drug shortage situation appears to be escalating across America. We need help on the front lines to ensure we will have the means to alleviate suffering from acutely painful conditions. This means exploring the creative solutions mentioned above as well as other innovative, science-supported approaches to provide timely access to analgesia. Certainly let's put a stop to the declared national opioid crises, but let's also enact long-term strategies to ensure sufficient opioid production and access for essential patient care. Opioids are an important tool in the armamentarium for pain treatment. While we apply temporary regional mitigation strategies to address critical drug shortages, a long-term solution that identifies and eliminates the root causes of the crisis must be mobilized. In the meantime, our attention should not be solely focused on the popularized opioid crisis. In the case of opioids while there is too much, we also have too little, too late.

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Continuous Intravenous Sub-Dissociative Dose Ketamine Infusion for Managing Pain in the Emergency Department

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Introduction: Our objective was to describe dosing, duration, and pre- and post-infusion analgesic administration of continuous intravenous sub-dissociative dose ketamine (SDK) infusion for managing a variety of painful conditions in the emergency department (ED).

Methods: We conducted a retrospective chart review of patients aged 18 and older presenting to the ED with acute and chronic painful conditions who received continuous SDK infusion in the ED for a period over six years (2010-2016). Primary data analyses included dosing and duration of infusion, rates of pre- and post-infusion analgesic administration, and final diagnoses. Secondary data included pre- and post-infusion pain scores and rates of side effects.

Results: A total of 104 patients were enrolled in the study. Average dosing of SDK infusion was 11.26 mg/hr, and the mean duration of infusion was 135.87 minutes. There was a 38% increase in patients not requiring post-infusion analgesia. The average decrease in pain score was 5.04. There were 12 reported adverse effects, with nausea being the most prevalent.

Conclusion: Continuous intravenous SDK infusion has a role in controlling pain of various etiologies in the ED with a potential to reduce the need for co-analgesics or rescue analgesic administration. There is a need for more robust, prospective, randomized trials that will further evaluate the analgesic efficacy and safety of this modality across a wide range of pain syndromes and different age groups in the ED. [West J Emerg Med. 2018;19(3)559-566.]

INTRODUCTION

Background

Ketamine is a non-competitive N-methyl-D-aspartate (NMDA)/glutamate receptor complex antagonist that reduces pain by diminishing central sensitization, hyperalgesia, and "wind-up" phenomenon at the level of the spinal cord (dorsal ganglion) and central nervous system.[1] Ketamine administration in a sub-dissociative dosing range (0.1-0.3 mg/kg) leads to anti-hyperalgesia, anti-allodynia, and anti-tolerance, making it useful in managing a variety of acute and chronic painful conditions without adversely affecting hemodynamics and cognition.[1-3] In the emergency department (ED), sub-dissociative dose ketamine (SDK) was found to be effective for patients with acute traumatic and non-traumatic pain, chronic and cancer pain, opioid-tolerant pain and opioid-induced hyperalgesia states.[4]

Importance

A large body of evidence supports the use of SDK analgesia administered either as an adjunct to opioids or as a single agent in the ED and in the prehospital setting that leads to significant pain relief and opioid sparing.[3-10] Several strategies of SDK administration in the ED exist that include intravenous (IV) push dose (over 2-5 minutes), which is associated with highest rates of minor but bothersome psychoperceptual side effects (feeling of unreality), or short infusion (over 15 minutes) that results in significant decrease of such side effects with preserved analgesic efficacy.[11,12] However, there is virtually no data evaluating the role of continuous SDK infusion in the ED. A study by Ahern et al. that evaluated analgesic efficacy of continuous ketamine infusion lasting for one hour in ED patients with acute pain demonstrated clinically significant pain reduction (change in numerical rating scale [NRS] >3) at 60 and 120 minutes post-administration in 65% and 68% patients, respectively.[5]

Goals of This Investigation

The goal of our investigation was to evaluate feasibility (dosing, duration and co-analgesics administration), analgesic efficacy, and side-effects profile of continuous SDK infusion in order to manage various acute and chronic painful conditions in the ED. We hypothesized that this analgesic modality can be used in the ED and its administration might result in adequate pain relief with minimal risk for adverse effects.

Population Health Research Capsule

What do we already know about this issue?
SDK analgesia administered either as an adjunct to opioids or as a single agent in the ED and in prehospital settings leads to significant pain relief and opioid sparing.

What was the research question?
We sought to evaluate the feasibility, analgesic efficacy and side-effects profile of continuous intravenous SDK infusion in the ED.

What was the major finding of the study?
The mean SDK dose was 11 mg/hr with mean duration of 136 minutes, and mean pain scores (NRS) were 7.6 and 2.6 pre-/post-infusion.

How does this improve population health?
Continuous SDK infusion can be used in the ED for a wide range of acute and chronic painful conditions and age groups either as an adjunct to opioid and non-opioid analgesics or as a single agent.

METHODS

Study Design and Setting

We retrospectively reviewed medical charts of patients who were admitted to our ED and received continuous SDK infusion over a six-year period (2010-2016). The study was conducted at a 711-bed urban community teaching hospital with an annual ED census of greater than 120,000 visits. In our ED, ketamine infusions are prepared by the ED pharmacists and administered by nursing staff via infusion pump. The continuous, weight-based SDK infusion order sets are built into our electronic medical record (EMR) system (Allscripts™) with a starting dose of 0.15mg/kg/hr that is titrated upward every 30 minutes by 2.5-5mg as determined by the treating physician. We defined pre-infusion analgesia as an administration of any analgesics deemed necessary by a treating ED clinician prior to initiation of continuous ketamine infusion. Post-infusion analgesia was defined as an administration of opioid and/or non-opioid analgesic from the end of the infusion until patient's final disposition from the ED. All data with respect to doses and types of analgesics administered to each patient enrolled in the study (ketamine bolus dose, opioid and non-opioid) was aggregated and described as a percentage of total amount of analgesics given pre- and post-infusion. All patients underwent continuous cardiac monitoring and pulse oximetry. This study was approved by the hospital's institutional review board.

Selection of Participants

Patients 18 and older presenting to the ED with a variety of acute and chronic painful conditions and receiving a continuous SDK infusion in the ED were eligible for the study. We excluded patients if they received a ketamine infusion for the purpose of sedation, end-of-life care, or received only a bolus dose of ketamine.

Methods and Measurements

We performed data collection by querying the ED EMR database. Extracted data included age, sex, chief complaint, final diagnoses, pre- and post-infusion NRS pain score, duration of infusion, analgesics given before and after infusion, and adverse effects.

Outcomes

The primary outcomes of the study were the following: 1) mean dose and duration of the continuous ketamine infusion, 2) percentage of patients receiving analgesics before and after ketamine infusion, and 3) percentage of patients receiving SDK bolus dose prior to continuous ketamine infusion. Secondary outcomes consisted of 1) change in pain score before and after infusion administration via standard 11-point

NRS score, and 2) overall rates of adverse effects.

Data Analysis

The data analyses consisted primarily of descriptive statistics. We described baseline characteristics of patients in each treatment group in terms of mean ± standard deviation for continuous variables and frequency (percent) for categorical variables. A student's t-test was used to compare simple group differences in terms of means (e.g., age), while we used the chi-square test to look at differences in terms of percent rates (e.g., sex). We carried out all statistical analyses using SPSS® version 24.

RESULTS

We reviewed 2,781 medical records containing orders for ketamine dosing, which occurred between January 2010 and December 2016. Of those, we excluded 2,677 patient records due to ketamine use other than a continuous infusion for analgesia. The remaining 104 subjects receiving a continuous SDK infusion for pain control were enrolled into our study (Figure 1).

The mean age was 49.5 years old respectively, with 43% male patients. Mean baseline NRS pain score was 7.63. Most patients presented with chief complaints related to musculoskeletal pain (40.4%) and abdominal pain (36.6%), which roughly correlated with final diagnoses (Tables 1 and 2).

Main Outcomes

The overall mean dose for SDK infusion was 11.26 mg/hr (6.0-22.50 mg/hr) with an overall mean duration of treatment of 135.87 minutes (20-480 minutes). When we compared dose and duration of infusion in four different age groups (18-29, 30-49, 50-69, 70-89), we found that patients in the 30-49 age group received the highest mean dose of continuous SDK infusion of 12.17 mg/hr, as well as the longest mean duration of infusion of 140.6 minutes. There was a trend towards lower dosing and shorter duration of infusion in patients 50 years of age and older (Figure 2).

Table 1. Characteristics of patients receiving continuous ketamine infusion for pain in the emergency department.

Patients (104)	
Characteristic	N (%)
Sex	
Male	45 (43.3)
Female	59 (56.7)
Age, mean (median)	49.51 (49)
Chief complaint	
Musculoskeletal pain	42 (40.4)
Abdominal pain	38 (36.6)
Flank pain	4 (3.8)
Sickle cell disease	4 (3.8)
Other (chronic, non-cancerous, neuropathic, soft tissue pain)	16 (15.4)

Table 3 shows the percentages of patients receiving analgesia before and after continuous ketamine infusion.

Non-opioid analgesics had the highest rates of pre-infusion administration (38.4% of patients). In addition, 11.5% of patients received no analgesics prior to infusion. Post-infusion, opioids constituted the largest class of analgesics administered (23.1% of patients) with 50% of patients receiving no additional analgesics. Furthermore, 59.6% of patients received an SDK bolus before the continuous infusion, and 11.5% of patients received the continuous SDK infusion alone.

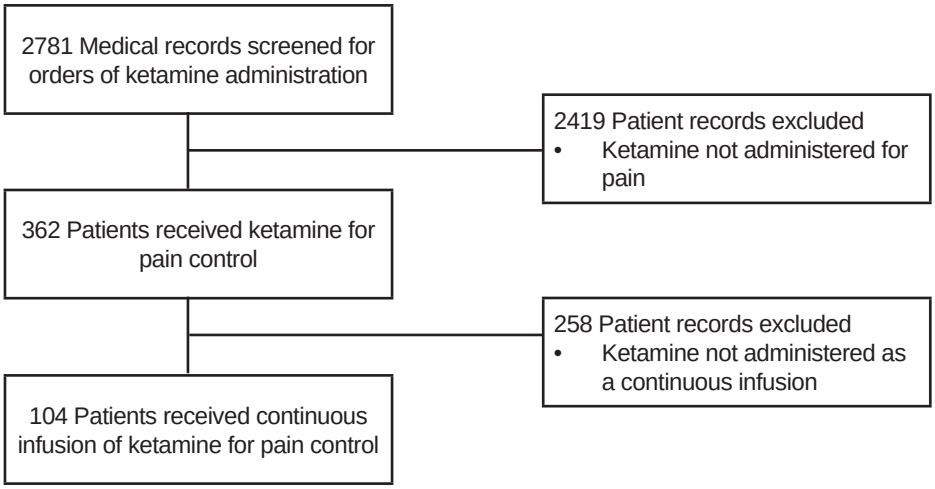

Figure 1. Study flow diagram for selection of patients who received continuous ketamine infusion for pain control.

Table 2. Patient clinical diagnosis.

Final diagnosis	N (%)
Abdominal pain (n=36)	
Non specific	21 (20.2)
Pancreatitis	6 (5.8)
Cyclic vomiting	3 (2.9)
Bowel obstruction	2 (1.9)
Gastroparesis	2 (1.9)
Gastritis	1 (1)
Cholecystitis	1 (1)
Musculoskeletal pain (n=19)	
Back (generalized/spasm)	10 (9.6)
Extremity (fracture/dislocation)	6 (5.8)
Ribs (trauma/fracture)	3 (2.9)
Neuropathic pain	20 (19.2)
Cancer pain	11 (10.6)
Chronic non-cancer pain	5 (4.8)
Sickle cell disease	4 (3.8)
Renal colic	3 (2.9)
Soft tissue pain	3 (2.9)
Headache	2 (1.9)
Other	1 (1)

Table 3. Analgesics administration pre- and post-ketamine infusion.

Type of Analgesic Pre-Infusion	N (%)
Opioid only	18 (17.3)
Non-opioid only	41 (38.4)
Opioid and Non-opioid	33 (31.7)
No analgesics administered	12 (11.5)
	Type of analgesic
Post-Infusion	N (%)
Opioid only	24 (23.1)
Non-opioid only	13 (12.5)
Opioid and non-opioid	15 (14.4)
No analgesics administered	52 (50)
	Ketamine Bolus
Pre-Infusion	N (%)
Ketamine bolus	
Administered	62 (59.6)
Not administered	42 (40.4)
Ketamine continuous infusion with no other analgesics	12 (11.5)

Furthermore, upon comparing the dose and duration of continuous SDK infusion across the nine final diagnoses, we found that patients with a clinical diagnoses of headache, renal colic, and chronic non-cancer pain received the highest doses of continuous ketamine infusion. Patients with a clinical diagnoses of soft tissue, chronic non-cancer, and abdominal pain on average had the longest duration of ketamine infusion (Figure 3).

Administration of analgesics before and after continuous SDK infusion varied greatly between the four most prevalent clinical diagnoses groups, most notably in patients with abdominal and cancer pain. Patients with abdominal pain demonstrated the largest difference in not receiving any analgesic from 2.8% pre-infusion to 61.1% post-infusion ($p<0.0001$). Patients with cancer pain also showed a significant difference of not receiving any analgesic from 9.1% pre-infusion to 63.6% post-infusion ($p<0.05$). These findings were noted despite the fact that abdominal-pain and cancer-pain patients received relatively lower doses of ketamine. While no definitive conclusion can be drawn from this observation, it may suggest a higher rate of analgesic efficacy in the two patient populations. Furthermore, patients with abdominal and cancer pain had reduced requirements for non-opioid analgesics post-continuous ketamine infusion ($p<0.05$) **(**Figure 4). Patients with musculoskeletal pain exhibited a significant decrease in non-opioid analgesic administration post infusion ($p<0.010$) while patients with neuropathic pain showed an increase in opioid-only analgesic administration ($p=0.064$) (Figure 4).

Secondary Outcomes

Complete NRS data was not available for all 104 patients. For 53.8% of patients with available pain scores, the mean NRS pain scores were 7.63 (±2.3) pre-infusion and 2.65 (±3.3) post-infusion, resulting in an average pain score decrease of 5.04 (95% confidence interval [CI] [4.07-6.00]; $p<0.0001$). Furthermore, for patients with one of the top three diagnoses of abdominal, musculoskeletal, and neuropathic pain with available pre- and post-pain scores, the mean decrease in pain score was 4.95 (95% CI [3.36- 6.53]; $p<0.0001$) for abdominal pain, 4.78 (95% CI [1.28-8.28]; $p<0.05$) for musculoskeletal pain, and 3.69 (95% CI [1.45-5.93]; $p<0.005$) for neuropathic pain. Five adverse effects were documented in a total of 12 patients: nausea (5.8%), headache (1.9%), dizziness (1.9%), rash (1.0%), and confusion (1.0%). Ninety-two (88.4%) patients had no documentation of any adverse effects. Two (1.9%) patients presenting with abdominal and renal colic pain required discontinuation of SDK infusion due to severe nausea. Thirty-six (34.6%) patients were admitted to the hospital for further pain control after infusion was completed, which included 13 (12.5%) with abdominal pain, six (5.8%) with cancer pain, five (4.8%) with musculoskeletal pain, five (4.8%) with neuropathic pain, three (2.9%) with sickle cell pain, three (2.9%) with chronic pain, and one (0.9%) with flank pain.

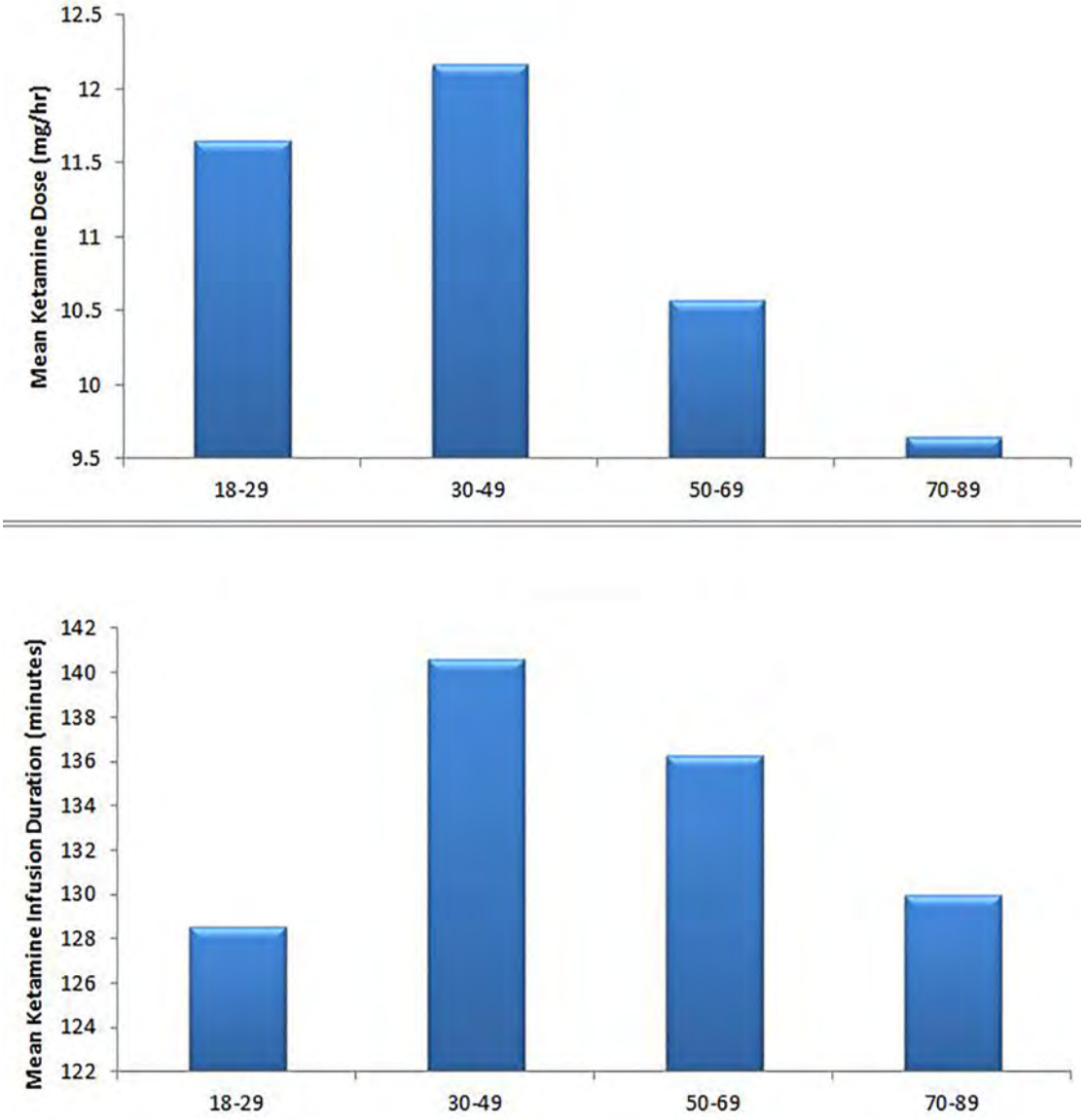

Figure 2. Mean ketamine infusion dose and duration for different age groups.

LIMITATIONS

The retrospective nature of our study, relatively small sample size, and lack of documented pain scores in 46.2% of patients were the major limitations. As a result, we could not fully evaluate and compare the analgesic efficacy of continuous SDK infusion between different age groups and between different pain syndromes; thus, we could not assert any recommendation with respect to overall pain relief. Furthermore, due to the fact that only 53.8% of patients had documented pre- and post-infusion pain scores and only 59.6% of patients received a ketamine bolus prior to the infusion we could not accurately and reliably compare the difference in improvement of pain scores between patients receiving a bolus dose followed by infusion to infusion only. Additionally, since the primary outcome of the study was the dosing regimen for continuous ketamine infusion, dosages for analgesics given to patients before and after infusion were not abstracted. Lastly, due to the retrospective nature of the study we cannot make any statements regarding the safety of continuous SDK infusion in our ED. Future prospective studies are needed to evaluate the safety and efficacy of SDK infusion in the ED.

DISCUSSION

SDK administration in the form of IV push or short infusion is becoming increasingly popular as a viable adjunct

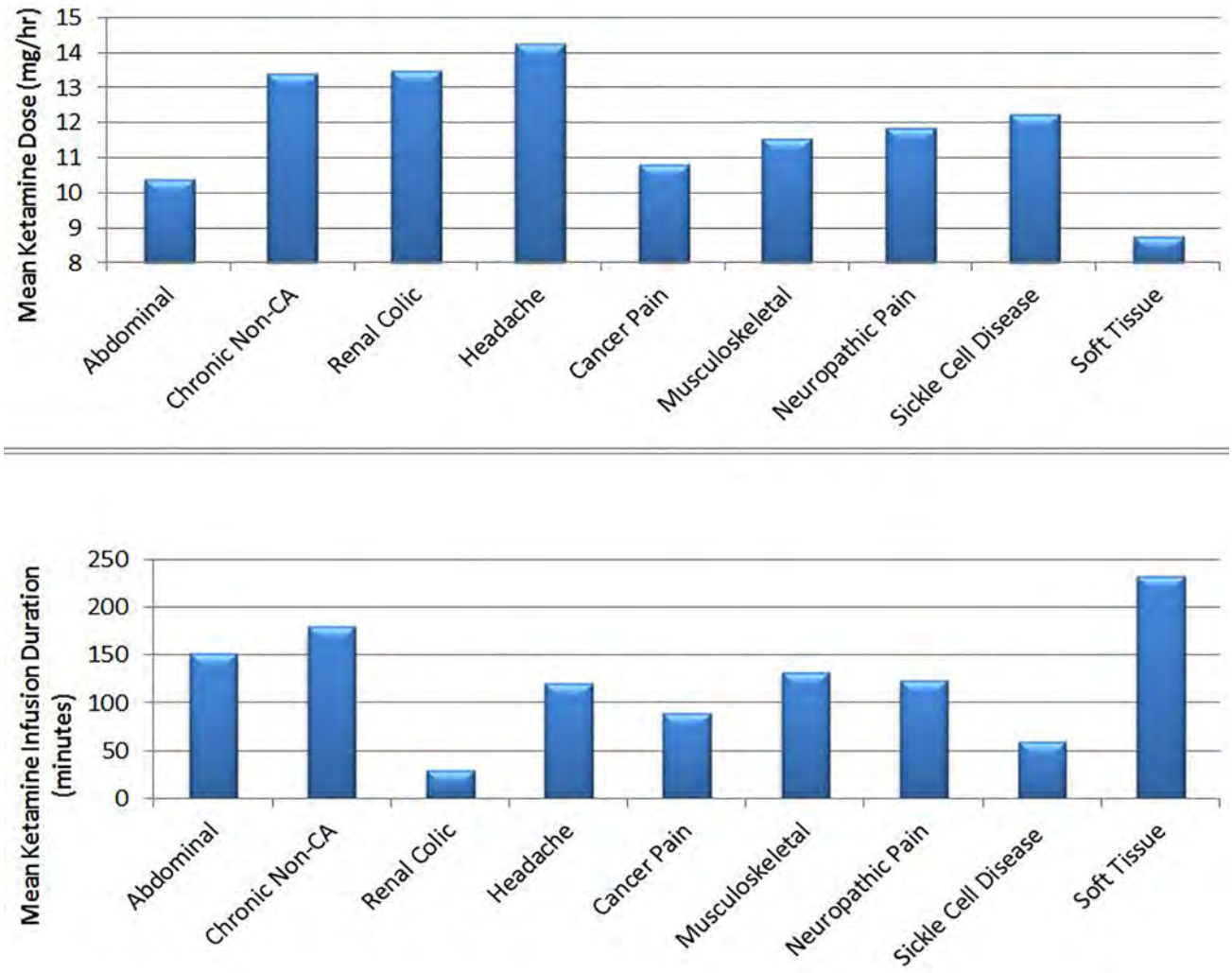

Figure 3. Mean ketamine infusion dose and duration for final diagnosis groups.

to or even a substitute for opioid analgesics in managing a variety of acute and chronic painful conditions in the ED.[3-12] To date, however, there is a paucity of data that supports the use of continuous SDK infusion (longer than one hour) in the ED. Ahern et al. prospectively administered 15 mg of IV SDK immediately followed by a continuous infusion of 20 mg/hr for one hour to 38 ED patients with acute pain. At the one-hour mark, 25 and 26 patients had significant pain relief (NRS reduction greater than 3) at 60 and 120 minutes, respectively.[5]

A growing body of literature advocates for use of continuous SDK infusion either as an adjunct to opioids or as a single agent for pediatric and adult patients with predominantly chronic painful conditions. A recent cohort study that included 230 hospitalized patients receiving continuous ketamine infusion demonstrated a 34% decrease in pain score after one day of treatment. In addition 58% of patients achieved equal or greater than 20% overall reduction in pain scores without psychotomimetic side effects requiring therapy. Furthermore, patients with cancer pain and patients with pancreatitis and Crohn's disease had greater reductions in pain scores.[13]

A retrospective chart review of five pediatric patients with sickle cell disease and acute vaso-occlusive crisis who received continuous ketamine infusion with a dosing range of 0.06 mg/kg/hr to 0.1 mg/kg/hr and duration of treatment from 19 to 90 hours, demonstrated a clinically significant pain reduction in two children and reduction in opioid consumption in one child. Two patients experienced side effects (mainly dysphoria) that resulted in treatment termination in one patient.[14] A case report of continuous ketamine infusion in adult patients with acute vaso-occlusive painful crisis administered for seven days resulted in 65% pain relief at the

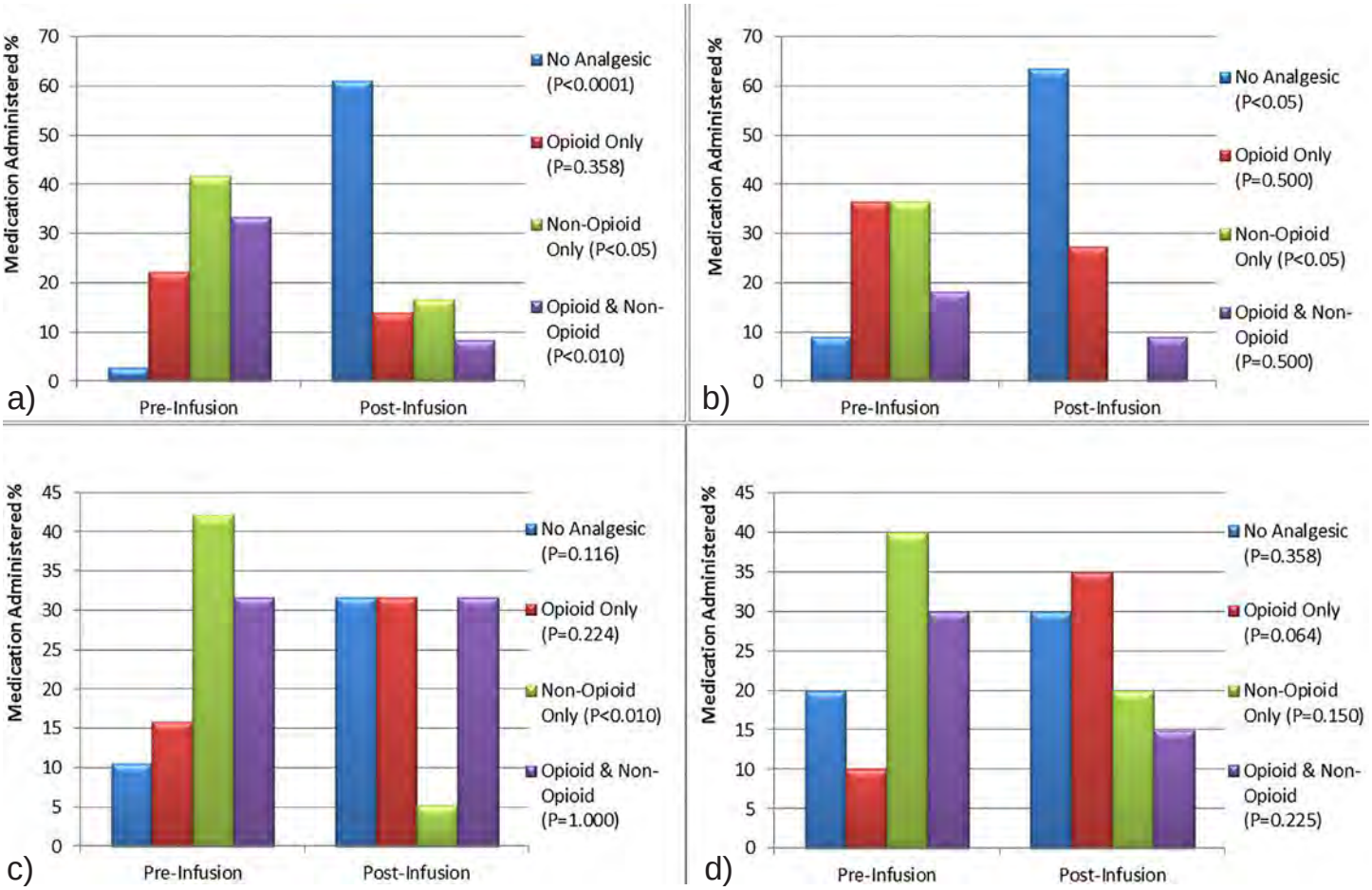

Figure 4. Analgesics administered pre- and post-ketamine infusion for most common final diagnoses; a) abdominal pain, b) cancer pain, c) musculoskeletal pain, d) neuropathic pain.

end of the treatment course without any psychoperceptual side effects.[15] Another case report of a patient with post-operative phantom pain and allodynia who was started on ultra-low dose (1.5-5 mg/hr) of continuous ketamine infusion for three days, demonstrated a 60% pain decrease during the initial hours of administration without any psychomimetic side effects.[16]

Our retrospective chart review demonstrates that continuous SDK infusion has the potential to be used in the ED across a wide range of acute and chronic painful conditions and age groups either as an adjunct to opioid and non-opioid analgesics or as a single agent. The fact that continuous SDK infusion alleviated the need for additional post-infusion analgesia in 60% and 55% of patients with abdominal pain and cancer pain is very encouraging even though we could not fully evaluate the analgesic efficacy of this analgesic modality due to the retrospective nature of this study. In addition, our chart review showed that patients with neuropathic pain and chronic non-cancer pain required higher rates of post-infusion opioid rescue analgesia and a longer duration of ketamine infusion, thus demonstrating that management of such painful conditions in the ED can be very challenging.

Lastly, our data showed that continuous SDK infusion can be employed for geriatric patients with a broad range of painful syndromes in the ED, thus adding an additional analgesic modality when opioids and non-steroidal anti-inflammatory drugs are contraindicated.

One of the possible barriers to use of continuous SDK infusion are potential administrative concerns regarding an off-label use of an anesthetic agent such as ketamine for managing pain in the ED and on the hospital wards. Departmental and interdisciplinary protocols with clearly specified, patient eligibility criteria as well as indications for and contraindications to SDK infusion should be in place before widespread use of this analgesic modality is considered for implementation.

CONCLUSION

Continuous intravenous SDK infusion does have a role in controlling pain of various etiologies in the ED with the potential added benefit of decreased need for additional

analgesia. There is a need for more robust, prospective, randomized trials that will further evaluate the analgesic efficacy and safety of this analgesic modality across a wide range of pain syndromes and different age groups.

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Retrospective Chart Review of Synthetic Cannabinoid Intoxication with Toxicologic Analysis

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Introduction: Use of synthetic cannabinoids (SC) has recently emerged as a new drug epidemic. Our emergency departments (EDs) received a surge of SC users presenting with lethargy and bradycardia, contrasting prior reports of SC-induced tachycardia and agitation.Our goal was to describe these novel presentations and characterize the compounds.

Methods: We present a case series of patients with SC intoxication who presented to our toxicology service covering two tertiary care EDs between 2/11/2015 and 6/23/2015. A retrospective chart review recorded initial vital signs, chief complaint and clinical course. Urine, blood and xenobiotic samples were analyzed using either liquid chromatography/mass spectrometry or gas chromatography/mass spectrometry. We compared resulting spectra against databases containing numerous SCs or metabolites and scored based on a reference comparison.

Results: Between 2/11/2015 and 6/23/2015, we identified 141 visits. Males comprised 139 visits (age range 21-68 years; median 35, interquartile range 20). Sixty-eight percent presented with lethargy or loss of consciousness. Hypotension (SBP <90 mmHg) and bradycardia (HR<60 bpm) were seen in 10% and 24% of visits, respectively. While most patients were discharged after observation, three were admitted to the intensive care unit and seven to telemetry. Admissions were for vital sign instability, bradycardia requiring pacing, prolonged sedation and respiratory failure requiring mechanical ventilation.
Laboratory analysis revealed SC in the XLR-11 family in 18/36 drug, 9/12 blood, and 23/31 urine samples. Carboxamide indazole derivative (CID) family compounds were detected in 13/36 drug samples, 21/31 urine samples, but no blood samples; 11/31 drug samples contained both XLR-11 and CID. Other compounds detected included PB-22 and nicotine. No JWH compounds, opiates, imidazoline receptor agonists, benzodiazepines or other sedative-hypnotics were detected.

Conclusion: Unlike their predecessors, novel SC may be associated with significant central nervous system depression and bradycardia. While prior reports indicated that SC mostly contained JWH compounds, none were detected in these samples. The most commonly identified compounds in this series were CID and alkyl SC derivatives, such as INACA compounds and XLR-11. These tend to be full agonists at the cannabinoid receptor and are presumably more potent. The lack of other depressants suggests that the clinical findings are due to the combination of these compounds and not coingestants or adulterants. SC intoxication should be considered for patients with undifferentiated psychomotor depression and bradycardia. [West J Emerg Med. 2018;19(3)567-572.]

INTRODUCTION

Synthetic cannabinoids (SC) are a class of drugs that are becoming increasingly popular throughout the United States and Europe. Also known as "K2," "spice," spike," or "legal marijuana," SC are causing intoxication requiring emergency department (ED) visits in epidemic and unparalleled numbers.[1] Patients present with a wide array of symptoms, ranging from nausea and vomiting to confusion, agitation, short-term memory loss, cognitive impairment, psychosis, seizures, arrhythmias, strokes and even death.[2] SC have often been associated with sympathomimetic effects such as mydriasis, hypertension and tachycardia.[2] We present a case series of patients with SC intoxication who presented atypically with central nervous system (CNS) and cardiovascular depression over a five-month period; in addition, we present an analysis of blood, urine and SC samples using mass spectrometry. Intoxication with SC products should be considered for patients with undifferentiated psychomotor depression and bradycardia in addition to the excitatory effects previously described.

Population Health Research Capsule

What do we already know about this issue?
Synthetic cannabinoid intoxication has emerged as an epidemic, and can present with a wide array of gastrointestinal, neuropsychiatric and cardiovascular symptoms.

What was the research question?
Are bradycardia and central nervous system (CNS) depression associated with novel synthetic cannabinoids, or coingestants or adulterants?

What was the major finding of the study?
Novel synthetic cannabinoids were detected with no coingestants and are associated with CNS depression and bradycardia.

How does this improve population health?
Synthetic cannabinoid intoxication should be considered for patients with undifferentiated CNS depression and bradycardia.

BACKGROUND

In early 2015 our suburban, tertiary care EDs experienced a large influx of patients presenting with lethargy and psychomotor depression, often requiring admission to the telemetry or intensive care units and rarely requiring intubation. The patients usually experienced sudden and complete resolution of symptoms after several hours in an obtunded state. Large cohorts of these patients simultaneously presented from a nearby psychiatric center that provided inpatient, outpatient and residential services. The increased volume of intoxications exacerbated ED crowding. Patients later admitted to SC use, and some produced samples of the plant material. Questions arose regarding the potential contamination of these substances with other agents, such as clonidine or digoxin, or whether these presentations were due to newer generation SC.

We selected cases for this series from the toxicology consult service database for patients suspected of SC use. Blood and urine samples were collected from the patients when possible. The unknown drug samples were analyzed and compared to a reference database to identify the compounds present.

MATERIALS AND METHODS

We included two tertiary care EDs in our case series. In total, 141 ED visits were selected by toxicologists from the consult service database based on abnormal triage vitals, history of SC use or an obtunded mental state upon presentation. Twelve blood and 31 urine samples were collected. The 36 samples of plant material provided by patients were collected and analyzed using liquid chromatography/mass spectrometry and gas chromatography/mass spectrometry (GC/MS). The samples were not correlated with specific patients. This retrospective chart review was approved by an institutional review board.

Standards and Reagents

We purchased chemical reagents, including ethyl acetate, methanol, water, and formic acid from VWR International (Bridgeport, NJ). All solvents were high performance liquid chromatography grade or better.

Sample Preparation

Samples were extracted with organic solvent and concentrated to isolate any drugs present on the plant material. Briefly, 5 mg aliquots of an unknown plant material, or 100 μL of submitted blood/urine, were transferred to screwtop centrifuge tubes. Two mL of ethyl acetate were added and the samples were thoroughly mixed. Samples were extracted for 10 minutes on a nutating mixer at 24 revolutions per minute. The solvent was transferred to clean test tubes and the extracts were evaporated to dryness under nitrogen at 45°C. Samples were reconstituted in 50 μL methanol and 50 μL 0.1% formic acid in water and transferred to conical autosampler vials for analysis by liquid chromatography time-of-flight (TOF) mass spectrometry. Similarly, samples were reconstituted in 50 μL ethyl acetate for GC/MS confirmation analysis. Biological samples underwent a 20-minute room temperature hydrolysis period prior to liquid-liquid extraction.

Liquid Chromatography Conditions

We used an Agilent Technologies 1290 liquid chromatograph (LC) equipped with a Zorbax Eclipse Plus C-18 column (2.1mm x 50mm x 1.8μm) for chromatographic separation of the unknown plant material extract. The LC columns were maintained at 50°C in the thermostated column compartment. Mobile phases consisted of 0.1% formic acid in deionized water (A) and 100% methanol (B). The mobile phase flow rate was set at 0.7 mL/min. Initial mobile phase conditions were held at 0%B for 0.5 minutes then increased to 95%B over five minutes. Mobile phase conditions returned to initial starting conditions for a final run time of six minutes.

Time-of-Flight Mass Spectrometry Conditions

We operated an Agilent Technologies 6230 TOF mass spectrometer with a Jetstream electrospray source in positive ion mode with the following common parameters: nitrogen drying gas temperature 350°C; nitrogen sheath gas temperature 400°C; nitrogen drying gas flow 10 L/min; nitrogen sheath gas flow 11 L/min; nebulizer pressure 45 psi; capillary voltage 4000 V; and nozzle voltage 1000 V. Accurate mass spectra were acquired at a rate of 1 spectra per second over the range of 100 – 1700 m/z.

TOF Data Analysis

We compared all acquired spectra against the Agilent Technologies Forensic Toxicology PCD Accurate Mass Database of over 7,500 compounds. All spectra were scored based on deviation from expected exact mass assignment (ΔPPM), chromatographic retention time, and peak abundance. Scores greater than 90% match were considered positive. Where available, unknown compounds were confirmed as positive by comparison to a known reference material.

Gas Chromatography Mass Spectrometry Conditions

We used an Agilent Technologies 7980A series gas chromatograph equipped with an HP-5MS column (30m x 0.25mm x 0.25μm), a 5975C series mass selective detector and a 7693 series autoinjector module for chromatographic separation of the unknown plant material extract. The transfer line temperature was 295°C. The oven program consisted of an equilibration time of 0.5 minutes, initial temperature of 100°C, ramp of 15°C/minute to a final temperature of 325°C. The total run time was 20 minutes. The inlet mode was splitless with a temperature of 265°C and an injection volume of 1μL.

GC/MS Data Analysis

We compared all acquired spectra against the Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) database. All spectra were scored based on the search quality of the generated spectrum in comparison to the reference spectrum. We considered search quality scores greater than or equal to 90% positively detected based on chromatographic retention time, and peak abundance. Where available, unknown compounds were confirmed as positive by comparison to a known reference material.

RESULTS

We identified 141 patient visits from 2/11/2015 to 6/23/2015 (Table 1). Of these patients, 139 (98%) were male with a median age of 35 (range 21-68 years old). Ninety-seven (68%) of the patients presented with lethargy or an altered level of consciousness. A smaller proportion presented with hypotension (systolic blood pressure < 90 mmHg) (10%) or bradycardia (heart rate < 60 bpm) (24%).

We analyzed 36 drug samples (Table 2) and found that the majority of them contained carboxamide indazole derivatives (CID) or XLR-11, an alkyl derivative. Eleven of the samples had both derivative classes detected in the mixture and 14 had no SC identified.

We found that 24 of 31 urine samples tested positive for a SC; 74% of urine samples contained XLR-11, and 35% contained carboxamide indazole derivatives (CID). Nine of the 12 blood samples (75%) contained suspected metabolite of XLR-11. None of the blood samples tested positive for CID. There were no JWH compounds, opioids, imidazoline receptor agonist or sedative-hypnotics detected in any of the material, urine or blood samples.

DISCUSSION

Hundreds of distinct SC compounds have been identified.[2] SCs are responsible for a rapidly growing number of presentations to EDs throughout the U.S. in the past several years.[1] SC use causes intense highs and has become popularized due to accessibility, affordability and limited detectability in common drug screens.[3] Intoxications often present in clusters due to local distribution of a single product and great variability in the herbal mixtures. One study found a range of 2.3-22.9 mg/g of cannabimimetics in the herbal mixtures.[4] In addition, SC have been found to be more potent than Δ^9-THC;[2] the SC 5F-ADB-PINACA, a CID compound similar to a SC detected in our study, is over 1,000 times more potent than Δ^9-THC.[5]

In March 2011 the U.S. Department of Justice categorized

Table 1. Patients presenting with symptoms of synthetic cannabinoid intoxication.

	Total number	%
Total visits	141	100
Male visits	139	98
Lethargy/LOC	97	68
Hypotension (<90 SBP)	14	10
Bradycardia (<60 HR)	34	24
ICU admissions	4	3
Telemetry admissions	10	7

LOC, loss of consciousness; *ICU*, intensive care unit.

Table 2. Analyses of samples for presence of synthetic cannabinoids.

Sample (total)	Any SC (%)	XLR-11 (%)	CID (%)	XLR-11 and CID (%)	Nicotine (%)	No SC definitively identified (%)
Drug (36)	22 (61)	18 (50)	13 (36)	11 (31)	5 (14)	14 (39)
Blood (12)	9 (75)	9* (75)	Not detected	Not detected	Not detected	3 (25)
Urine (31)	24 (77)	23* (74)	21 (68)	20 (65)	Not detected	7 (23)

CID, carboxamide indazole derivatives, *SC*, synthetic cannabinoids.
*Suspected metabolite of XLR-11 (UR-144 compounds).

the five most commonly abused SCs (JWH-018, JWH-073, JWH-200, CP-47,497 and its C8 homolog) as Schedule I drugs under 21 U.S.C.811(h) of the Controlled Substances Act.[6,7,8] As local outbreaks continued, the novel compounds (detected in this study) were identified and added to the Controlled Substances Act.

ED visits increased from 11,406 in 2010 to 28,531 in 2011.[9,10] Visits from patients 12-17 years old more than doubled from 3,780 to 7,584, while visits from patients18-20 years old increased from 1,881 to 8,212.[9,10] In 2011, SCs were the second most commonly used drug in the 10th grade and the third most common in eighth grade following marijuana and inhalants.[2,11] Despite the federal ban on SCs that year, there was no decline in frequency of use in high school students the following year. However, use declined in each of the next three years.[11] Users of SCs vary greatly in both demographics and motivation, but are typically males aged 13-59, most with polydrug use and are found in larger, urban populations.[2,12]

SCs are known to interact with the cannabinoid receptors, CB_1 and CB_2, leading to changes in levels of multiple neurotransmitters including acetylcholine, dopamine, noradrenaline, glutamine and GABA.[2] Genetic polymorphisms in enzymes responsible for metabolism of SCs can lead to increased blood levels of the parent compound and prolonged duration of action, and therefore a potential increased risk of adverse events.[10,13] In addition, many SC metabolites retain biological activity.[10,13] Combination of these metabolites with accumulation of the parent drug creates complex pharmacodynamics, especially when the multitude of other compounds typically found within herbal mixtures is considered.

SCs have been reported to exhibit a wide array of effects. CNS effects include psychosis, anxiety, agitation, irritability, memory changes, sedation, confusion and hallucinations,[14] in addition to lowering the seizure threshold in susceptible individuals.[15] Reported cardiovascular effects include tachycardia, chest pain, dysrhythmias, myocardial ischemia[13] and cerebrovascular accident caused by embolisms due to cardiac arrhythmias or reversible cerebral vasoconstriction syndrome.[16,17] In an analysis of a Centers for Disease Control and Prevention report of 3,573 calls to poison control for SC-related adverse events, the most common effects were agitation (35%), tachycardia (29%), drowsiness or lethargy (26%), vomiting (16%), and confusion (4%).[1]

In early 2010, JWH-018 was detected in 100% of SC products. However, as legislation regarding SCs changed in 2010 and 2011, the incidence of JWH-018 decreased, while similar yet compositionally distinct compounds appeared. By the end of 2012, JWH-018 was not detected in samples, and XLR-11 became the most common SC detected,[18] as exhibited in our sample analysis.

In our case series, CID and alkyl SC derivatives, such as INACA compounds and XLR-11,[19] were the most commonly detected with no opiates, imidazoline receptor agonists, benzodiazepines or other sedative-hypnotics detected that might explain the atypical presentations. Sixty-one percent of the confiscated products contained a SC and 31% contained both XLR-11 and CID. Seventy-five percent of blood samples and 77% of urine samples tested positive for SC. Unlike their predecessors, novel SC appear to be associated with significant CNS depression and bradycardia. The compounds detected in our case series tended to be full agonists at the cannabinoid receptor and are more potent than Δ9-THC.[20] The lack of other CNS and cardiovascular depressants suggests that the clinical findings are due to the combination of these compounds and not coingestants or adulterants.

It is important to note that many substances detected in the plant samples were not detected in the blood or urine samples. Some examples include 5-Fluoro-NNEI 2'-naphthyl isomer, 5-fluoropentylindole, NM-2201 and NPB-22. There are multiple explanations for these findings. The patient may have used SC products that were not included in our plant samples and therefore would not be associated with the urine and blood samples. It is also possible that the metabolites of the compound were not in the database or that the level was below the LC TOF detection limits. Furthermore, the metabolite may have been metabolized to a common XLR metabolite that was detected, or the drug had already been eliminated from the body.

LIMITATIONS

Our case series demonstrates some of the severe effects these novel compounds can cause. However, the study has a number of important limitations. First, the selection of patients was based on the judgment of our ED team and toxicologists based on abnormal vital signs, subjective history from the patient, presentation of decreased mental status and clinical judgment. Many intoxicated patients may have been evaluated

and treated without being included in the study. In addition, patients may have had altered mental status for reasons other than SC intoxication and may have been erroneously included in the study because their ED arrival was associated with other patients with SC intoxication. Although there were 141 visits, several patients with recurrent intoxications were included as multiple visits in the study.

The SC samples were provided by patients, but it should not be assumed that the specific sample was necessarily the cause of their intoxication. Furthermore, the samples were collected anonymously, without designation to a specific patient, and therefore we were unable to identify which of the patients presenting with bradycardia tested positive for certain compounds. This significantly diminished our ability to conclude that certain types of SC are associated with more profound presentations of bradycardia and psychomotor depression. Lastly, the majority of the patients presented from a large, nearby psychiatric center. The patients often presented as groups, possibly due to simultaneous drug use with the same sample. This patient population tends to have multiple comorbidities, and members may be taking neuroleptic medications that may increase the opportunity for interactions with the cannabinoids. This is a population with an increased risk of substance use, and therefore the results of our case series cannot necessarily be extrapolated to other populations.

CONCLUSION

SC products are inexpensive, easily obtained, avoid common drug detection screens and cause a wide array of signs and symptoms. The changing composition of available SCs corresponds to the variability exhibited in patient presentations. SC intoxication should be considered for patients with varied clinical effects, including undifferentiated psychomotor depression, loss of consciousness, hypotension and bradycardia.

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Occult Suicidality and Psychiatric Disease Among Emergency Department Patients with Low-acuity Chief Complaints

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Introduction: Patients presenting to emergency departments (ED) are often screened for suicidality, even when their chief complaint does not involve mental health concerns. Patient receptiveness to ED-based mental health screening and intervention is unknown, particularly among patients with low-acuity chief complaints, who often prioritize rapid evaluation and discharge.

Methods: This cross-sectional study included adults with low-acuity chief complaints presenting to an urban, academic ED in the Northeastern United States during daytime and evening hours, from 2015 to 2016. Participants completed validated mental health screening instruments, including the Suicide Behaviors Questionnaire-Revised and the Patient Health Questionnaire-4. Participants were also asked to rate the importance of addressing mental health concerns during their ED visit.

Results: We approached 1,688 patients, and 816 (48.4%) consented to participate in the study. Of these, 27% screened positive for anxiety and 25% screened positive for depression. Even among patients with no prior depression history, 17% were at high risk of depression. Eleven percent of participants were at high risk for suicidal behavior, including 5% of those with no reported history of depression or bipolar disorder. Thirty-five percent of patients at risk for suicide and 53% of those at high risk of depression thought it was important or very important to address these issues during the ED visit.

Conclusion: Symptoms of mental health disorders were common among this group of ED patients presenting with low-acuity chief complaints. Patients often desired to address these mental health concerns as part of their ED visit. [West J Emerg Med.2018;19(3)573–578.]

INTRODUCTION

Suicide is a leading cause of death in the United States, particularly among younger adults.[1-3] Each year U.S. emergency departments (ED) treat approximately half a million patients for attempted self-harm or suicide.[4] Prior studies have demonstrated that patients seeking ED care for issues not related to mental health have significant rates of depression and occult suicidal thoughts.[5,6] As a result, the Joint Commission has mandated that U.S. EDs screen all patients for suicidal ideation.[7] Despite this mandate, little is known about the effectiveness of broadly implemented mental health screening programs, and the U.S. Preventive Services Task Force has concluded that insufficient evidence exists to support generalized screening for suicide risk.[8] Importantly, the link between screening for mental health disorders and improved patient outcomes depends in part on the receptiveness of patients to interventions that might be implemented when screening suggests the presence of a disorder such as suicidal ideation.

Patients presenting to the ED with low-acuity chief complaints comprise up to two-thirds of ED visits, and may face unique barriers to mental health screening.[9] For example,

because these patients are often rapidly treated and discharged, and because they often prioritize limiting their time spent in the ED, they may not be receptive to interventions unrelated to the medical problem that prompted their ED visit. Despite the significant proportion of ED patients who present seeking care for low-acuity complaints, little study has been devoted to examining the baseline mental health of this population. Consequently, the receptiveness of this population to mental health screening and ED-based interventions is unknown. The goal of this study was to determine the prevalence of occult suicidal ideation and other mental health disorders among ED patients presenting with low-acuity chief complaints, along with the receptiveness of these patients to ED-based mental health interventions.

Population Health Research Capsule

What do we already know about this issue?
Symptoms of severe depression and occult suicidality are common among emergency department patients, and screening of ED patients for suicidal thoughts is required by the Joint Commission.

What was the research question?
Among low-acuity ED patients, how common are suicidal thoughts and how willing are patients to address them during the ED visit?

What was the major finding of the study?
Of 816 participants, 11% were at high risk for suicide. Many were receptive to addressing mental health issues during the ED visit.

How does this improve population health?
These findings suggest that screening low acuity ED patients for mental health concerns may be useful, though studies assessing the impact of screening on patient-oriented outcomes are needed.

METHODS

Study Design, Setting, and Selection of Participants

This prospective cross-sectional survey study was performed in the Cooper University Hospital ED, an urban academic department with an annual volume of about 80,000 patients per year, which provides care for a socioeconomically diverse community in the Northeastern United States. Medical care is provided by either an attending physician or by residents or nurse practitioners under the supervision of an attending physician. The study was approved by the institutional review board, and all subjects provided signed informed consent to participate.

Patients were eligible for participation if they were aged 18 years or older and had an Emergency Severity Index (ESI) triage score of 4 or 5, indicating a low-acuity presentation, as documented by a triage nurse experienced in the use of the ESI system. Approximately 25% of the patient visits evaluated in the ED met this definition for a low-acuity presentation. Patients were excluded if they did not speak English, if they suffered from dementia or other cognitive impairment, if they presented to the ED for treatment of an acute psychiatric emergency, if they were intoxicated, or if they were incarcerated at the time of their ED visit.

Research assistants (RA) were initially trained in the study methods via a didactic lecture. An investigator then provided additional individualized training and observation until they deemed each RA proficient at independently screening subjects, obtaining informed consent, and performing data collection, after which the RAs independently performed these tasks. Subjects were enrolled between 9 a.m. and 10 p.m. during randomly selected two-hour blocks, seven days a week, between June 2015 and April 2016. We used random time-block sampling to minimize sampling bias due to convenience sampling, given limited resources available for data collection.

Measurements

Participants completed two previously validated mental health screening instruments, the Patient Health Questionnaire for Depression and Anxiety (PHQ-4) and the Suicide Behaviors Questionnaire–Revised (SBQ-R).[10,11] The PHQ-4 has been validated as a screening tool for depression and anxiety in both general and primary-care populations. Participants with scores of three or more (out of six) on either the anxiety or depression subscales were considered to be at risk for these specific disorders. Overall PHQ-4 scores of 0-2 indicate no psychological distress, 3-5 indicate mild distress, 6-8 indicate moderate distress, and scores of 9-12 indicate severe psychological distress.[10,12] The SBQ-R is a tool that has been used to detect suicidality in both a general population and among patients with known, mental health disorders. A score of seven or greater was considered to identify individuals at risk of suicide.[11] When RAs identified a patient as being at high risk of suicide, they alerted the treating ED clinician to this information, and the clinician determined what immediate steps, if any, would be taken as a result.

Participants also provided information regarding the use and abuse of alcohol, tobacco, recreational drugs, and prescription drugs used for reasons other than prescribed. We defined binge drinking as five or more drinks in one sitting for men, and four or more for women. Additionally, patients were asked how important it was for providers to address problems related to both

mental health and substance abuse during their current ED visit (for example, "How important is it that today's emergency department visit address any mental health concerns you may have?"), and they could choose from the following responses: not important, minor importance, important, or very important.

The study instrument was assessed for content validity by a panel of individuals with expertise in urban health, barriers to healthcare access, ED care, and survey administration. One study author administered the survey during a pilot phase prior to beginning enrollment with no changes made to the survey instrument afterward.

Statistical Analysis

We estimated that a sample size of at least 800 participants would provide a 2% margin of error based on a 95% confidence interval for the detection of occult suicidality, assuming an estimated prevalence of 8% among patients within an urban ED population.[13] Study data were saved in a secure electronic database created using REDCap, and were analyzed in 2017.[14] Descriptive data are presented, including proportions, median with interquartile range, and mean with standard deviation. We performed no imputation for missing data, and we excluded from analyses cases with missing data, relying on the missing data on a pair-wise basis. We used chi-square testing to compare data between categorical variables. P values < 0.05 were considered statistically significant, and we did not adjust p values for the performance of multiple comparisons. We performed data analysis using SPSS v 20.0 (IBM Corp, Armonk, NY).

Table 1. Characteristics of patients (N=816) with low-acuity presentation to the emergency department who participated in mental health screening.

Patient characteristics	Frequency; N (%)
Sex	
Female	466 (57)
Age, median (IQR)	34 (26-49)
Race	
Black	397(49)
White	216 (27)
Other	181 (22)
Ethnicity	
Hispanic	220 (27)
Insurance status	
Private insurance	80 (10)
Medicare	98 (12)
Medicaid	442 (54)
Uninsured	107 (13)
Other/no answer	89 (11)
Has a primary care provider	588 (72)
Mental health history	
Depression	181 (22)
Bipolar disorder	66 (8)
Schizophrenia	19 (2)

IQR, interquartile range.

RESULTS

There were 14,571 low-acuity visits during the study period. Of these, 2,016 presented during approximately 400 two-hour enrollment windows and were screened for inclusion. From these potentially eligible patients, 328 were excluded: 195 did not speak English; 114 were intoxicated; nine were cognitively impaired; and 10 were prisoners. Of the remaining 1,688 eligible patients, 816 (48%) agreed to participate. Participants were diverse with respect to race, ethnicity, and insurance status, and 22% reported a past medical history of depression (Table 1).

Within this cohort, 27% of patients screened positive for anxiety, and 25% screened positive for depression, including 17% of those participants with no known history of depression. Evidence of moderate psychological distress was present in 9%, and severe psychological distress was present in another 13%. Eleven percent of all participants were found to be at significant risk of suicide (SBQ-R ≥ 7), and 5% of those with no history of depression or bipolar disorder were at risk of suicide. Race and sex were not associated with suicide risk, though risk of suicide was associated with a past history of depression (32% vs 5%, p < 0.001) or bipolar disorder (38% vs 9%, p <0.001 for both). Suicide risk was also associated with a reported history of heroin use (35% vs. 10%, p < 0.001) and cocaine use (32% vs. 10%, p = 0.001). Binge drinking monthly or more was also weakly associated with risk for suicide (15% vs 10%, p = 0.40).

Among participants at risk of suicide based on the SBQ-R, 35% felt that it was either important or very important for suicidal thoughts to be addressed during the ED visit (Table 3).

Table 2. Results of mental health screening using the SBQ-R for suicidality and PHQ-4 for psychological distress.

Survey Metric	N (%)
Suicidality (n = 802)	
SBQ-R Total score ≥7	89 (10.9)
Psychological Distress (n = 772)	
PHQ-4 Score 3-5 (Mild)	123 (15.2)
PHQ-4 Score 6-8 (Moderate)	74 (9.1)
PHQ-4 Score 9-12 (Severe)	105 (12.9)
PHQ-4 Anxiety Score ≥3	209 (25.6)
PHQ-4 Depression Score ≥3	196 (24.1)

SBQ-R, Suicide Behaviors Questionnaire-Revised; *PHQ-4,* Patient Health Questionnaire-4.

Thirteen percent felt that addressing suicidal thoughts in the ED was not very important, and 52% felt that it was not important at all. Of those subjects found to be at significant risk of depression 53% felt that it was important or very important for the ED visit to address mental health concerns, while 16% thought this was not very important and 31% thought this was not important at all. Among the 105 participants with severe psychological distress, 67 (64%) felt that addressing mental health concerns in the ED was important or very important.

Reported substance abuse was common within this cohort, with 23% of participants binge drinking alcohol monthly or more. About one-third (280, 34.5%) used tobacco products daily or almost daily. Twelve percent reported using recreational drugs monthly or more, including 6% who used these drugs daily or almost daily. Six percent reported abusing prescription drugs for reasons other than prescribed. Of the 179 participants with monthly binge alcohol drinking, just 31 (17%) thought that receiving assistance with substance abuse during the ED visit was important or very important. Of the 96 participants with monthly recreational drug use, 33 (34%) felt that addressing this issue in the ED was important or very important.

DISCUSSION

In this large cohort of ED patients with low-acuity chief complaints, we observed that a significant proportion of patients who presented with a chief complaint not suggestive of psychiatric disease had mental health concerns that were apparent on screening, including 11% with a significant risk of suicide. Between approximately one-third and two-thirds of these patients with evidence of significant psychiatric concerns were open to ED-based interventions targeting their mental health.

These results are consistent with prior studies describing the under-diagnosis of depression and other mental health disorders among ED patients,[15, 16] along with the presence of passive suicidal ideation among approximately 6%-12% of patients who are evaluated in the ED for non-psychiatric reasons.[5,6,13,17] The effectiveness of ED-based screening programs can be improved through the use of performance improvement methodologies, as well as careful training of the staff members who perform these screenings.[17] These methods are relatively resource-intensive, however, thus raising the question of whether screening every ED patient for suicidality is necessary.

In particular, patients with low-acuity complaints are often managed through ED triage and evaluation processes that are distinct from higher-acuity patients, resulting in their rapid evaluation and discharge that limits opportunities for careful mental health screening. Our results suggest that even among these lower-acuity patients, mental health screening may have value. However, perhaps due to the expectation that visits for low-acuity complaints would be both rapid and focused, a significant proportion of patients at risk for suicide, based on their SBQ-R score, indicated that they did not want to address mental health concerns during the ED visit. Significant additional work is needed to ensure that the benefits of screening justify the costs involved.

Before any widespread screening program is initiated, it is important to both confirm the existence of effective treatments such that the anticipated benefits of screening will outweigh anticipated harms, and to assess the resources required to achieve these outcomes. With respect to ED-based screening for suicidality there are a number of existing interventions that may be helpful in reducing the incidence of suicide among at-risk patients. These include linkage to specialist care, the development of a safety plan, and counseling about modifiable risk factors such as access to firearms.[18,19]

Table 3. Perceived importance of addressing psychiatric concerns among patients reporting mental health symptoms.

Mental health screening result	Not important at all	Not very important	Important	Very important
How important is it that today's Emergency Department visit address any suicidal thoughts or ideations you may have? N (%)				
Suicidal Risk (SBQ-R ≥7); n = 89	46 (52)	12 (13)	10 (11)	21 (24)
How important is it that today's Emergency Department visit address any mental health concerns you may have? N (%)				
Psychological Distress				
PHQ-4 Score 3-5 (Mild) ; n = 122[1]	53 (43)	16 (13)	24 (20)	29 (24)
PHQ-4 Score 6-8 (Moderate); n = 74	34 (46)	11 (15)	14 (19)	15 (20)
PHQ-4 Score 9-12 (Severe); n = 105	23 (22)	15 (14)	21 (20)	46 (44)
PHQ-4 Anxiety Score ≥3; n = 209	72 (34)	28 (13)	40 (19)	69 (33)
PHQ-4 Depression Score ≥3; n = 195[1]	60 (31)	31 (16)	40 (21)	64 (33)

SBQ-R, Suicide Behaviors Questionnaire-Revised; *PHQ-4,* Patient Health Questionnaire-4.
[1] One case excluded due to missing data.

However, very few studies have evaluated the long-term impact of these interventions on patient outcomes. For example, despite showing the feasibility of using a mobile crisis team to establish linkage to care among suicidal patients who are discharged from the ED, this intervention did not improve long-term symptom burdens.[20] Another recent study of patients with active or recent suicidal ideation showed that combining universal suicide-risk screening with interventions aimed at reducing suicidal behavior was associated with a decrease in suicide attempts at one year, suggesting that coupling screening with a defined intervention is more effective than screening alone.[21] Future studies are needed to explicitely assess the impact of mental health screening programs on patient-oriented health outcomes, such as suicide completion and symptom burden.

Additionally, we did not assess the resource burden required to effectively screen a non-targeted population of ED patients for mental health disorders, though this is another key question that ideally would have been addressed before widespread screening was implemented.[7] Relevant ED costs include staff time for screening, opportunity costs of screening during brief ED visits, time required to follow up on patients who screen positive, and the potential for increasing the length of stay when patients screen positive. Other relevant costs include the expense and limited availability of mental health resources that get devoted to those who screen positive, risks of false-positive screening, and potential harms to patients who are labeled as having a mental health diagnosis. These concerns are all particularly important when screening an untargeted population in which the disorder of interest is relatively uncommon, and when the effectiveness of subsequent interventions is not well established.

LIMITATIONS

This study is subject to several important limitations that should be considered when interpreting these results. First, participants were recruited from a single academic ED within the U.S. between 9 a.m. and 10 p.m. While most low-acuity patients present to EDs during daytime hours and our sample was diverse with respect to race, ethnicity, and access to healthcare, results from other populations may differ.[22] In particular, it is likely that patients presenting during nighttime hours with low-acuity complaints systematically differ from patients presenting during daytime and evening hours. Second, about half of the patients we approached for enrollment declined, possibly reflecting a combination of patient discomfort due to pain or other acute symptoms, as well as a limited tolerance for anything that might have increased the ED visit duration among low-acuity patients expecting rapid evaluation and discharge.

Therefore, it is likely that sampling bias impacted our observed results. For example, rates of occult mental health disorders may differ between respondents and non-respondents. Furthermore, even if rates of occult mental health disorders are similar between respondents and non-respondents, there may be differences between these groups in patients' willingness to report mental health symptoms. Also, compared to those patients who chose not to participate, study participants might have been more open to receiving ED-based interventions for mental health disorders not related to their chief complaint, which would have limited the utility of routine mental health screening among this population.

Additionally, we used the ESI triage system as applied by an experienced triage nurse to identify a low-acuity patient cohort. The admission rate of study participants was just 7%, which supports this assumption, though ESI is not perfect in this regard. We used the SBQ-R to assess suicidality, which has been validated to predict long-term suicidal behavior. While this instrument is one of several recommended by the Joint Commission for use as a screening tool, it has not been validated for use in predicting short-term suicide completion.[7] Similarly, our questions addressing the perceived importance of addressing mental health concerns have not been previously validated. Finally, while we determined the prevalence of occult mental health disorders among this patient cohort and assessed receptiveness to ED-based interventions aimed at addressing these issues, we did not explore either the effectiveness or the risks of any specific interventions. Both steps should be undertaken prior to implementing any intervention aimed at addressing these issues.

CONCLUSION

Among this cohort of ED patients presenting for non-psychiatric reasons with low-acuity chief complaints, a significant portion were at risk for suicidal behavior. Further, approximately one-quarter of patients screened positive for moderate to severe psychological distress. A substantial proportion of patients with mental health disorders unrelated to their chief complaints were open to addressing these disorders during the ED visit.

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Substance Use in Pregnant Women Using the Emergency Department: Undertested And Overlooked?

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Introduction: The objective was to determine if pregnant women visiting the emergency department (ED) are tested for substance use as frequently as non-pregnant women.

Methods: We captured all ED visits over a six-year period (2010-2016) from a single community hospital and identified women of childbearing age, defined for our study as 11-50 years old. We collected demographic data including age in years, ethnicity, body mass index, marital status, disposition, last encounter department, method of arrival, and day of week. An independent binary variable was created based on whether the woman was tested for alcohol or drugs (amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, opioids) during her visit. We then compared rates of testing for substance use by pregnancy status.

Results: We identified 61,222 ED visits by women of childbearing age (range 11-50, mean 30.5, standard deviation 9.6) over a six-year period from 2010-2016. Of the 57,360 non-pregnant women, 4.14% were tested compared to 1.04% of the 3,862 pregnant women tested with a relative risk of 0.25 (p<0.001, 95% confidence interval [CI] [0.183-0.341]). The most highly tested chief complaints for all women – psychiatric or substance use concerns – showed pregnant women were still 37% and 54% less likely to be tested, respectively (risk ratio [RR] 0.46, 95% CI [0.19-1.13]; RR 0.63, 95% CI [0.41-0.96]). Beyond pregnancy status, we found no significant interaction between patient demographics and substance use testing.

Conclusion: Pregnant women presenting to the ED were 75% less likely to be tested for drug or alcohol use than non-pregnant women. Our study showed only pregnancy status as a statistically significant variable in drug- and alcohol-screening rates when pregnant and non-pregnant patient chief complaints and demographics were compared. Increased attention to the screening of pregnant women for substance use may be necessary to provide adequate care and intervention to this population. [West J Emerg Med. 2018;19(3)579-584.]

INTRODUCTION

Alcohol and drug use among women of childbearing age represents an increasing burden to society and healthcare providers across the United States. Substance use during pregnancy is associated with increased rates of obstetric complications, fewer prenatal visits, and poor perinatal outcomes.[1-4] Fetal alcohol spectrum disorder (FASD), a serious consequence of prenatal alcohol exposure, is the leading preventable cause of birth defects and neurodevelopmental disability in the U.S. It often reoccurs within sibships and the

mortality among birth mothers of children diagnosed with an FASD is increased by nearly 39-fold.[2,5,6] Recent data demonstrate that 11.9% of non-pregnant women and 5.3% of pregnant women age 15-44 reported illicit drug use in November, 2016.[1] Alcohol use at levels meeting criteria for binge or heavy drinking was reported by 23.7% of non-pregnant women and 2.8% of pregnant women.[1]

According to the National Institute on Drug Abuse, of the more than 130 million visits to emergency departments (ED) in 2009, 2.1 million (2.73%) were for drug abuse.[7] From 2004 to 2009 ED visits for non-medical use of drugs increased 98% (nearly 20% per year), with 32% of patients reporting concurrent alcohol use.[7] In 2005 the National Alcohol Survey found that 24% of individuals presenting to the ED reported high-risk drinking behaviors.[8,9]

Approximately 50% of pregnancies in the U.S. are unplanned, with fetal first trimester exposure rates of 56% for all women and 78.9% for women with recent alcohol dependence.[10] While the majority of women cease or reduce alcohol consumption during pregnancy, in the U.S. alone every year around 80,000 women report drinking during all three trimesters.[11]Women meeting criteria for a substance use disorder used ED services 57% more frequently than women who did not have a substance use disorder and were hospitalized 67 % more frequently.[1] Given the high prevalence of substance use in the patient population most using ED services, this setting presents a unique opportunity to screen a high-risk population for substance use. However, limited data exist to examine the nuances of the screening process in the ED for substance use. In this study, we compared rates of screening for substance use among pregnant and non-pregnant women seeking care at an ED facility.

Population Health Research Capsule

What do we already know about this issue?
In November 2016, 11.9% of non-pregnant women reported illicit drug use and 23.7% reported heavy drinking compared to pregnant women with 5.3% reporting drug use and 2.8% heavy drinking.

What was the research question?
Do emergency departments appropriately screen all women for substance abuse? Does pregnancy status modify screening rates?

What was the major finding of the study?
Pregnant women were screened for substance abuse only one-fourth as often as non-pregnant women.

How does this improve population health?
Improving screening for pregnant women may improve detection of substance abuse and allow for intervention during pregnancy and reduce risk for exposure during the next pregnancy.

METHODS

The project was approved by the Altru Health System Institutional Review Board and the University of North Dakota Institutional Review Board. We captured all ED records of women from a single community hospital for the years 2010 to 2016 (n=61,222). A woman was considered pregnant if her pregnancy status was recorded as "pregnant." All other women were classified as not pregnant. Demographic data included age in years, race/ethnicity (White, American Indian/Alaskan Native, Hispanic, Black, and Other, which included Asian, Chinese, Filipino, Korean, Hawaiian, Pacific Islander, Nepalese, Samoan, Somalian, Vietnamese and unknown or refused), marital status (married, single, "Other," which included life partner, significant other, fiancé, divorced, legally separated, widowed, other and unknown), and body mass index (BMI). We categorized data on how the woman arrived at the ED as either ambulatory or assisted (crutches/walker, wheelchair, cart/stretcher, or carried).

We created a dependent binary variable based on whether the woman was tested for alcohol or drugs during her ED visit or not tested. We examined the electronic medical record and the lab record for any test for substance use that was ordered or completed by the lab. Testing modalities included blood, urine, hair, or breathalyzer readings. We included testing for amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, opioids, and alcohol.

The 399 unique chief complaint ICD-9 codes were then further grouped into 20 categories (Table 2). The last department used by the woman was categorized as ED, urgent care, or other (which included cardiac, ICU, obstetrics, oncology, orthopedics, surgical, and women's and children's units). Their dispositions were combined into two groups, internal (admitted, sent to labor and delivery, psychiatric care or transferred) or external (deceased, discharged, left against medical advice before or after triage, or referred to observation).

Statistical Analysis

We compared the association between pregnancy status and drug/alcohol testing using the chi-square statistic with relative risk and 95% confidence intervals (CI). This association was assessed for the demographic covariates. The risk of drug/alcohol testing for pregnant woman relative to non-pregnant women was produced for levels of other variables using relative risk and 95% CIs. We tested interactions between pregnancy status and the

demographic variables using the Breslow-Day test for homogeneity in odds ratios. Logistic regression was then used to test for interactions between pregnancy status and demographics or ED visit characteristics. We used SAS version 9.4 for analyses.

RESULTS

We identified 61,222 visits by women age 11-50 years over the time period of 2010 to 2016. Table 1 summarizes the study subjects' demographic information. The mean age was 30.5 (standard deviation [SD] 9.6 years) ranging from 11-50. We located data on BMI for 26,177 women with a mean value of 30.4 (SD 8.6) ranging from 11.5 to 85.9. The majority of women (78.5%) were White, 12% were American Indian / Alaska Native, 4.3% were Hispanic, and 2.4% were Black / African American. In the sample 3,862 (6.7%) were reported to be pregnant and 57,360 (93.3%) were not pregnant. Based on recorded pregnancy status, 4.14% of the 57,360 non-pregnant women were tested for drug or alcohol use and 1.04% of the 3,862 pregnant women were tested. The relative risk (RR) of a pregnant woman being tested was one-fourth that of a non-pregnant woman (RR=0.25; 95% CI [0.18 to 0.34]; p<0.001).

To check for effects of other variables that might have influenced this risk, we first tested the data using demographic variables age, BMI, race, marital status, and day of the week. While there was some variation, we found no significant interaction between the demographics and pregnancy associated with testing (Table 1). The RR for being tested was somewhat lower for single women, Whites, and on weekends and Thursdays. For both populations, not being married increased the risk of being tested but this was significant only for non-pregnant women (odds ratio=1.6) (95% CI [1.4 to 1.9]). We examined day of the week because in our community substance use increases on weekends.

Psychiatric concerns and substance use were the two most commonly tested presenting complaints (Table 2). Pregnant women presenting with substance use had a risk of being tested that was just less than half that of a non-pregnant woman (RR=0.46) (95% CI [0.19 to 1.13]). Women who were pregnant and presented with psychiatric complaints had a risk two-thirds of non-pregnant women (RR=.63) (95% CI [0.41 to 0.96]). Additional data on differences between groups by presenting complaint is shown in Table 2. The patient's final disposition status showed some influence on testing risk. Based on pregnancy status, 30.05% (n=1,376) of the 4,579 non-pregnant women who were admitted to the ED were tested for drugs or alcohol, while only 9.29% (n=21) of the 226 pregnant women were tested. Of the 50,413 non-pregnant women discharged, 1.43% (n=723) were tested for drugs or alcohol, while only 0.56% (n=18) of 3,243 pregnant women discharged were tested. Additional detail about patient disposition status is shown in Table 3.

DISCUSSION

Our study found that pregnant women presenting to the ED were 75% less likely to be tested for substance use than non-pregnant women. Even among the most-tested presenting complaints for all women (psychiatric or substance use concerns),

Table 1. Patient characteristics of women upon arrival to the emergency department.

Characteristic	Non-pregnant	Tested	%	Pregnant	Tested	%
Pregnancy status, n (%)	57,360	2,377	4.14	3,862	40	1.04
Age, n (mean)	54,983 (30.77)	2,377	31.58	3,822 (25.96)	40	27.25
BMI, n (mean)	23,113 (30.53)	1,613	28.71	1,367 (30.11)	24	27.22
Race, n (%)						
White	45,291	1,874	4.14	2,742	22	0.805
AI/AN	6,886	354	5.14	459	12	2.61
Hispanic	2,431	78	3.21	193	1	0.52
Black	1,283	31	2.42	203	5	2.46
Other	1,469	40	2.72	265	0	
Marital status, n (%)						
Married	19,249	532	2.76	1,830	15	0.82
Single	29,475	1,391	4.72	1,728	20	1.16
Other	8,636	454	5.26	304	5	1.64
Arrival, n (%)						
Ambulatory	51,210	1,360	2.16	3,505	22	0.63
Assisted	5,011	848	16.92	249	14	5.62

BMI, body mass index; *AI/AN*, American Indian/Alaska Native.

Table 2. Presenting complaints for 61,222 women attending the emergency department from 2010 to 2016. The women were grouped by pregnancy status (pregnant and non-pregnant) to compare proportions tested for substance use.

Presenting complaint	Non-pregnant	Tested	%	Pregnant	Tested	%
Psychiatric, n (%)	1744	848	48.62	49	15	30.61
Substance use, n (%)	695	563	81.01	8	3	37.50
Other	n	n	%	n	n	%
Gastrointestinal	11980	132	1.10	871	5	0.57
Musculoskeletal	11519	80	0.69	384	3	0.78
Neurologic	6347	318	5.01	407	6	1.47
Immunologic	3835	16	0.42	234	0	0
Trauma	3472	154	4.44	166	4	2.41
Cardiac	2421	85	3.51	94	0	0
Oral	2314	1	0.04	155	0	0
Respiratory	2195	41	1.87	134	1	0.75
Genitourinary	2089	7	0.34	93	0	0
Gynecologic	1290	2	0.16	592	0	0
Treatment	1575	27	1.71	61	0	0
Dermatologic	1348	4	0.30	81	0	0
Ear	1137	0	0	77	0	0
Ocular	773	0	0		35	0
Pregnancy	187	0	0	136	3	2.21
Hematologic	150	4	2.68	8	0	0
Endocrine	140	13	9.29	5	0	0
Miscellaneous	1660	76	4.58	88	0	0
NA	489	6	1.23	184	0	0

pregnant women were still 37%-54% less likely to be tested. These data may suggest a relatively lower index of suspicion for substance use among pregnant women seeking care in the ED. This difference by pregnancy status was present even for women with similar presenting complaints and demographics in the ED.

While no prophylactic treatment exists at this time, early screening and counseling is the best practice to support women in decreasing the risk of the serious consequences associated with prenatal substance exposure.[12] Identification of prenatal alcohol exposure is of particular importance as the long-term implications of alcohol exposure for the fetus have shown significant consequences in comparison to other substance exposures.[3,13-15] With fetal first-trimester alcohol exposure rates of 56% for all women and 78.9% for women with recent alcohol dependence,[10] the ED presents a unique opportunity to address a population of women with a greater than average incidence of alcohol and drug use. The opportunity to provide education and intervention at this stage is especially compelling among women of low socioeconomic status who are seen in the ED more frequently than in primary practice.[16] Women who received treatment based on positive drug/alcohol screening results have been shown to subsequently have fewer future ED visits, injuries and hospitalization.[4,17]

LIMITATIONS

Extrapolation of the results of this study is limited due to the small sample of women – pregnant or non-pregnant – tested in the ED for drugs and alcohol. An unknown portion of women with substance use may have been identified by history or observation and were not in need of additional testing. Additionally, in accordance with regional demographics the sampled population is largely White/Caucasian, which may limit the generalizability of this data to other populations. The power to detect significant risk differences between the two groups (when psychiatric concerns were the presenting complaint) for this sample size was 0.72 and when substance use was the presenting complaint the power was 0.82. Power for other diagnoses (prevalences > 0% for both groups) was low and ranged from 0.07 to 0.26.

While substance use does not equate to substance abuse, any use of alcohol or illicit drugs during pregnancy is contraindicated. Although not a factor in these data, a negative test does not rule

Table 3. Patient disposition from emergency department visits for 61,222 women seen from 2010 to 2016. The women were grouped by pregnancy status (pregnant and non-pregnant) to compare proportions tested for substance use.

Characteristic	Non-pregnant	Tested	%	Pregnant	Tested	%
Discharged, n	50,413	723	1.43	3,243	18	0.56
Admitted, n	4,579	1,376	30.05	226	21	9.29
Other	n	n	%	n	n	%
LWBS after triage	582	4	0.69	46	0	0
AMA	233	28	12.02	15	0	0
Refer to observation	207	50	24.15	7	0	0
Send to psych	171	122	71.35	1	0	0
Eloped	104	8	7.69	7	0	0
LWBS before triage	95	0	0	6	0	0
Transferred	81	37	45.68	3	1	33.33
Send to L&D	5	0	0	44	0	0
Deceased	5	0	0	0	0	0

LWBS, left without being seen; *AMA*, against medical advice; *L&D*, labor and delivery.

out substance use in all women. The rates of testing in other ED services across the U.S. may differ. The data we collected do not allow for determination as to why clinicians select non-pregnant women for substance use screening 75% more often than pregnant women. This is an area for further research.

CONCLUSION

The use of alcohol, prescription drugs, and illicit drugs is an important and growing public health problem. The ED presents a unique opportunity to address, intervene, and offer education to a population of women with a greater than average incidence of alcohol and drug use. Our research shows that increased attention to substance use in ED settings is warranted and that pregnancy status should not allay clinician concerns about substance use.

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Effect of an Educational Intervention on Medical Student Scripting and Patient Satisfaction: A Randomized Trial

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Introduction: Effective communication between clinicians and patients has been shown to improve patient outcomes, reduce malpractice liability, and is now being tied to reimbursement. Use of a communication strategy known as "scripting" has been suggested to improve patient satisfaction in multiple hospital settings, but the frequency with which medical students use this strategy and whether this affects patient perception of medical student care is unknown. Our objective was to measure the use of targeted communication skills after an educational intervention as well as to further clarify the relationship between communication element usage and patient satisfaction.

Methods: Medical students were block randomized into the control or intervention group. Those in the intervention group received refresher training in scripted communication. Those in the control group received no instruction or other intervention related to communication. Use of six explicit communication behaviors were recorded by trained study observers: 1) acknowledging the patient by name, 2) introducing themselves as medical students, 3) explaining their role in the patient's care, 4) explaining the care plan, 5) providing an estimated duration of time to be spent in the emergency department (ED), and 6) notifying the patient that another provider would also be seeing them. Patients then completed a survey regarding their satisfaction with the medical student encounter.

Results: We observed 474 medical student-patient encounters in the ED (231 in the control group and 243 in the intervention group). We were unable to detect a statistically significant difference in communication element use between the intervention and control groups. One of the communication elements, explaining steps in the care plan, was positively associated with patient perception of the medical student's overall communication skills. Otherwise, there was no statistically significant association between element use and patient satisfaction.

Conclusion: We were unable to demonstrate any improvement in student use of communication elements or in patient satisfaction after refresher training in scripted communication. Furthermore, there was little variation in patient satisfaction based on the use of scripted communication elements. Effective communication with patients in the ED is complicated and requires further investigation on how to provide this skill set. [West J Emerg Med. 2018;19(3)585-592.]

INTRODUCTION

The medical community has embraced the importance of sound communication in the physician-patient relationship. Effective communication has been associated with improved patient outcomes[1,2] and patient satisfaction.[3] Patient satisfaction, in turn, has become an important benchmark for many hospital systems.

Communication skills are difficult to teach, implement, and evaluate. Recent advancements in undergraduate medical curricula have sought to improve communication skills.[4-7] Some medical schools have recognized communication as a competency to further emphasize development of this important skill.[8] Despite these recent advancements, there is still a need for improvement. Research suggests that medical students, likely more focused on expanding their medical knowledge, under-appreciate the importance of communication skills in the practice of medicine.[9]

Healthcare consultants have suggested scripting as one method to improve communication with patients. Scripting has previously been shown to have a positive impact on patient satisfaction[10,11] and elopement rates[12] from the emergency department (ED). We thus undertook a previous pilot study to assess the association of scripted communication elements with patient satisfaction in the ED, an environment that presents a unique set of communication challenges, especially for novice learners.[13]

In the pilot study, we chose to use a modified version of the Studer Group's AIDET® mnemonic to teach scripted communication elements to medical students rotating through the ED. The mnemonic reminds the provider of simple communication elements: acknowledging the patient by name, introducing themselves by name, providing an expected duration, and explaining the steps in the patient's care plan.

Our pilot study found that medical students use these targeted communication elements inconsistently, but that their use was associated with improved patient satisfaction. The low rate with which medical students used basic communication skills, such as acknowledging the patient by name, confirmed the need for additional education in this area.[13] Based on this preliminary data, we implemented an educational intervention emphasizing scripting to improve communication.

The objectives of this study were to measure the use of targeted communication skills after a refresher educational intervention as well as to further clarify their relationship with patient satisfaction. We hypothesized that students who received the refresher training would be more likely to use scripted communication and that this would be associated with higher patient satisfaction scores.

Population Health Research Capsule

What do we already know about this issue?
Effective communication in the physician-patient relationship improves patient outcomes and patient satisfaction. Scripting is a suggested method to improve these skills.

What was the research question?
Does an educational intervention improve medical student use of communication skills and improve patient satisfaction?

What was the major finding of the study?
Patient satisfaction did not improve with the use of scripted communication or the educational intervention.

How does this improve population health?
Improving communication within the physician-patient relationship is a multifactorial construct and cannot rely on scripted communication elements alone.

METHODS

Design and Setting

This was a randomized controlled trial conducted between July 2014 and April 2015 in the EDs of two urban teaching hospitals affiliated with the Indiana University School of Medicine. The Sidney and Lois Eskenazi Hospital (Hospital A) is a county hospital with approximately 100,000 patient visits annually. Indiana University Health Methodist Hospital (Hospital B) is a tertiary referral center, also with approximately 100,000 patient visits annually. The study was approved by the Indiana University Institutional Review Board.

Participants

Fourth-year medical students were enrolled on a volunteer basis and provided written consent at the orientation to their emergency medicine (EM) clerkship, a required 4-week clinical course at Indiana University School of Medicine. There was no incentive for participation. Study information was given and consent was obtained by an EM resident who was not responsible for their grade. Students participating in the study were informed that they would be observed while on shift in the ED but were otherwise kept blind as to what was being observed.

Patients who could provide verbal consent (>18 years old or had a parent present to consent) in English or Spanish and who were evaluated by a participating medical student were given the option to participate in a patient satisfaction survey. Surveys were not administered to patients with the following conditions: incarcerated, altered mental status, psychiatric

chief complaint (suicidal ideation, homicidal ideation, aggressive behavior, depression, anxiety, or psychosis), or critical illness (unstable vital signs, respiratory distress, or triaged to the high acuity area of the ED).

Intervention and Randomization

All students at Indiana University School of Medicine participate in a brief session introducing scripted communication prior to starting their third-year clinical rotations (13-20 months prior to participation in our study). For this study, students participating in the clerkship each month were block randomized by rotation site, using a block size of six, to receive additional refresher training on scripted communication (intervention group) or no additional training (control group). The randomization schedule is shown in Table 1. The refresher training consisted of a 10-minute video presentation about scripted communication provided on the first day of the rotation. This presentation carried the logo of the respective healthcare system and was shown to the students during their clinical site orientation rather than at the course orientation to keep students blind regarding the association of the presentation with the study and the clerkship. Students randomized to the intervention were also provided a handout emphasizing the importance of scripted communication. The control group was not provided with these materials prior to their clerkship, but they were provided with this education at the conclusion of the study.

Outcome Measures

Six communication elements were previously chosen for observation as outlined in our pilot study.[13] The elements are shown in Table 2. They are based on AIDET®, a patient communication framework by The Studer Group. We assessed patient satisfaction through the same four-part survey used in that study (Appendix A). The primary outcome of interest was change in the frequency of "yes" responses to questions about likelihood to return to the ED or likelihood to refer a loved one to the ED. Secondary outcomes of interest included frequency of use of each of the six elements, improvement in the patient's perception of the student's overall communication skill, and improvement in score on the Communication Assessment Tool (CAT). The CAT is a previously validated instrument that assesses interpersonal and communication skills using a 15-item survey with a five-point Likert scale (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent).[14] We modified the survey by removing one question, "The doctor's staff treated me with respect," to keep focus on the student-patient interaction rather than the patient's overall experience.

Table 1. Randomization by site of med students participating in research on scripted communication with patients.

	Hospital A	Hospital B
July 2014	Intervention	Intervention
August 2014	Intervention	Control
September 2014	Control	Intervention
November 2014	Control	Control
January 2015	Intervention	Control
February 2015	Control	Intervention

Table 2. Observed communication elements.

Did the student acknowledge the patient using the patient's name?
Did the student introduce himself/herself by name?
Did the student explain his/her role as a medical student?
Did the student explain some of the steps (including diagnostic testing, medication administration, or observation) that would be used to address the patient's complaint?
Did the student explain that additional providers (such as a resident or attending physician) would also be evaluating the patient?
Did the student offer an estimated duration of time that the patient would spend in the ED?†

†For estimated duration, a general statement of time (e.g. ,"overnight" or "a few hours") was considered acceptable; a specific number was not required.

Observers and Study Procedure

Four observers, all students in the pre-medical program at Indiana University-Purdue University Indianapolis, were trained by study investigators to navigate participating EDs and record elements of patient-student interactions on a data collection form. Data collection forms included whether or not the student used each of the six communication elements as well as whether the student performed 17 additional "dummy" data points, which were chosen by study investigators as actions commonly performed by students. These were added to keep the student and observers blind to what elements were of interest for the study. Refer to Appendix B for the complete data collection sheet with all "dummy" data points.

As part of their training, the four observers viewed 31 simulated video recordings of interactions between a patient and a provider and marked whether the provider used each of the six communication elements of interest as well as whether they performed each of the 17 "dummy" data points. Responses for each of the observers were compared to "criterion standard" responses from a fifth observer, the Masters of Public Health student who had performed all observations in our previous study.[13] We calculated agreement of the observers with the criterion standard as kappa and percent agreement.

Each month, the four observers were scheduled for a variety of shifts across multiple days and times. For each shift, the observer was assigned to follow 1-3 participating medical

students. Observers followed their assigned students and completed the data collection sheet for each patient encounter.

After the student-patient encounter but before discharge or admission, the observer returned to the patient's room and verbally administered the patient satisfaction survey. At this time, the observer presented the patient with a picture of the student and stressed that the questions applied specifically to the patient's interaction with that student and not other aspects of the patient's care in the ED. The satisfaction survey was done without the students' knowledge.

Following each shift, all data from the data collection forms and associated patient satisfaction surveys were stored in RedCap.[15] REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies.

Power Analysis

The length of this study was determined by the usage of communication elements in our pilot study as well as data provided by hospital administration on expected baseline patient satisfaction. We estimated from this data that the baseline rate of "yes" responses would be between 50-60% for Hospital B and 30-40% for Hospital A. We recognized this value would fluctuate month to month, but the randomized design and the fact that intervention and control subjects would be studied in back-to-back months would help control for that variance. With 20 students rotating at the study sites per month and >100,000 visits annually at each ED, preliminary power calculation estimates with α=0.05, an effect size of 10%, change in score from 45% to 55% between groups and N=750 encounters per group yielded a power of 97%.

Data Analysis

We used chi-square test ($p<0.05$ significant) to test the bivariate association of communication elements with likelihood to return, likelihood to refer, and excellent overall communication skill. Two-tailed t-tests and chi-square tests were used to determine if student characteristics differed by randomization group. We used chi-square tests to determine if the dichotomous items (each of the six communication elements, referral to ED, return to ED, and excellent overall communication) differed by randomization group, while two-tailed t-tests were used to determine if the overall CAT score differed by the intervention.

Since multiple assessments were done on each student, we also performed mixed effects regressions (logistic for dichotomous outcomes and linear for continuous outcomes) to account for repeated measures across students. For these models, intervention was included as the only fixed effect, while a random effect for student was included to account for repeated measurements across students. Additionally, we ran models adjusting for student characteristics (gender, age, intended specialty, and rotation site). Results were similar; therefore, we only report those results with no adjustment. All analyses were performed using SAS v9.4.

RESULTS

During the simulated encounters used for observer training, there was high level of agreement between the four observers for each of the six primary data points (Appendix C).

Demographics

Eighty medical students were observed during the eight-month study period. One student declined to participate. Forty-five of the students were male. Twenty-nine planned to pursue emergency medicine (EM), and 51 planned to pursue other specialties (including anesthesiology, family medicine, general surgery, internal medicine, neurology, neurosurgery, obstetrics-gynecology, otolaryngology, orthopedic surgery, pathology, psychiatry, radiology, other surgical specialty, other non-surgical specialty, and multiple/unsure). There was no statistically significant difference between the groups in terms of the percentage of students pursuing a specialty in EM ($p = 0.062$). Four hundred seventy-four medical student-patient encounters were observed (231 in the control group and 243 in the intervention group). All observations that were begun were completed. Table 3 provides additional characteristics of the observed students.

Communication Element Use

Data for the use of communication elements in the control and intervention groups is shown in the Figure. The most frequently used element in both the control and intervention groups was the student introducing himself or herself by name, which occurred during 96.1% and 97.9% of encounters in the control and intervention groups, respectively. The least frequently used element was providing the patient with an expected duration of stay, which occurred during 11.3% and 13.1% of encounters in the control and intervention groups, respectively.

Table 3. Characteristics of med students who participated in an eight-month study of patient satisfaction with student communication.

	Control (n=40)	Intervention (n=40)	P value
Site			1.000
% Hospital A (n)	55.0 (22)	55.0 (22)	
% Hospital B (n)	45.0 (18)	45.0 (18)	
% Male (n)	52.5 (21)	60.0 (24)	0.652
% Emergency medicine (n)	25.0 (10)	47.5 (19)	0.062
Mean age (SD)	26.6 (2.6)	26.6 (1.6)	0.628

SD, standard deviation.

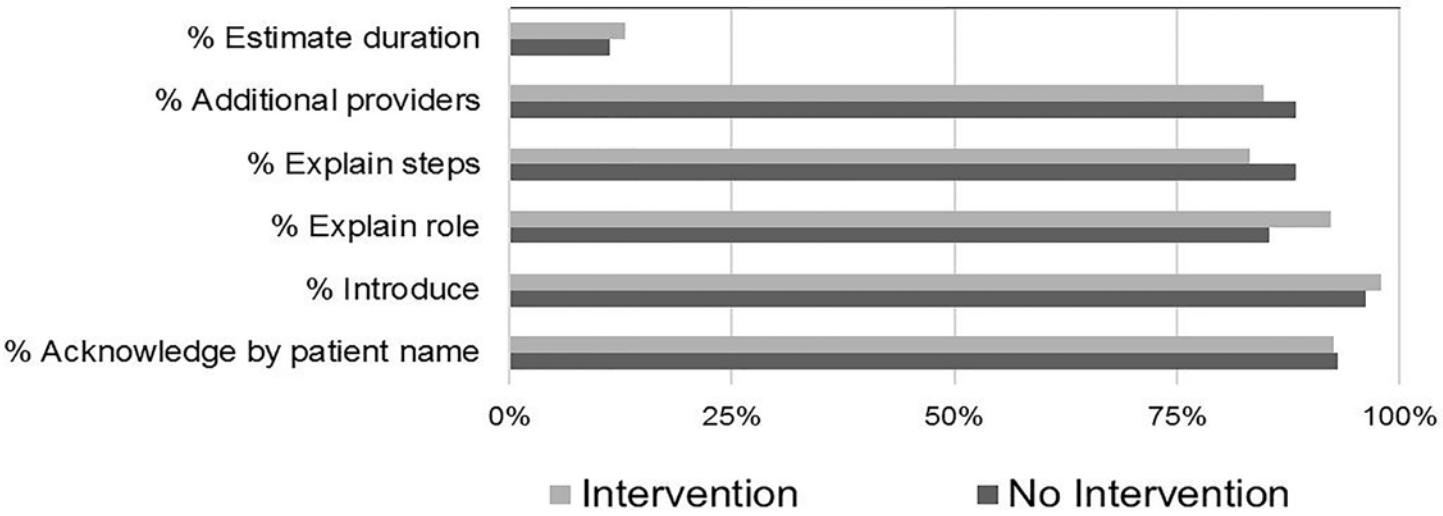

Figure. Rate of communication element use by group.

Comparative Data

Table 4 displays the association between each of the six communication elements and patient satisfaction outcomes. Explaining steps in the care plan was associated with an increased likelihood that the patient would give the student an "excellent" rating in overall communication skills. Otherwise, there was no statistically significant association between element use and patient satisfaction.

Table 5 shows the association of the outcome measures with placement in the control or intervention groups. There were no statistically significant associations between group and outcome measures. The intervention group did receive a slightly, but not statistically significant, higher frequency of "yes" responses to the questions about likelihood to return and to refer, a higher percentage of excellent ratings in overall communication skill, and a higher mean score on the CAT.

DISCUSSION

Our previous study demonstrated that medical student use of specific communication elements was associated with increased patient satisfaction but that medical students use these elements inconsistently.[13] Additionally, baseline medical student use of what may be considered the most basic of communication elements – such as acknowledging the patient by name – was surprisingly low (61%) in our previous study. We therefore developed and tested an educational intervention in an attempt to increase student use of these communication elements and further explore the association of these communication elements with patient satisfaction. In contrast to our previous results, the current study found no increase in patient satisfaction with our intervention and little association between use of scripting and patient satisfaction. The single significant association between the intervention group and use of the explaining role element was possibly due to chance given the number of outcomes analyzed and lost significance in the mixed-effects model.

Interestingly, baseline medical student (non-intervention) use of all communication elements in this study was much higher than in our previous study. Such a high baseline use of scripting may have contributed to the failure of the intervention to increase usage above that baseline rate. The reason for this increased utilization is unclear. To our knowledge, medical students did not receive any new formalized communication training in comparison to the previous study group, and observer training was also unchanged. It is possible that increased emphasis on communication throughout the medical school has resulted in improved modeling of good communication by faculty and teachers, or that medical student admissions processes have adapted to address communication skills among those accepted to the school. Additionally, the higher than anticipated baseline use of elements certainly affected the power of our study as we used much lower rates in our power analysis.

Our previous study found a strong association between use of several of the communication elements and increased rates of patient satisfaction as measured by our selected outcomes. The current study did not confirm this association. Only one element-outcome pair, "Explain-Overall Communication Skill" maintained statistical significance in this study. With 18 element-outcome pairs, it is possible that this single association occurred by chance. However, the fact that this "Explain-Overall Communication Skill" pair was also significant in our pilot study raises the possibility that this represents a result of the intervention rather than a chance event.

Table 4. Association of element use with patient satisfaction outcomes.

	Student encounter would make patient choose ED again (%)	Student encounter would make patient refer a loved one to the ED (%)	% Rate student's overall communication skill = 5 (Excellent)
Student did not acknowledge patient by name (n=34)	91.2	91.2	76.5
Student acknowledge patient by name (n=440)	91.5	96.1	85.9
P-value	0.320	0.194	0.193
Student did not introduce themselves by name (n=14)	100.0	100.0	85.7
Student introduced themselves by name (n=460)	94.8	95.6	85.0
P-value	0.796	0.903	0.928
Student did not describe role as a medical student (n=53)	96.2	96.2	84.9
Student described role as a medical student (n=422)	94.8	95.7	85.1
P-value	0.657	0.868	0.995
Student did not explain any steps in care plan (n=67)	95.5	95.5	73.1
Student explained some steps in care plan (n=403)	94.8	95.8	86.8
P-value	0.802	0.923	0.010
Student did not explain other providers would see patient (n=64)	95.3	95.3	82.8
Student explained other providers would see patient (n=411)	94.9	95.9	85.4
P-value	0.887	0.840	0.578
Student did not provide estimated duration (n=410)	94.6	95.4	86.1
Student provided estimated duration (n=57)	96.5	98.3	77.2
P-value	0.559	0.342	0.059

ED, emergency department.

Table 5. Association of intervention with patient satisfaction outcomes.

	No intervention (n=231)	Intervention (n=243)	P value	Mixed effects P-value*
% Acknowledge by patient name (n)	93.1 (215)	92.6 (225)	0.839	0.858
% Introduce (n)	96.1 (223)	97.9 (237)	0.244	0.318
% Explain role (n)	85.3 (198)	92.2 (224)	0.018	0.304
% Explain steps (n)	88.4 (205)	83.2 (198)	0.109	0.453
% Additional providers (n)	88.4 (205)	84.8 (206)	0.252	0.537
% Estimate duration (n)	11.3 (26)	13.1 (31)	0.558	0.647
% Return to ED (n)	94.4 (219)	95.5 (232)	0.592	0.595
% Refer friend to ED (n)	94.8 (220)	96.7 (235)	0.308	0.315
% Overall skill excellent (n)	82.3 (191)	87.7 (213)	0.104	0.110
Mean # CAT items excellent (SD)	12.3 (3.3)	12.7 (2.8)	0.184	0.238

ED, emergency department; *SD,* standard deviation.
* Mixed effect model only contained a fixed effect for intervention group and a random effect for student.

The other statistically significant associations found in the pilot study lost their significance in the current study. Two of the significant associations from the pilot study, the "Acknowledge-Refer" and "Acknowledge-Overall Communication Skill" pairs showed a small trend toward a positive association in the current study. It is possible that significance was lost due to much higher element use across the board, making it more difficult to show a difference.

In the current study, patient satisfaction scores were not significantly improved in students randomized to our intervention. This is not surprising given the failure of the intervention to significantly increase student use of most of the scripted elements that were emphasized. Our intervention was brief, and it is possible that a more robust intervention might have increased the use of scripted elements. However, it is still unknown if this would have had a positive effect on patient satisfaction. Even if there is some effect of the use of scripted communication elements on satisfaction, our current results suggest that the magnitude of this effect seems to be small.

The most likely explanation for the failure of this study to show an association between the selected scripted communication elements and patient satisfaction is that improving patient satisfaction is a multifactorial construct and the contribution of adding scripted communication elements is very small. Using scripted communication as a strategy to improve patient satisfaction is only a small piece of a much larger puzzle. Scripted communication may help providers remember a baseline level of communication, and this study does not indicate that initial training in scripted communication is not valuable. However, our study indicates refresher training in scripting itself is not enough to improve communication beyond a baseline level. The effect of refresher training and of scripted communication in general may also be influenced by experience and level of training, and it is possible that different results would be obtained with different levels of providers. Future research should focus beyond a simple communication checkbox. Perhaps there would be benefit with interventions that help providers better understand the patient's perspective, experience, and expectation.

LIMITATIONS

There were several limitations to this study. The study group consisted of a sample of medical students from a single medical school. While we attempted to blind the students to the nature of the study, the Hawthorne effect resulting from the knowledge that they were being observed may have contributed to increased use of all communication elements in both groups, limiting our ability to show a difference between groups. Also, while we took measures to avoid the intervention group influencing the control group (such as holding the intervention at clinical site orientation rather than the clerkship orientation), there is no guarantee that the groups did not communicate about the intervention.

Additionally, the study is limited by the lack of explicit testing of the validity of the outcome measures. The patient satisfaction survey is similar to actual surveys that are widely used in hospital systems like ours, and the CAT tool has been previously validated for other purposes. However, both tools were modified for the purposes of our study, which could threaten their validity. Finally, although we stressed to the patient that the survey pertained only to their encounter with the student, it is possible that other aspects of their visit – including interactions with other providers – influenced survey results. It is also likely that other unmeasured verbal and non-verbal aspects of communication may have influenced results. We were also not able to control medical student exposure to other forms of communication education and did not examine medical student retention of the information covered during our education intervention.

CONCLUSION

We hypothesized that an educational intervention to increase use of scripted communication elements would result in increased patient satisfaction. Unfortunately, our intervention did not result in any increase in either use of scripting by students or patient satisfaction. Additionally, this study failed to confirm earlier findings of an association between scripted communication elements and patient satisfaction. Communicating effectively with patients is likely much more complex than using a sample of scripted communication elements, and further research on optimizing patient-provider communication is urgently needed.

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Scholarly Tracks in Emergency Medicine Residency Programs Are Associated with Increased Choice of Academic Career

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Introduction: Career preparation in residency training is not standardized. Scholarly tracks have emerged in emergency medicine (EM) residencies to allow specialized training in an area of focus. The characteristics of these tracks and their value and impact on resident career choice are unknown. We aim to describe the current state of scholarly tracks in residency training programs and their association with pursuit of an academic career.

Methods: Program leaders at EM training programs completed an online survey consisting of multiple-choice items with free-text option. Additionally, participants completed a matrix of dropdown items identifying the immediately chosen post-residency position and applicable track of each member of their graduating class. Descriptive statistics were calculated and reported for multiple-choice items. We performed comparative statistics using chi-squared and Wilcoxon rank-sum tests. Free-text responses were analyzed using a thematic approach.

Results: 113/157(72%) programs participated, 51 with and 62 without tracks. Tracks were more common in four-year programs (odds ratio [OR]=4.8;[2.0-11.9]) and larger programs (chi-sq, p=0.001). Perceived benefits of tracks from programs with them included advanced training (46/50; 92%), career guidance (44/50; 88%), mentorship (44/50; 88%), and preparation for an academic career (40/50; 80%). Residents often participated in a single track (37/50; 74%) usually during their later residency years. Programs with tracks were more likely to graduate residents to an academic career, OR 1.8;[1.3-2.4].

Conclusion: This study describes the current characteristics and perceptions of scholarly tracks in EM residencies. Scholarly tracks are associated with an academic position immediately following residency. The results of this study may inform the development and use of scholarly tracks in residency training programs. [West J Emerg Med. 2018;19(3)593–599.]

INTRODUCTION

Residency training is designed to prepare residents for careers as practicing physicians who deliver high-quality clinical care to patients. The Accreditation Council for Graduate Medical Education (ACGME) has outlined specific requirements for each specialty training program, including emergency medicine (EM).[1] However, the ACGME does not provide specific requirements for career preparation, so career preparation is not standardized among EM programs, and residents at different training programs may have different experiences.

It is unknown if we are providing appropriate career guidance and preparation, particularly for careers in academic medicine. Adding to the challenge is the fact that career choice is a complex decision and multiple influential factors play a role,

including personal and financial preferences as well as training program characteristics.[2-12] Prior literature has demonstrated that residents may feel ill-prepared for a career in academic medicine due to lack of training, research skills, and mentorship.[2,13] To meet this need, some programs have implemented "scholarly tracks": longitudinal curricular experiences with clear goals and objectives to allow residents to explore and develop skills in a particular clinical or academic area of focus within EM.[14] In addition to exposure to a specific area of concentration, tracks may increase scholarly activity, academic success, and selection of a career in academic medicine.[14-16] Despite these potential benefits and suggested strategies for implementation, a recent review of publicly available data demonstrated that specialized tracks are not widespread in EM training programs.[14,17] The reasons for this are unclear. Additionally, the value of specialized tracks and impact on resident career choice remains unknown.

The purpose of this study was to assess the prevalence and characteristics of specialized tracks as well as perceived benefits and barriers to implementation in EM residency training programs. Additionally, we sought to evaluate the relationship between tracks and resident career choice and whether there is an association between tracks and choosing an academic career.

Population Health Research Capsule

What do we already know about this issue?
Scholarly tracks have emerged in emergency medicine residency training programs, but their value and impact on resident career choice is unknown.

What was the research question?
What is the current state of scholarly tracks? Is there an association between scholarly tracks and pursuit of an academic career?

What was the major finding of the study?
Residency programs with scholarly tracks were more likely to graduate residents to an academic career.

How does this improve population health?
These results may inform the development and usage of scholarly tracks in residency training programs.

METHODS

Study Setting and Participants

We identified ACGME-accredited EM training programs through their accreditation data system.[18] To prevent duplication, one member of program leadership from each program was invited to participate based on available contact information with preference for seniority (i.e., program director [PD] over assistant/associate program director [APD]). We collected data between March 2017 and June 2017. This study was deemed exempt by the institutional review board of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.

Study Design

This was a cross-sectional survey study. We identified contact information for potential participants through the ACGME accreditation data system, Society for Academic Emergency Medicine Residency Directory, Internet search, and personal knowledge of study team members.[18,19] We sent email invitations with a link to an Internet-based survey administered by SurveyMonkey® to potential participants.[20] Two follow-up emails were sent at bi-weekly intervals to non-responders. Informed consent was implied by those participants who chose to click on the survey link.

Instrument Development

The instrument was developed by our study group of EM education researchers based on literature review and our prior research in this area according to established guidelines for survey research.[17,21] The survey consisted of multiple-choice items. For items where an "other" choice was available, participants were permitted to enter a free-text response. Participants were asked to complete a matrix of dropdown menus identifying the career choice and track (if present) for each resident in their graduating class. All items were read aloud and discussed among members of the study group to ensure response process validity. We then piloted the survey among a small group of representative subjects, and made revisions based on feedback from pilot testing. The final survey instrument is available in Appendix A. To incorporate all available data and maximize response rate, completion of all survey questions was not required.

Statistical Analysis

Residency-associated variables included whether tracks were offered, geographic region (West, Southwest, Midwest, Southeast, and Northeast), format (PGY1-3 vs. PGY1-4), total number of residents in the program, number of fellowships offered, and types of fellowships. The tracks were further categorized by whether the tracks were "clinical" (critical care, hyperbarics, pediatric EM, sports medicine, toxicology, ultrasound, wilderness medicine) or "non-clinical" (administration, education, emergency medical services, global health, research, simulation). Resident-level variables included type of track (if the resident came from a

program that offered tracks), and the intended educational or employment position after completion of residency. To answer the broad question of whether or not tracks were associated with an academic career, career options were further categorized into academic (academic full-time, academic part-time, fellowship) vs. non-academic (community practice non-teaching, community practice with teaching, other residency, non-clinical career, unknown). Fellowship was included in the academic category as this has been associated with academic career, and fellowship training is strongly recommended by experts in EM as a prelude to an academic career.[7,22,23]

All data were entered into Microsoft Excel (Microsoft Corporation, Redmond, WA) and transferred to SAS 9.4 (SAS Institute, Cary, NC) for analysis. We calculated and reported descriptive statistics for multiple- choice items. We report the results of comparisons between categorical variables, such as tracks and career choice, using odds ratios and proportions with exact binomial confidence intervals. To compare two cohorts (e.g., tracks vs. those without tracks or academic career vs. non-academic career) with respect to a multi-level categorical predictor (e.g., region), we used the chi-squared test. When comparing continuous variables, such as the number of fellowships offered, we described medians with interquartile ranges and used the non-parametric Wilcoxon rank-sum test. To adjust for potential correlations of residents within residency programs, we used a generalized estimating equation to adjust for clustering by program. Free-text responses were analyzed using a thematic approach.

RESULTS

General Results

A total of 113/157 (72%) programs completed the survey. Fifty-one programs reported having tracks. Characteristics of programs with and without specialized tracks are listed in Table 1. There was no significant difference in location between programs with tracks vs. those without (p= 0.6). Tracks were more common in four-year programs (OR = 4.8; [2.0-11.9]) and larger programs (chi-sq, p = 0.001). Programs with tracks were also more likely to offer a greater number of fellowships than those without tracks with medians of 5[2-6] and 3[1-5] respectively; p=0.03. The most common reasons reported for not having tracks was insufficient faculty manpower (28/57;49.1%). Additional reasons are described in Table 2. Written comments from respondents who selected "other" as a reason identified three major themes: 1) the program was in the process of developing tracks; 2) the program or program leadership was new; or 3) an individualized approach to career needs was preferred.

Table 1. Comparison of characteristics between residency programs with and without tracks.

	Programs without tracks (n= 62)*	Programs with tracks (n= 51)*
Region		
West	11/57 (19.3%)	8/50 (16.0%)
Southwest	5/57 (8.8%)	4/50 (8.0%)
Midwest	16/57 (28.1%)	12/50 (24.0%)
Southeast	13/57 (22.8%)	8/50 (16.0%)
Northeast	12/57 (21.1%)	18/50 (36.0%)
Program format		
PGY-1-3	48/57 (84.2%)	28/50 (56%)
PGY-1-4	9/57 (15.8%	22/50 (44.0%)
Other	0/57 (0%)	0/50 (0%)
Total number of residents		
15 or less	0/57 (0%)	0/50 (0%)
16-30	23/57 (40.4%)	7/50 (14.0%)
31-45	22/57 (38.6%)	18/50 (36.0%)
46-60	8/57 (14.0%)	16/50 (320%)
61 or more	4/57 (7.0%)	9/50 (9.0%)
Number of fellowships		
Median, [interquartile range]	3 [1-5]	5 [2-6]
Fellowships currently offered		
Administration	18/57 (31.6%)	22/50 (44.0%)
Critical care	8/57 (14.0%)	14/50 (28.0%)
Education	14/57 (24.6%)	21/50 (42.0%)
EMS	22/57 (38.6%)	26/50 (52.0%)
Global health	16/57 (28.1%)	17/50 (34.0%)
Hyperbarics	2/57 (3.5%)	0/50 (0%)
Pediatrics	18/57 (31.6%)	20/50 (40.0%)
Research	15/57 (26.3%)	23/50 (46.0%)
Simulation	12/57 (21.1%)	14/50 (28.0%)
Sports medicine	7/57 (12.3%)	12/50 (24.0%)
Toxicology	10/57 (17.5%)	14/50 (28.0%)
Ultrasound	35/57 (61.4%)	37/50 (74.0%)
Wilderness medicine	6/57 (10.5%)	5/50 (10.0%)
None	9/57 (15.8%)	6/50 (12.0%)
Other	6/57 (10.5%)	7/50 (14.0%)

EMS, emergency medical services; *PGY*, post-graduate year.
*6 Participants, 5 from programs without tracks and 1 from a program with tracks, answered the question about the presence of tracks, but did not complete any additional questions in the survey.

Description of Tracks

For those programs with tracks, track characteristics are listed in Table 3. Programs had various years of experience with tracks. Track participation was mandatory in 40% (20/50) of programs, usually during the later years in residency. Residents commonly participated in a single track (37/50; 74%) and/or participated continuously (33/50; 66%). Written responses from those selecting "other" for how residents participate in tracks revealed two major themes: residents

Table 2. Reasons residency programs do not have tracks.

	n (%) Total n = 57
We don't have the faculty manpower to support tracks	28 (49.1%)
There is insufficient time in the resident schedule	19 (33.3%)
We don't have administrative resources to support tracks	16 (28.1%)
We do not feel that tracks would be helpful	15 (26.3%)
Our residents don't want tracks	15 (26.3%)
Other	14 (24.6%)
There is inadequate funding to support tracks	12 (21.1%)
We don't have leadership support for tracks	8 (14.0%)
We don't have enough faculty expertise to offer tracks	7 (12.3%)
We don't know how to implement a track program	5 (8.8%)

rotate through all tracks as an intern and then select one in later years, and residents participate in as many tracks as they choose. The most commonly perceived benefits of tracks to residents were an opportunity for advanced training in an area of focus (46/50; 92%), career guidance/exploration/selection (44/50; 88.0%), mentorship (44/50; 88.0%), and preparation for an academic career (40/50; 80.0%) (Table 4).

Tracks and Careers

Immediate post-residency career is shown in Table 5. Programs with tracks were more likely to graduate residents to an academic position, OR= 1.8 [1.3-2.4]. The type of track pursued, clinical vs. nonclinical was not significantly associated with immediate post-residency academic career, OR = 1.0,[0.6-1.9].

DISCUSSION

In this study we found that residency programs with tracks were more likely to graduate residents to an academic career. This is not surprising, as tracks offer the opportunity for advanced training, scholarship, and directed mentorship, which have been previously identified as being associated with an academic career.[7] A four-year program format has also been associated with academic career choice, and in our study we found that tracks were more common in four-year programs.[10] Interestingly, we did not find an association between type of track completed, clinical vs. nonclinical, and academic career. This was somewhat surprising as one might imagine that residents with an interest and additional training in areas such as administration, education, and research may be more likely to pursue an academic career. However, academicians may have primary job roles that are both non-clinical (i.e., research director, PD) and clinical (i.e. ultrasound director, pediatric EM director).

It is important to note that this study found an association between scholarly tracks and an initial academic position, but this does not necessarily indicate causation. It is not known if the tracks themselves increase the likelihood of choosing an academic career or if the presence of tracks is simply an indicator that a program has more resources and/or specifically encourages academic endeavors as part of its mission. Residents who have a predetermined academic career preference may select training programs with this type of curricular offering to better meet their needs. Some literature demonstrates that residents may not feel well prepared for an academic career.[2,13]

In our study population, the majority of residents entered community practice (with and without teaching) immediately following residency. This is similar to what has been reported previously for EM residents.[10] In contrast to Lubavin's study in 2004, we found a greater percentage of residents entering fellowships and less an academic career straight after residency.[10] However, if these categories (fellowships and those who assume an academic position directly after residency) are combined, then our results are similar. Securing an academic position may have become more competitive in recent years, necessitating applicants to gain additional skills and experience. EM leaders strongly recommend fellowship as a precursor to an academic career.[22,23] Fellowship affords protected time to develop expertise in a specific niche without the multiple competing demands of an academic position.

Programs with tracks noted multiple benefits, including advanced training, career guidance, mentorship, and preparation for an academic career. Despite these benefits as well as prior literature suggesting strategies for successful implementation, we found that tracks are not highly prevalent (though there were additional programs in the process of developing tracks).[14] The most notable reasons for not having tracks in this study were lack of faculty manpower, insufficient time, and lack of administrative resources. These barriers may explain why tracks were

Table 3. Characteristics of residency program tracks

	Response rate (%)
Length of time program has had tracks	
Less than 1 year	9/50 (18.0%)
1-3 years	14/50 (28.0%)
4-6 years	15/50 (30.0%)
7 or more years	12/50 (24.0%)
Track participation is mandatory	
Yes	20/50 (40.0%)
No	30/50 (60.0%)
Years that residents participate in tracks	
PGY-1	26/50 (52.0%)
PGY-2	41/50 (82.0%)
PGY-3	48/50 (96%)
PGY-4	22/50 (44.0%)
Other	2/50 (4.0%)
Total time residents engage in tracks during residency	
1-4 weeks	2/50 (4.0%)
5-8 weeks	2/50 (4.0%)
9-12 weeks	6/50 (12.0%)
13-16 weeks	3/50 (6.0%)
More than 16 weeks	0/50 (0%)
Continuously	33/50 (66%)
Other	4/50 (8.0%)
Track participation format	
Residents rotate through all available tracks	0/50 (0%)
Residents rotate through multiple tracks	1/50 (0%)
Residents select one track to participate in	37/50 (74%)
Other	12/50 (24.0%)
Tracks offered	
Administration	34/50 (68.0%)
Critical care	21/50 (42.0%)
Education	39/50 (78.0%)
EMS	36/50 (72.0%)
Global health	29/50 (58.0%)
Hyperbarics	2/50 (4.0%)
Pediatrics	14/50 (28.0%)
Research	27/50 (54.0%)
Simulation	22/50 (44.0%)
Sports medicine	12/50 (24.0%)
Toxicology	24/50 (48.0%)
Ultrasound	40/50 (80.0%)
Wilderness medicine	19/50 (38.0%)
Other	12/50 (24.0%)

EMS, emergency medical services; *PGY*, post-graduate year.

more common in larger programs and those with a four-year format as these programs may have a larger faculty to share the workload, greater administrative resources, and more time and flexibility to incorporate such curricula. As there is scant literature defining and reporting objective outcomes resulting from implementing tracks, programs may also be hesitant to devote resources to their development and implementation until further research is done.

For those programs with tracks, our study found that residents usually participate in one track continuously in their later years, with some offering an exploratory rotation through tracks in the earlier years. This likely is by design to meet the overall objectives of such curricula. Trainees need time to consider and select an area of focus that most interests them. Concentrating on a single area with focused mentorship facilitates the development of specialized expertise, allowing for consistent growth and accomplishment of scholarly work.

LIMITATIONS

This was a survey study and the results are subject to the limitations inherent to this type of data collection. As this was a cross-sectional study, only one period of time was evaluated and it is possible that results may vary if multiple years were incorporated, longitudinally. Additionally, data were collected from only one member of the residency leadership team. This may have led to limited insight in the free-response section, and confirmation of accuracy of individual data was not available. Although the survey response rate was 72%, since we do not have information on the non-respondents, there may have been selection bias.

Additionally, not all respondents completed every survey item, and thus, we may have missed some information. Despite these limitations, we feel this study provides important information regarding scholarly tracks. Our results suggest there is an association between programs with scholarly tracks and selection of an academic career. Furthermore, many perceive benefits of tracks. There are still many questions left unanswered, and research should focus on defining objective outcomes from implementing tracks and whether the association between tracks and the selection of an academic career is due to the tracks themselves or the self-selection of residents.

CONCLUSION

This study describes the current prevalence, characteristics, and perceived benefits of scholarly tracks in residency training. Scholarly tracks are associated with an academic position immediately following residency. The results of this study may inform the development and usage of scholarly tracks in residency programs.

Table 4. Perceived benefits of tracks.

	n (%) Total n = 50
Advanced training in an area of focus	46 (92.0%)
Career guidance/exploration/selection	44 (88.0%)
Directed mentorship	44 (88.0%)
Development of a niche	42 (84.0%)
Preparation for an academic career	40 (80.0%)
Preparation for a leadership role	32 (64.0%)
Creation of a collaborative network	25 (50.0%)
Increased scholarly productivity	25 (50.0%)
Improved wellness during residency	17 (34.0%)
Improved clinical skills	7(14.0%)
Other	3 (6.0%)
None	0 (0%)

Table 5. Immediate post-residency career.

Career category	Immediate post-residency career	Residents from programs without tracks n (%), total n= 517	Residents from programs with tracks n (%), total n= 267	All residents n (%), total n= 784
Academic				
	Academic- full time	33 (6.4%)	26 (9.7%)	59 (7.5%)
	Academic- part time	22 (4.3%)	7 (2.6%)	29 (3.7%)
	Fellowship	95 (18.4%)	82 (30.7%)	177 (22.6%)
Non-academic				
	Community practice non-teaching	271 (52.4%)	108 (40.4%)	379 (48.3%)
	Community practice with teaching	78 (15.1%)	41 (15.4%)	119 (15.2%)
	Other residency	1 (0.2%)	0 (0%)	1 (0.1%)
	Non-clinical practice	1 (0.2%)	0 (0%)	1 (0.1%)
	Unknown	16 (3.1%)	3 (1.1%)	19 (2.4%)

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Free Open Access Medical Education (FOAM) in Emergency Medicine: The Global Distribution of Users in 2016

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Introduction: Free open-access medical education (FOAM) is a collection of interactive online medical education resources—free and accessible to students, physicians and other learners. This novel approach to medical education has the potential to reach learners across the globe; however, the extent of its global uptake is unknown.

Methods: This descriptive report evaluates the 2016 web analytics data from a convenience sample of FOAM blogs and websites with a focus on emergency medicine (EM) and critical care. The number of times a site was accessed, or "sessions", was categorized by country of access, cross-referenced with World Bank data for population and income level, and then analyzed using simple descriptive statistics and geographic mapping.

Results: We analyzed 12 FOAM blogs published from six countries, with a total reported volume of approximately 18.7 million sessions worldwide in 2016. High-income countries accounted for 73.7% of population-weighted FOAM blog and website sessions in 2016, while upper-middle income countries, lower-middle income countries and low-income countries accounted for 17.5%, 8.5% and 0.3%, respectively.

Conclusion: FOAM, while largely used in high-income countries, is used in low- and middle-income countries as well. The potential to provide free, online training resources for EM in places where formal training is limited is significant and thus is prime for further investigation. [West J Emerg Med.2018;19(3)600–605.]

INTRODUCTION

Free open-access medical education (FOAM) is a collection of interactive online medical education resources—free and accessible to students, physicians, nurses, paramedics and other learners.[1] FOAM uses multiple online platforms such as blogs, podcasts, tweets, videos and other web-based media to form a community that shares ideas and accelerates the translation of research into clinical practice.[1-3] Physicians in emergency medicine (EM) and critical care have been leaders in the trend to rapidly increase the number of online resources that share FOAM content, and recently there have been calls to formally integrate online learning into residency education in the United States.[4,5]

Formal training in EM is lacking in many low- and middle-income countries (LMICs) but must be prioritized in order to reach key development priorities for emergency care systems.[6,7] FOAM has the potential to fill certain gaps in EM training resources in LMICs. The current content of FOAM represents a diverse array of learning resources from core emergency care basics to cutting-edge techniques such as extracorporeal membrane oxygenation. Although the latter is unlikely to be relevant in low-resource contexts, there

is potential for content to be customized to the resources and cultural context of a country, as opposed to textbooks written predominantly for high-resourced settings. However, awareness of FOAM resources may in fact be lowest in those LMIC settings where formal resources (e.g. textbooks, lecturers, instructors, simulations) are least available.[8] This descriptive report assesses the global uptake of FOAM via the geographical distribution of blog and website users in 2016.

Population Health Research Capsule

What do we already know about this issue?
Free open-access medical education (FOAM) is a novel approach to education that has potential to reach emergency medicine (EM) learners worldwide.

What was the research question?
To what extent is FOAM being used by EM learners around the globe?

What was the major finding of the study?
FOAM is mostly used in high-income countries, but there are notable users in several middle-income countries.

How does this improve population health?
FOAM is prime for further research regarding its ability to train EM providers around the world.

METHODS

A convenience sample of popular FOAM blogs and websites—known to the authors or identified via a Google search using the term "emergency medicine FOAM"—were approached for inclusion via email inquiries. We identified additional sites by referral of the site administrators that responded to emails. Sites were included if they were free, fully accessible, had actively published new content in 2016, and specifically addressed mainstream topics in EM and critical care. We excluded sites if they solely produced niche content that is less applicable to the wider global audience (e.g. emergency subspecialties such as wilderness medicine). Web analytics data for all sites were collected via Google Analytics to ascertain the location of de-identified users accessing the blog or website in the calendar year 2016. No individual Internet protocol addresses were collected, nor are they available from the version of Google Analytics used. We grouped the number of sessions—or unique interactions between a user and the site—by country of access.

For each country, we calculated a cumulative number of sessions from all websites and blogs, which was then cross-referenced with World Bank data for population and income level. To account for large differences in population sizes between countries (and therefore large differences in potential FOAM users), population-weighted session counts (sessions per million people) were calculated by dividing the gross number of sessions by the 2016 World Bank population figure for each country, then multiplied by one million.

We then grouped countries as high income, upper-middle income, lower-middle income and low income by 2016 World Bank classification. Gross session counts and population-weighted session counts for each economic stratum were again calculated in the manner described above.

All data were aggregated in Microsoft Excel (v.14.5.5, Redmond, WA) and analyzed via simple descriptive statistics. We mapped cumulative and population-weighted session counts for visualization of the global distribution using Infogram (Infogram Software Inc., San Francisco, CA).

RESULTS

We included 12 FOAM blogs and websites from six countries for analysis (Table 1). The majority of sites were published in English, while one site (MDU Chile) was published in Spanish and another (FOAM EM) aggregated blog postings from multiple languages. The combined reported annual sessions of these FOAM sites totaled approximately 18.7 million sessions worldwide in 2016. The number of unique countries accessing each site ranged from 82 to 209.

The 20 countries with the highest gross annual sessions in 2016 are listed in Figure 1. The United States, Australia, the United Kingdom and India had cumulative session counts greater than one million. Figure 2 maps the global distribution of users by gross annual session counts. Figure 3 shows the population-weighted session counts for the 20 countries with the most FOAM activity, and Figure 4 maps the global distribution of users by population-weighted session counts.

When population-weighted session counts were grouped by World Bank income classification, we noted diminishing usage of FOAM blogs and websites as income level decreased. High-income countries accounted for 73.7% of population-weighted FOAM blog and website sessions in 2016, while upper-middle income countries, lower-middle countries and low-income countries accounted for 17.5%, 8.5% and 0.3%, respectively (Table 2).

DISCUSSION

The majority of users of FOAM blogs and websites are concentrated in a small number of countries, many of which are also the primary producers of FOAM content such as the U.S., Australia, Canada, and the United Kingdom. Conversely, there are large gaps in FOAM use in many regions of South America, central Africa, and Asia where language and economic

Table 1. Description of FOAM blogs and websites included for analysis, 2016.

Site	Country of origin	Language	Annual sessions	Number of countries accessing
Life in the fast lane	Australia	English	17,436,575	209
ALiEM	USA	English	568,521	196
Pediatric EM morsels	USA	English	245,264	187
FOAM EM	UK	Multiple	196,628	187
ER cast	USA	English	119,388	170
Intensive blog	Australia	English	76,026	169
Broome docs	Australia	English	57,401	170
SOC MOB	Canada	English	44,097	158
EM tutorials	New Zealand	English	39,818	168
SCGH ED	Australia	English	33,969	156
Manu Et corde	Canada	English	27,606	156
Blunt dissection	Australia	English	16,628	139
MDU Chile	Chile	Spanish	10,941	80
EM/IM doc	USA	English	4,164	82

FOAM, free open access medical education; *ALiEM*, Academic Life in Emergency Medicine; *EM*, emergency medicine; *ER*, emergency room; *SOC MOB*, standing on the corner, minding my own business; *SCGH ED*, Sir Charles Gairdner Hospital Emergency Department; *MDU*, Medicine de Urgencia; *IM*, Internal Medicine; *USA*, United States of America; *UK*, United Kingdom.

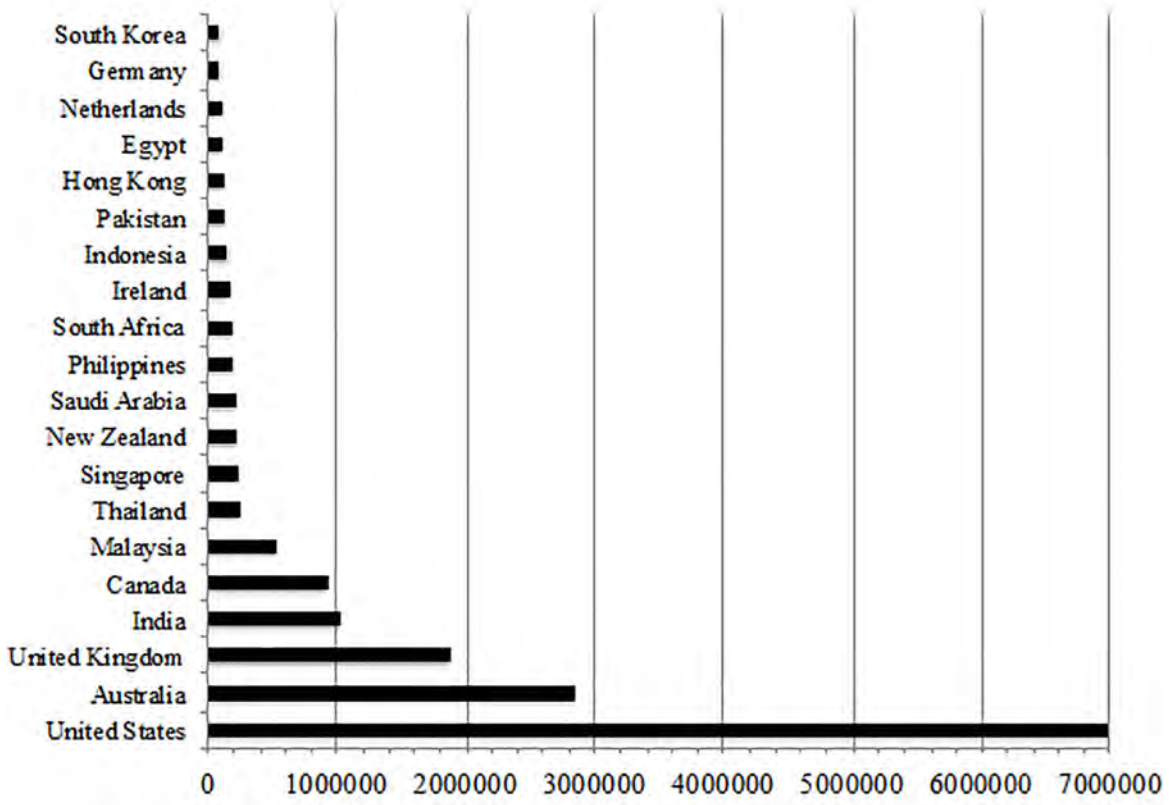

Figure 1. Gross annual sessions from FOAM users in the top 20 countries, 2016.
FOAM, Free Open Access Medical education.

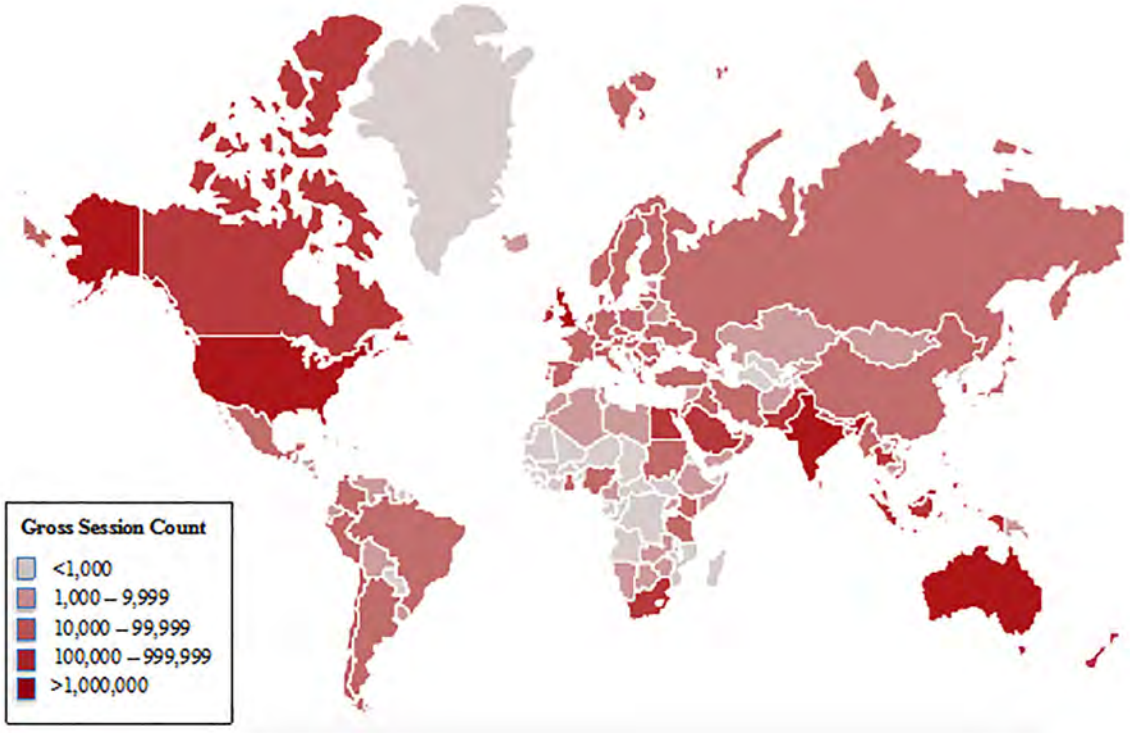

Figure 2. Global FOAM distribution- Gross annual session counts by country, 2016.
FOAM, Free Open Access Medical education.

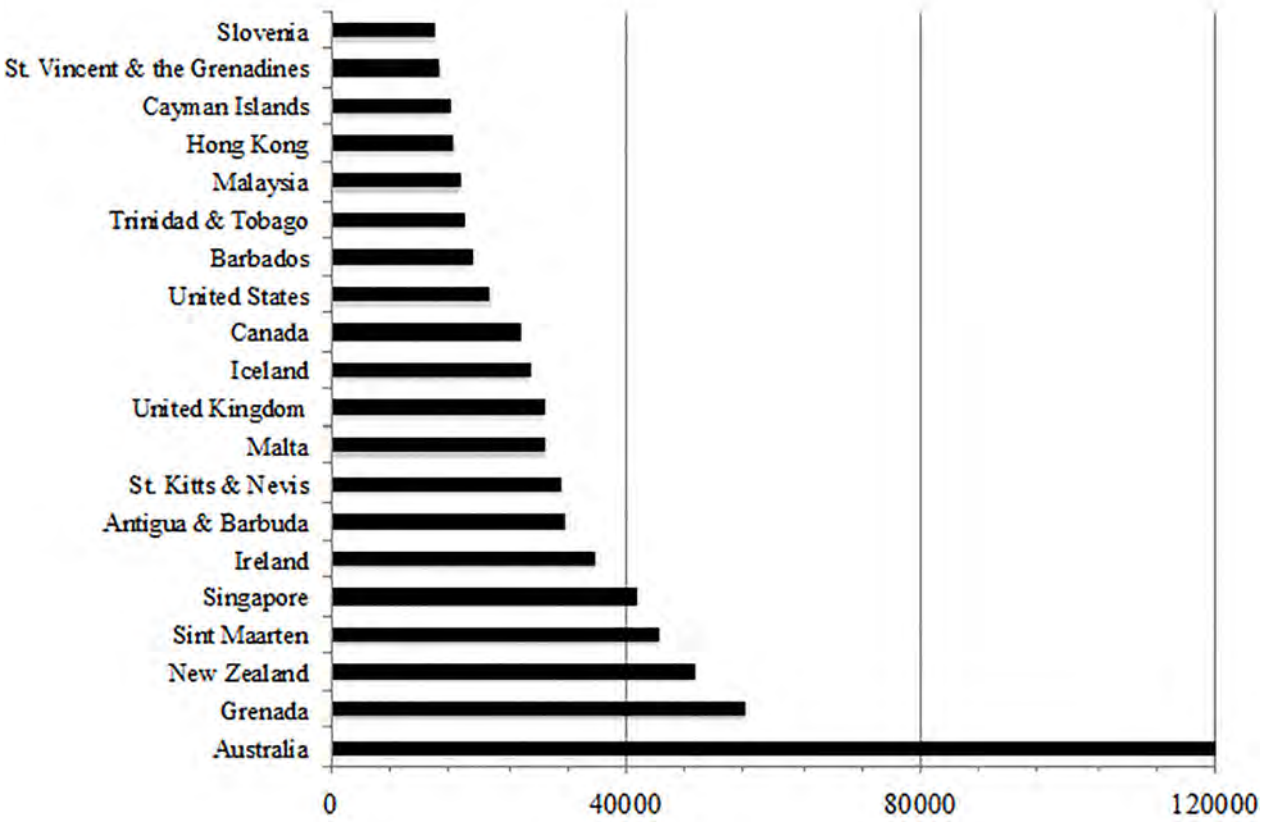

Figure 3. Population-weighted session counts from FOAM users in the top 20 countries, 2016 (per million people).
FOAM, Free Open Access Medical education.

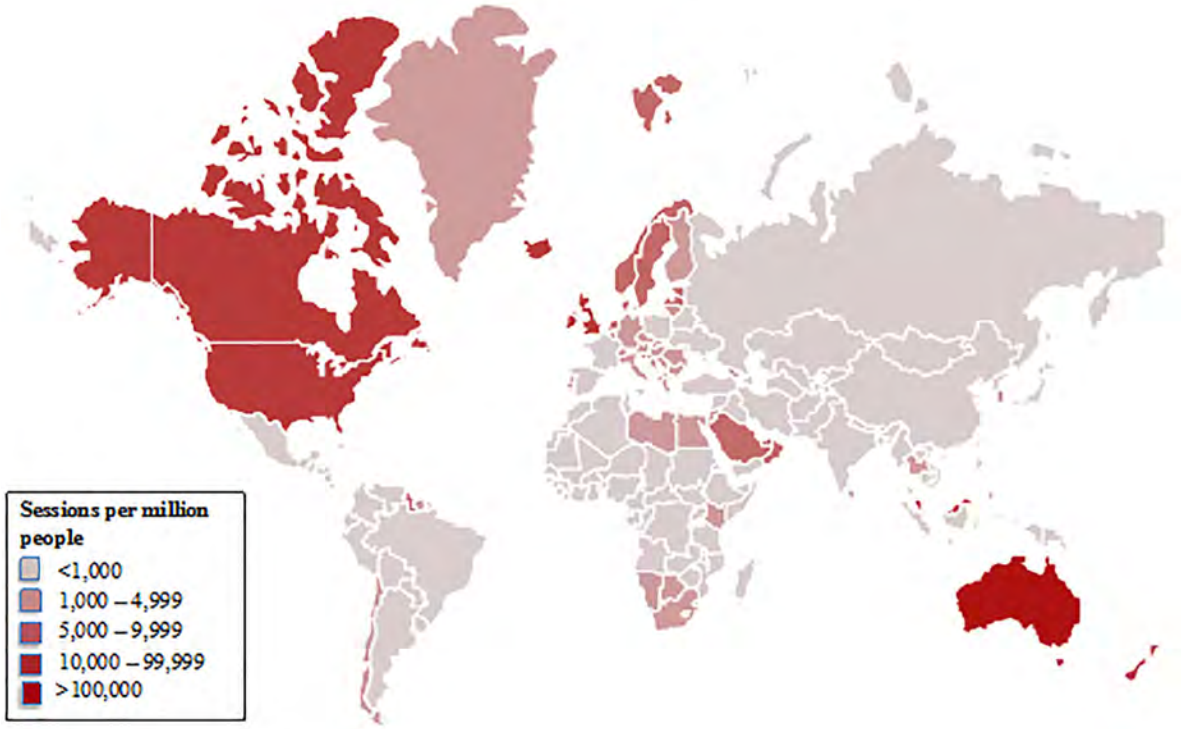

Figure 4. Global FOAM distribution- Population-weighted session counts by country, 2016.
FOAM, Free Open Access Medical education.

Table 2. Distribution of FOAM sessions by World Bank income level, 2016.

Income level*	Total sessions	% of Total sessions	Sessions per million people	% of Sessions per million people
High-income	14,067,663	75.30%	806,043	73.72%
Upper-middle income	1,604,520	8.59%	190,835	17.45%
Lower-middle income	2,933,755	15.70%	93,350	8.54%
Low-income	77,229	0.41%	3,219	0.29%

FOAM, Free Open Access Medical education.
*Income level grouped by World Bank classification, 2016.

development might present challenges to access and use. Other potential barriers to FOAM use in these regions include web accessibility and speed, device availability, censorship, and lack of awareness.

Despite the majority of FOAM users clustering in high-income countries, there is a notable signal of user activity in several middle-income countries, which suggests a potential audience for FOAM content beyond the current high-income users. For example, South Africa is an upper-middle income country that accounted for 195,070 of the gross FOAM sessions in 2016. The country is also home to several graduate EM training programs dating back to 2001, which may explain the relative increase in FOAM users as compared to other LMICs.[9]

These findings, although a single snapshot of FOAM usage, represent a baseline index that can be used in future years to assess the growth and penetration of FOAM resources into LMICs. Since FOAM users have begun to emerge in many LMICs, we suggest that FOAM content creators consider developing a subset of FOAM that is particularly relevant to resource-limited contexts. Additionally, we encourage a partnership between experienced FOAM creators with clinicians and educators in LMICs that have an interest in developing their own FOAM content. This type of mentorship will provide a vehicle for clinicians in LMICs to publish educational materials and to diversify the current scope of FOAM.

LIMITATIONS

There are several limitations to the generalizability of our findings. Due to the lack of standardized cataloguing of FOAM resources, we were unaware of a truly systematic method of sampling all FOAM sites. Instead, our convenience sample was limited to those sites that were already known to

the authors, readily identified as top hits by a Google search, or referred by other site administrators. In many cases there was no response to email inquiries; thus, no website data could be obtained. We exclusively sampled FOAM blogs and websites related to EM and critical care. Our results may not be fully representative of other platforms of FOAM, such as podcasts or videos, or FOAM content tailored to other medical and surgical specialties. Ten out of the 12 sites were published in English. Unless this language allocation is truly representative of the published FOAM content, our findings likely under-report the number of sessions from non-English speaking countries.

Although we posit that the number of sessions originating from a particular country approximates the number of users in that country, this may only loosely estimate the true distribution of users. The advantage of this method is that it takes into account both the number of users and their degree of activity (number of unique visits to a site) over the course of the year. However, we were unable to determine if a smaller core of very active users gain more from FOAM resources than a larger audience of infrequent users. Our method also assumes that a negligible number of FOAM users are accessing virtual private networks, which would falsely lower the session counts from a particular country.

Ideally, a weighted session count would be cross-referenced by the number of healthcare providers (i.e., end users of FOAM) in a given country. However, these data were not readily available for most countries, so session counts were weighted by country population size instead. In many island nations such as Grenada the population size is small, but weighted session counts may be easily skewed by the presence of medical schools that draw from the international community.

Finally, this study does not answer important questions about barriers to awareness and use of FOAM in LMICs. Further investigation is needed to understand the potential impact of FOAM on EM training, the availability of the Internet and web-enabled devices required to access FOAM, the growth of FOAM over time, and the applicability of FOAM content to practicing in low-resource settings. A needs assessment of learners in LMICs would be helpful to understand the gaps in educational resources and whether FOAM has the potential to fill those gaps.

CONCLUSION

Our findings suggest that FOAM is largely being used in a select number of high-income countries. However, there are significant numbers of users in middle-income countries as well. The potential to provide free, online training resources for emergency medicine in places where formal training is limited is prime for further investigation.

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Implementation of an Emergency Medicine Research Associates Program: Sharing 20 Years of Experience

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Introduction: The use of research associates (RA) programs to facilitate study enrollment in the emergency department was initiated during the mid-1990s. The University of Rochester Medical Center (URMC) was an early adopting site for this model, which has experienced considerable growth and development over the past 20 years.

Methods: Our goal was to detail the Emergency Department Research Associates (EDRA) program processes developed at the URMC that has led to our program's sustainability and productivity. These processes, and the lessons learned during their development, can assist institutions seeking to establish an RA program or refine an existing program.

Results: Defined procedures for selecting, training, and monitoring EDRAs have been created and refined with the goal of maximizing study enrollment and minimizing protocol deviations. Our EDRA program functions as a paid service center for investigators, and our EDRAs engage in a variety of study-related activities including screening and enrolling patients, administering surveys, collecting bio-specimens, and making follow-up calls. Over the past two years, our program has averaged 222 enrollments/month (standard deviation = 79.93), gathering roughly 25 participants per study per month.

Conclusion: Our EDRA model has consistently resulted in some of the highest number of enrollments across a variety of recently funded, multi-center studies. Maintaining a high-quality EDRA program requires continual investment on the part of the leadership team, though the benefits to investigators within and outside the department outweigh these costs. [West J Emerg Med. 2018;19(3)606-612.]

INTRODUCTION

Research in emergency medicine has been accelerating rapidly over the past several decades, with increasing quality and quantity of publications and grant mechanisms. Concomitant to the increased output have been maturations in processes and procedures for conducting widely heterogeneous research in the emergency department (ED) setting. In the fast-paced ED environment, practicing clinicians have historically found it difficult to identify and enroll patients into their research studies.[1] One particular innovation that has been adopted and refined with considerable success is the use of a research associates (RA) program for study enrollment and procedures in the ED.[2-5]

In the mid-1990s, Drs. Judd Hollander,[6] Keith Bradley,[2] and others pioneered the use of undergraduate, pre-health

profession students to enroll subjects into investigator-initiated research studies and perform basic study procedures. This early work has led to the development of numerous RA programs across the United States and significant expansion of the scope of research performed in emergency medicine. The Department of Emergency Medicine at the University of Rochester Medical Center (URMC) was a very early adopter of this model.[7] Our 20-year-old RA program has experienced considerable development and expansion since its inception. In the past 10 years alone, over 20,000 study participants have been enrolled by the URMC Emergency Department RA (EDRA) program into a wide variety of research studies. The EDRA program has been responsible for URMC being among the top enrolling institutions in the majority of the recent multi-center ED studies in which we participate.

For example, in the past year our center (a) was the second among 22 participating centers to meet the enrollment goal in a National Cancer Institute-supported study of ED utilization by patients with active cancer, despite being late to join the consortium; (b) was the highest enrolling site among 11 sites, enrolling over 1,000 subjects (accounting for 30% of total enrollment), into a National Heart, Lung, & Blood Institute-funded multi-center study of syncope in older adults; and (c) was the top enrolling site in several industry-sponsored, multisite clinical trials and validation studies on mild traumatic brain injury. Recent research using our program has been published in outlets including *Academic Emergency Medicine, Journal of Emergency Medicine, Annals of Emergency Medicine, Western Journal of Emergency Medicine, the American Journal of Emergency Medicine, PLOS One, Prehospital Emergency Care, Pediatric Emergency Care, Prehospital and Disaster Medicine, Journal of Trauma, JAMA Oncology, Journal of the American Geriatric Society,* and *Psychiatric Services*. Given this success, our team is frequently asked to share our model with collaborators across the country. Our goal here was to describe the evolution of our RA program model from its early roots, present quantitative evidence of our program activities, and provide a brief overview of our structure and processes for investigators interested in program creation, refinement, and/or expansion.

THE EDRA PROGRAM AT THE UNIVERSITY OF ROCHESTER

Our EDRA program aims to maximize recruitment for research studies within the department. Each faculty member in the research division of our ED has published using EDRA-collected data. Furthermore, more clinically focused EM faculty have also frequently published using our EDRA program, as the program strengths in data acquisition complement the clinical knowledge of these providers. Our program has also established a significant institutional profile, as investigators from numerous other departments and divisions frequently use our EDRA program to recruit patients into their studies. For example, in the past six months alone, our program has worked with the departments/divisions of infectious disease, laboratory medicine, obstetrics, psychiatry, and pediatrics, among others. For context, Strong Memorial Hospital (SMH), where the vast majority of our EDRA-related research takes place, is a Level I ACS trauma center, regional stroke center, regional heart center, and burn center with 830 beds. The ED in which the program is housed employs 85 fulltime faculty members and 42 residents (14 per class; three-year program). The SMH ED, including the pediatric ED, is a 29,000 square-foot unit that in 2016 saw over 116,000 patients. The University of Rochester, directly next door to SMH, had an enrollment of 6,170 fulltime undergraduate students during the 2016-2017 academic year.

Over the past 20 years,[7] the procedures and infrastructure governing our EDRA program have been formalized and refined to enhance its effectiveness and efficiency. The program is currently structured with (a) a faculty advisor who provides scientific oversight of proposed research and long-term direction (5% salary support provided); (b) a program director who interacts with study teams interested in using the EDRA program and oversees the EDRA coordinator and supervisor (25% effort); (c) a full-time post-baccalaureate supervisor who is responsible for hiring and training EDRAs, scheduling coverage of the ED by EDRAs, generating quotes for EDRA program usage by study teams, and formalizing and implementing study-specific protocols; (d) a half-time college senior/post-baccalaureate coordinator responsible for assisting the EDRA supervisor and piloting study protocols in the ED; and (e) 18-35 hourly-paid undergraduate EDRAs (see Figure 1). Over the past two years (including summer months), we have averaged 30.79 EDRAs on the payroll per month (standard deviation [SD] = 4.51).

Our EDRA program is structured as a university service center, with funding received from investigators using our services and as-needed support from the ED. (Institutional funding is eliminated when the program is fully funded by investigators). The need for departmental support is mitigated through monthly budget reconciliation meetings where program costs and revenues are discussed and managed to avoid propagation of a deficit. Program costs consist primarily of faculty/administrative effort, EDRA salaries (students are paid an hourly wage), and training expenses (including hourly EDRA costs, administrative fees, and phlebotomy course registrations), resulting in a fixed hourly rate for program utilization. This hourly rate is adjusted annually with the goal of cost neutrality in accordance with cost center status.

Investigators interested in using our program contact our team, meet with the program director, supervisor, and coordinator to discuss their project and potential levels of EDRA involvement, and then work with our team on planning the operationalization of their protocol. Pertinent information for this process includes the length of the study, the amount of initial and continuing study-specific training required, the

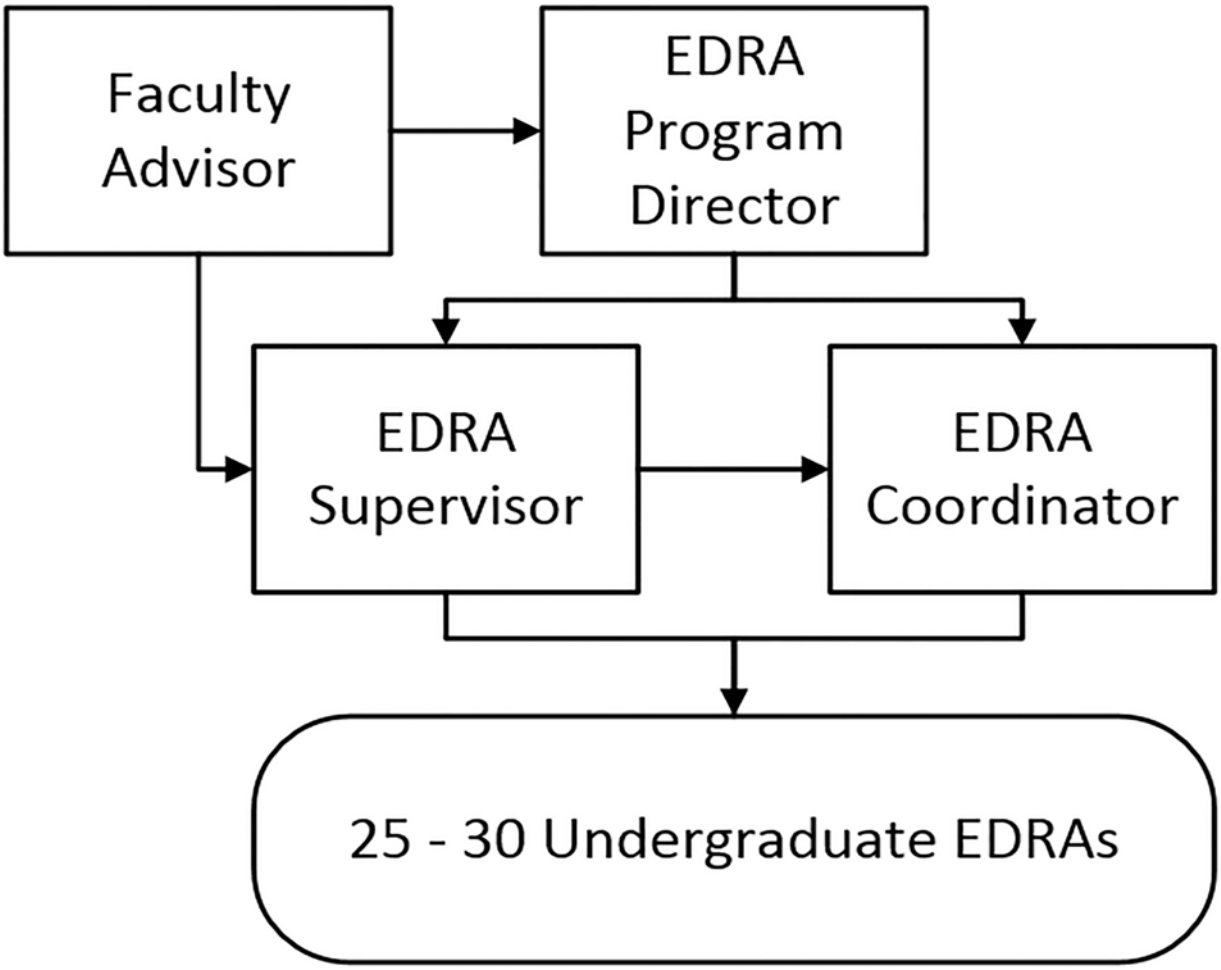

Figure 1. Emergency Department Research Associates (EDRA) program personnel structure.

number of patients expected to be screened (determined by eligibility criteria and estimates following electronic medical record [EMR] data abstraction performed by the EDRA staff), expected patient enrollment, and duration of EDRA study procedures (in minutes) including screening, consent, enrollment, and/or follow-up. This phase is particularly important for investigators from other departments as they often require guidance regarding the clinical workflow of the ED and our developed best practices for facilitating enrollment and study success.

Investigators then work with our team to develop an acceptable quote for service based on our annually fixed program rate and the agreed-upon amount of time EDRAs would devote to the specific project. EDRA time includes administrative startup time and continual program oversight, EDRA training, and EDRA coverage of the ED for 16 hours per day, seven days per week, with 8-12 of those hours necessitating two EDRAs to keep up with the patient volume and study demands. The total investigator cost for using our program is highly variable, from short-term studies with simple screening and referral requirements that cost as little as $1,000 to larger studies with more extensive EDRA involvement entailing program budgets in excess of $65,000 over the course of four years. The EDRA budget for any given study is modified, as needed, as the project progresses.

Importantly, our EDRA leadership team is closely linked with our departmental research review committee (chaired by the EDRA faculty advisor), which evaluates research protocols involving the ED for potential human subjects, clinical flow, and scientific concerns before investigators can receive institutional review board approval. This involvement allows the EDRA program to assist investigators in the creation of effective, efficient, and ethical research protocols. Given our track record of successful completion of enrollment protocols, human subjects training, and leadership oversight, our program has applied for and received "umbrella approval" from the URMC review board

for EDRA involvement in enrollment, consent, and basic study procedures (e.g., survey administration, interviews, nasal swabs) across different research studies. When an investigator references this annually reviewed umbrella protocol, it allows our team of EDRAs to participate in disparate research projects without the potentially burdensome paperwork associated with including each EDRA as study personnel on each project.

HIRING AND TRAINING EDRAS

Our program compensates the EDRAs both experientially and monetarily, as students are hired as part-time staff. While other models for RA programs have demonstrated considerable success[3,5,7,8], we have found the paid-enroller model to be most successful at our institution with regard to the quality of student applicants and retention of employees.

The University of Rochester has an undergraduate population that is very enthusiastic about careers in health sciences given the proximity and accessibility of the URMC (campuses directly adjacent). This close proximity to an exceptional undergraduate population is, no doubt, a strong asset to our program and significantly contributes to our program's success (though high-quality RA programs in settings with much looser connection to an undergraduate population have demonstrated considerable success[8]). Although there is no set criteria for who will be successful in this position, there are a few key indicators that help identify potentially successful candidates from the perennially large applicant pool, including grade point average, academic major, research experience at the college level, professional and/or volunteer experience working with people, favorable recommendations from previous employers, and communication skills demonstrated during the interviews for the position.

Given that the EDRA position is paid and has demonstrated significant student post-graduate success, we are fortunate to receive a competitive pool of applicants during each hiring cycle (i.e., approximately 15-20 applicants per position). It is not only our reputation and compensation that ensures our high quality EDRA team. We ask our senior EDRAs for recommendations of peers who they think would be successful in the position, send solicitations via e-mail to apply for an EDRA position to pre-medical and health-science student groups, give announcements to traditional pre-medical curriculum classes when the application periods are open, and attend Student Employment Office (SEO) events such as the bi-annual undergraduate job fair.

Once applications have been submitted to the SEO, additional paper applications are sent to all interested applicants that solicit short answers regarding previous work, clinical experiences, and research involvement. From the paper applications, roughly 25% of these applicants are granted half-hour interviews to further evaluate their ability and experience, of whom roughly one-third are accepted. The total number of EDRA position offers made during each hiring cycle is based on position needs. Over the past two years, we have averaged seven new EDRAs across five hiring classes. The majority of our accepted EDRAs are in their second or third year of undergraduate education. This ensures that our EDRAs are committed to their future in healthcare and have had sufficient time to acclimate to the college atmosphere, as well as reduces the amount of new hires that leave the position before providing the program with at least a year of service. As a result, the average length of time EDRAs have served in the program, based on completed terms of employment since Fall 2013, is 20.0 months (SD = 8.90).

Training for each EDRA is extensive and consistent (Figure 2). Initial training consists of 40 hours of classroom time and 12 hours of supervised clinical time before they are cleared to work independently in the ED. The classroom learning topics include EDRA and URMC policies and guidelines, university-sanctioned Health Insurance Portability and Accountability Act training (including Collaborative Institutional Training Initiative certification), the informed consent process (both practical application and historical context), study-specific trainings, professional interaction development, survey administration, and standardized good-documentation practices. Once the classroom portion of the initial training is complete, EDRAs are given a two-hour, in-depth guided tour of the ED. The new EDRAs then work two four-hour "shadow shifts" where they observe the on-shift behavior of a senior EDRA. The new hires then work one complete four-hour shift while the program coordinator observes them and evaluates their readiness to function independently based on their (a) facility with our EMR; (b) ability to appropriately consent patients; (c) knowledge of and aptitude in study procedures; (d) communication timing and quality with clinical providers on shift; and (e) navigation of the ED.

Due to the longevity of EDRAs in the program and the length of certain studies, the initial training is insufficient to maintain a high quality of work. EDRAs receive weekly update notifications via e-mail. Monthly staff meetings are held to communicate major updates and protocol changes, as well as providing EDRAs an opportunity to discuss any obstacles they may have encountered. This opportunity for peer interaction and problem solving afforded by these meetings has proven to be a very effective means of developing and communicating best practices relative to specific trials. When new studies are accepted, EDRAs are called in for new study-specific trainings.

For more involved protocols, in-service "boot camp" training sessions are held with the entire EDRA staff, including a review of all study documents, procedures, and best practices in patient approach. These in-service trainings occur 1-2 months after the initiation of the protocol and again every six months for the duration of the protocol. A similar investment in continuing education is the quality assurance process that the

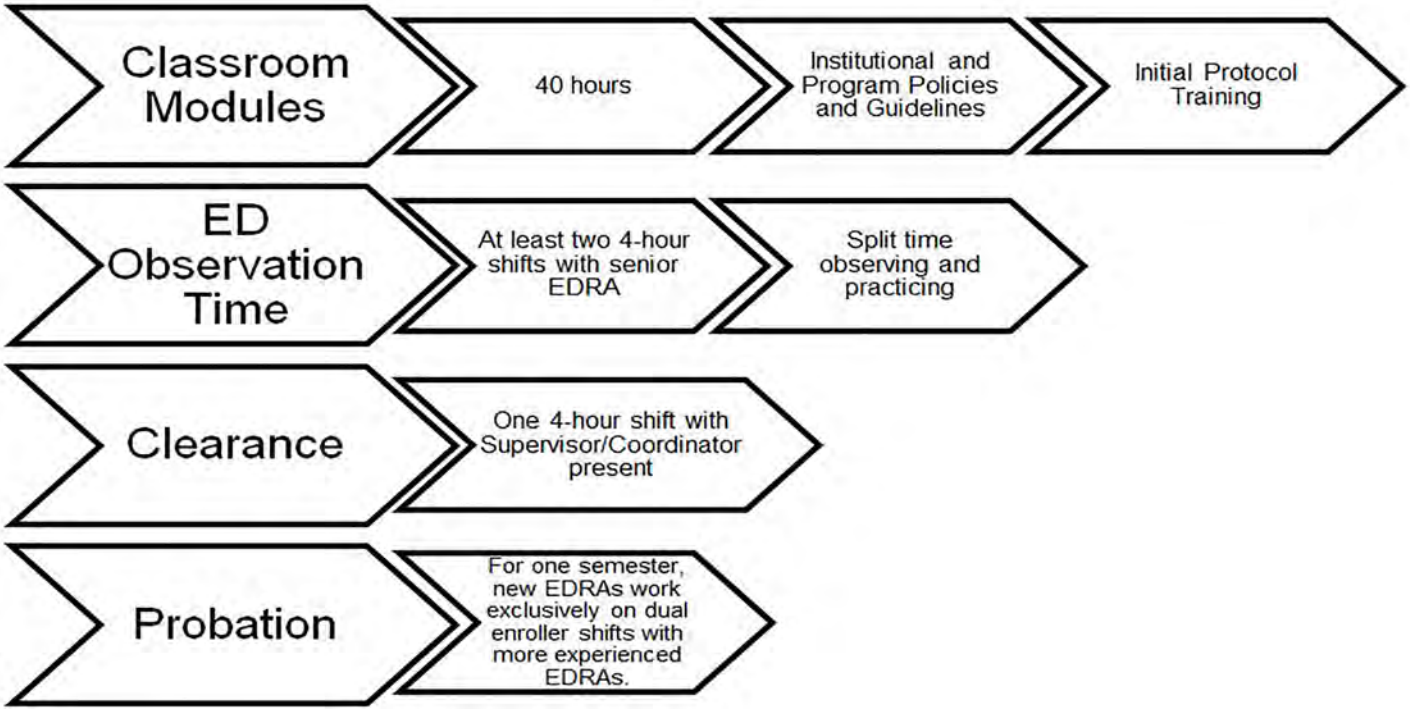

Figure 2. Emergency Department Research Associates (EDRA) initial training timeline.

program undertakes. All errors in screening, enrollment, or other study-related procedures and guidelines are addressed individually within one week. This time-sensitive response allows for the mistake to be promptly corrected and for the EDRA to learn from the mistake.

Because the EDRAs are college students, there are often long periods of excused absence while they are with the program (e.g., summer recess, semester abroad). During these absences, other EDRAs increase their hours spent enrolling (e.g., a subset of EDRAs work ≥ 30 hours/week during the summer) or additional EDRAs are hired to sustain the quality of service provided by our program. Those EDRAs who enroll on a more intensive schedule during the winter and/or summer breaks tend to develop rapidly, as they are afforded greater opportunities to refine their patient-approach style. To maintain the quality of the work upon an EDRA's return from an absence, EDRAs have three learning modules to complete: an online policy review with a competency check; a classroom review of study and training updates; and an abbreviated evaluation shift with the EDRA coordinator.

In addition to our extensive training protocols, we have developed a rigorous quality assurance (QA) process for monitoring study progress and efficiency, as well as for providing quantifiable, formative feedback to the EDRAs. Specifically, EDRAs are required to maintain a shift chart including the name, medical record number, chief complaint, and research disposition of all eligible patients arriving to the ED during enrollment hours. Twice a month, every visit to the ED is pulled in an EMR report for age, sex, chief complaint, method of arrival, and diagnosis. These data are then compared to the hard-copy shift charts that the EDRAs use to ensure that all potentially eligible patients are being screened during enrollment hours. The shift chart allows the EDRA to demonstrate that work is being done, even on patients who are not eligible, who refuse to participate, or who are missed for other reasons.

Formal performance assessments are done quarterly throughout the program, as well as at the end of the EDRA's time as a student or at the request of the individual. These assessments are based on feedback from clinical and research staff, and focus on five core competencies identified in successful EDRAs: communication skills, community interaction skills, critical thinking, personal presentation, and policy adherence. EDRAs are also assessed on their enrollment performance and any quality assurance and improvement concerns that have arisen. These assessments also serve as a mechanism by which EDRA readiness can be evaluated for additional clinical and research opportunities.

TYPICAL EDRA RESEARCH ACTIVITIES

Monitoring of patients presenting to the ED is required for nearly all of the studies that our EDRA program engages in. As representatives of the Department of EmergencyMedicine, our EDRAs are able to use the URMC EMR track-board to monitor the basic characteristics of patients presenting to the

ED. Each EDRA has a separate EMR login with rights to view information on ED patients, and each login is monitored by hospital administration for appropriate usage (e.g., only viewing study-related information; limiting access to sensitive behavioral/psychiatric health information). EDRAs use this tool to initially screen patients for eligibility (e.g., age range, presenting complaint, method of arrival). Some studies then require the EDRA to contact a principal investigator or study coordinator to alert them of a potentially eligible patient, at which point our program involvement with the patient may be complete. Other studies require the EDRA to approach those patients who meet the inclusion criteria in the EMR. EDRAs then introduce themselves and the study to the patient, offer to answer any questions, determine capacity for providing consent using standardized procedures appropriate for the particular study,[9] and obtain and document informed consent (whether verbal or written).

Over the past 26 months, EDRAs have averaged 222 enrolled participants per month (SD = 79.92; see Figure 3). This average actually underrepresents EDRA recruitment activities, as it does not include enrollments in studies where EDRAs are only responsible for identifying potential participants and notifying study teams. During this same time period, our program has been actively enrolling for an average of 8.98 studies at a time (SD = 1.61; range = 7 - 12). Importantly, across the wide variety of studies our EDRAs enroll in, we have demonstrated a monthly average rate of 2.99 enrollments for every patient refusal (SD = 1.10).

The responsibilities of our EDRAs following consent are highly variable. Certain research protocols require the EDRA to contact the contracted study team to hand off the consented patient, while others require the EDRA to perform study procedures. These procedures could include administering surveys, obtaining specimens (e.g., nasal swabs, saliva, blood), or performing brief interventions (e.g., brief motivational interviewing, referral to treatment).

Our EDRAs are also often required to approach and survey providers (e.g., emergency physicians, nurses, emergency medical technicians) involved in the care of enrolled patients. We have developed procedures for collecting needed study information without hampering clinical efforts, and clinical leadership provides consistent support for our research efforts.

OPPORTUNITIES FOR EXCEPTIONAL EDRAS

Our program at URMC has developed a system for both rewarding EDRAs who demonstrate excellence and facilitating sustainability/institutional memory long term. Specifically, the breadth and depth of studies that our program is simultaneously engaged in often requires additional performance analysis, data management, and administrative work. Those EDRAs who perform well enrolling patients and who demonstrate an interest in expanding their experience level are used to fill these roles on a temporary basis (e.g., 2-3 weeks to three months). Developing this experience base greatly assists our long-term efforts for the program, as we primarily hire into the EDRA supervisor and coordinator positions from within the program.

Our program is also relatively unique among RA programs with regard to clinical integration. Specifically, since the summer of 2010 senior members of the EDRA program who show significant aptitude have been offered positions as a provider assistant and liaison (PAL). The PAL position provides an undergraduate support staff person to attending

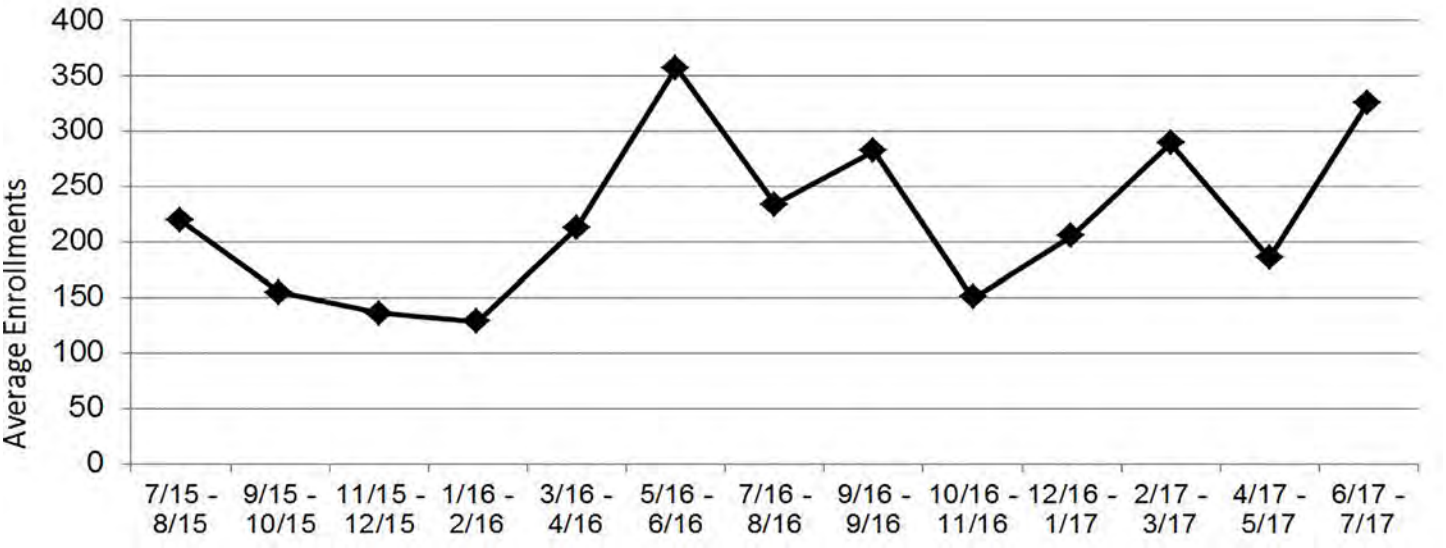

Figure 3. Emergency Department Research Associates monthly enrollments over time.

emergency physicians in the ED during peak hours to improve provider productivity, residency teaching and tracking, and patient satisfaction. PALs work side by side with attending physicians to help maintain assessments details (e.g., expedite delivery of lab and imaging results when needed), make phone calls (e.g., contacting primary care physicians and hospital consults), coordinate discharge resources, care for patient comfort needs, assist with traumas and critically ill patients in a non-medical role, and assist visitors. We have received consistent feedback from providers that the PAL program helps improve ED efficiency. Over the past five years, PALs have provided an average of 142.18 hours of service in the ED per month (SD = 48.56).

We also offer exceptional EDRAs study-specific training opportunities that will generalize to their future work. For example, a subset of our EDRA team recently received phlebotomy training and certification to better facilitate enrollment on several of our ongoing studies. Other EDRAs have become certified to work in a clinical laboratory as a way to enhance the efficiency of a set of studies examining biomarkers among ED patients. These students are then able to perform study-related procedures outside of the ED. Our program aims to continually develop these types of skills among our EDRAs to enhance our capacity for engaging in a broad set of research protocols.

CONCLUSION

The EDRA program at URMC has evolved significantly over its 20 years of service to the university. Our current model has consistently resulted in high enrollment rates across a variety of recently funded, multi-center studies. Much of this success can be attributed to (a) the formalized, extensive, and continuous training of the EDRAs, and (b) program efforts to integrate EDRAs into the clinical environment (i.e., dedicated space in the ED, access to electronic medical records). Nascent programs are encouraged to place much of their efforts into these specific areas of program development, as well as identifying and formalizing methods for accessing high-quality, engaged enrollers (e.g., undergraduate institutions, non-profit organizations, etc.). The design of our program has allowed for continual improvement in the quality of the enroller workforce, with the majority of students applying for and enrolling in post-graduate education in the health professions. This improvement and expansion in the URMC EDRA program requires continual investment on the part of the leadership team and ED, as a whole, though the benefits to investigators within and outside the department significantly outweigh these costs.

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3 for the Price of 1: Teaching Chest Pain Risk Stratification in a Multidisciplinary, Problem-based Learning Workshop

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Introduction: Chest pain is a common chief complaint among patients presenting to health systems and often leads to complex and intensive evaluations. While these patients are often cared for by a multidisciplinary team (primary care, emergency medicine, and cardiology), medical students usually learn about the care of these patients in a fragmented, single-specialty paradigm. The present and future care of patients with chest pain is multidisciplinary, and the education of medical students on the subject should be as well. Our objective was to evaluate the effectiveness of a multidisciplinary, problem-based learning workshop to teach third-year medical students about risk assessment for patients presenting with chest pain, specifically focusing on acute coronary syndromes.

Methods: To create an educational experience consistent with multidisciplinary team-based care, we designed a multidisciplinary, problem-based learning workshop to provide medical students with an understanding of how patients with chest pain are cared for in a systems-based manner to improve outcomes. Participants included third-year medical students (n=219) at a single, tertiary care, academic medical center. Knowledge acquisition was tested in a pre-/post-retention test study design.

Results: Following the workshop, students achieved a 19.7% (95% confidence interval [CI] [17.3-22.2%]) absolute increase in scores on post-testing as compared to pre-testing. In addition, students maintained an 11.1% (95% CI [7.2-15.0%]) increase on a retention test vs. the pre-test.

Conclusion: A multidisciplinary, problem-based learning workshop is an effective method of producing lasting gains in student knowledge about chest pain risk stratification. [West J Emerg Med. 2018;19(3)613-618.]

INTRODUCTION

Chest pain is a common medical complaint, accounting for 8-10 million emergency department (ED) visits annually.[1] Health systems care for patients with acute chest pain by using multiple medical disciplines (emergency physicians, primary care physicians, and cardiologists) working as a team. Patients with chest pain typically present to the ED or are seen first by their primary care provider and then sent to the ED. After ED evaluation, low-risk patients are often asked to follow up with primary care, while high-risk patients and those having acute coronary syndrome (ACS) events receive cardiology consultations and are hospitalized for further care. Despite its frequency, the evaluation of patients with chest pain remains complex and nuanced. Although most patients do not have a life-threatening illness, inadvertent discharge of a patient with ACS can result in serious morbidity or mortality.[2]

To avoid missing ACS, while also avoiding over-testing of very low-risk patients, many health systems have adopted

objective and multidisciplinary, risk-stratification care pathways.[3]

Given the frequency of chest pain as a chief complaint, third-year medical students have ample exposure to patients with acute chest pain while on their emergency medicine (EM) and internal medicine (IM) clerkships. However, the structure of the traditional third-year curriculum, in which a student rotates within a single discipline and sees a patient through one discipline's lens, may lead to suboptimal understanding of the patient's multidisciplinary care. To foster greater understanding of a multidisciplinary, team-based approach to the care of patients with acute chest pain, we developed a multidisciplinary, problem-based learning workshop (MD-PBW).

Prior studies on multidisciplinary education have generally been small, with a focus on measuring the satisfaction of learners and educators.[4,5]. While these are important metrics to ensure sustainability of an educational tool, the ability of the tool to deliver and encourage retention of knowledge is at the core of most educational endeavors. In this analysis, we tested whether our MD-PBW increased the medical student's knowledge of chest pain risk-stratification care and whether they retained this knowledge. We hypothesized that students would demonstrate improved knowledge and would retain a significant portion of this knowledge, as evidenced by scores on pre-tests, post-tests, and knowledge-retention tests, as a result of this educational intervention.

Population Health Research Capsule

What do we already know about this issue?
Student and teacher satisfaction for multidisciplinary, problem-based learning workshops (MD-PBW) has been established, but outcomes data testing their effectiveness are limited.

What was the research question?
Does teaching cardiac risk stratification in a MD-PBW produce demonstrable improvement in student knowledge?

What was the major finding of the study?
Results of this study show that cardiac risk-stratification concepts can be effectively taught in a MD-PBW.

How does this improve population health?
Teaching cardiac risk stratification is critical for patient care. Doing so in a multidisciplinary manner reflects the teamwork needed for efficient care.

METHODS

Study Design

This is a pre-/post-retention test study designed to assess the knowledge acquisition and retention of medical students participating in a MD-PBW focused on chest pain risk stratification. Third-year medical students participated in this study as part of their required IM clerkship. This study was reviewed by the institutional review board of the sponsoring organization and met criteria for exemption based on category 1.

Population

All participants in this study were third-year medical students enrolled in Wake Forest School of Medicine, an allopathic medical school with an annual enrollment of about 120 students, located in Winston-Salem, NC. These students participated in the educational intervention at varying times during the third-year of medical school, during their required 12-week IM clerkship. This clerkship includes nine weeks of inpatient care, of which two are cardiology. Roughly half of the students had experienced the required four-week EM clerkship and four-week family medicine clerkship prior to their IM clerkship, so presumably would have been exposed to the evaluation of patients presenting with chest pain.

Workshop

During the 10th week of their IM clerkship, students participated in two complementary educational events. First was a video presentation, developed in the style of the whiteboard videos made famous by Kahn Academy, viewed by the students detailing the complexities of evaluating patients with chest pain. The video included details of typical and atypical presentations, risk factors for coronary artery disease (CAD), and the use of the HEART Pathway[6] to risk stratify patients with chest pain.

Following the pre-learn video, students attended a 1.5-hour cardiac risk assessment workshop. During the workshop, students divided into small groups of 8-10 students, each led by three facilitators, with one facilitator from each discipline: EM, general IM, and cardiology. Each small group worked through three simulated patient cases in a PBL-based format. Cases were developed to represent low, intermediate, and high-risk presentations for ACS. Throughout the session, the students were guided by multidisciplinary faculty to organize, synthesize and prioritize the patient's medical data into an appropriate differential diagnosis and management plan. Facilitators focused on using a multidisciplinary, team-based approach and incorporating objective tools, such as the HEART Pathway,[6] to more accurately risk stratify patients with acute chest pain.

Testing

Prior to viewing the animated whiteboard video on chest pain evaluation, students completed a pre-test. Following the MD-PBW, students completed the post-test within one week. One month after the MD-PBW students were invited to complete a retention test. Each test had 10 questions from a question bank. These questions were developed by CB, KA, and SM, and four of the 15 questions were used and showed evidence of validity in a previous investigation by Hartman et al.[7] Some of the questions on the post-test or retention test were seen on previous tests given during the intervention. Students had 30 minutes to complete each test. Tests were taken electronically using an online testing platform. Students were given a week to take the pre-test and post-test at their own convenience. Retention tests could be taken for up to five months after the MD-PBW.

Analysis

We analyzed test scores using descriptive statistics, such as mean and standard deviation (SD). Mean percent correct and differences between mean pre-, post-, and retention tests were calculated along with corresponding 95% confidence intervals (CI). To assess for significant differences in test scores we compared the pre-, post-, and retention-test scores using paired t-testing. Statistical analysis was performed using SAS 9.4 (Cary, North Carolina).

RESULTS

From July 2014 to July 2016, 219 medical students participated in the MD-PBW. Among these students, 219 (117 male, 112 female) completed a pre-test, 195 completed a post-test, and 84 completed a retention test. The mean percentage of questions answered correctly on the pre-test was 69.8% (SD 15.7%, 95% CI [67.7-71.2%]), compared to 89.6% (SD 11.4%, 95% CI [88.0-91.2%]) for the post-test, and 81.2% (SD 13%, 95% CI [78.4-84.0%]) for the retention test. Mean test scores are summarized in Table 1 and graphically represented in Figure 1.

Paired comparison of test scores identified 190 students with complete pre-tests and post-tests. Among these students the average increase in score from pre-test to post-test was 19.7 (SD 16.9%, 95% CI [17.3-22.2%]). For the retention portion, 84 students finished both a pre-test and retention test, yielding an average increase in score of 11.1% (SD 17.5%, 95% CI [7.2-15.0%]). Post-tests and retention tests were both completed by 81 students. Among those students, scores decreased by 9.8% (SD 17.6%, 95% CI [5.9-13.6%]). Paired changes in test scores are summarized in Table 2 and graphically represented in Figure 2.

DISCUSSION

In an ever-changing medical environment, physicians must learn to practice as members of a multidisciplinary team to optimize patient care. Given how commonly patients with chest pain seek care and the relative infrequency with which they are found to have acutely life-threatening disease, it is paramount that budding physicians learn how to make the best use of the available resources within various care settings to optimize outcomes and reduce resource utilization. A focus on service lines and multidisciplinary care to manage these patients has been growing for decades. The number and success of chest pain centers and emergency department chest pain units are prime examples of this trend,[8,9] though education about risk stratification of chest pain is still frequently siloed in a specialty-by-specialty approach. This study aimed to institute and evaluate a multidisciplinary educational intervention to teach students about current practice in risk stratification of patients who present with chest pain.

In our study, medical students demonstrated improved knowledge, both immediately following the intervention as well as up to five months afterward. Variation in the pre-workshop knowledge base of the students is likely related to pre-intervention experience, regarding time in third year as a whole, as well as other clerkships completed. At our institution, third-year medical students have eight required, third-year clinical clerkships, with IM and EM occurring in opposite semesters. This workshop was housed within the IM clerkship, so during the early part of the year, students had fairly limited exposure to the evaluation of patients with chest pain. On the other hand, during the latter half of the year, the majority of students involved in the workshop had completed the EM clerkship, so they were already exposed to the early evaluation of this patient subset. As expected, some of the improvements in knowledge demonstrated by students on the post-test immediately following the workshop diminished over time, as evidenced by performance on the retention test. However, students still had significantly better scores on the

Table 1. Mean performance on pre/post/retention tests.

Test phase	Mean	SD	95% CI lower limit	95% CI upper limit
Pre-test	69.8	15.7	67.7	71.9
Post-test	89.6	11.4	88	91.2
Retention test	81.2	13	78.4	84

SD, standard deviation; *CI*, confidence interval.

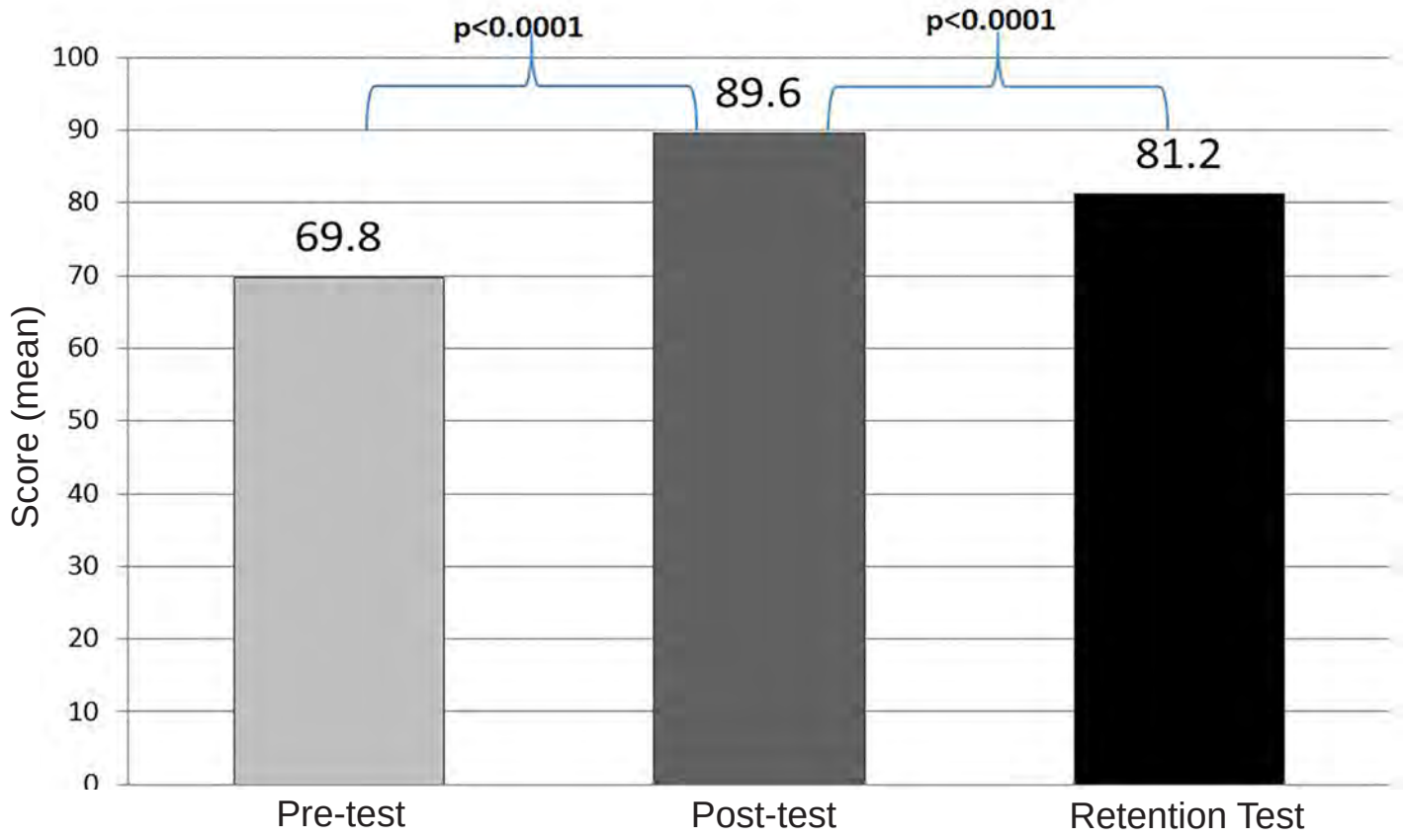

Figure 1. Mean student performance on pre-, post-, and retention test.

retention compared to the pre-test, demonstrating retention of much of the knowledge gained.

These results are promising for a number of reasons. In the changing medical landscape, team-based, coordinated patient care is more and more important. Our results demonstrate that our multidisciplinary, team-based approach to teaching risk stratification of patients with acute chest pain to medical students can produce lasting improvements in knowledge that ideally will translate into better patient care and improved patient outcomes. We believe that a multidisciplinary approach more closely mimics real-world practice, recognizing that patients with chest pain may seek care in a variety of settings, and once they have been initially evaluated and treated, they continue to need evaluation and treatment to ensure that those at high risk are receiving appropriately aggressive care, while lower-risk patients have further evaluation to determine the likely non-cardiac cause of their pain, frequently in the outpatient setting.

We also introduced the students to the HEART Pathway,[6] a risk-stratification tool used in patients with chest pain concerning for ACS. By including in our discussion a risk-stratification tool designed to focus more resource-intensive

Table 2. Difference in performance on testing before and after intervention.

Paired T-test	Mean	SD	95% CI lower limit	95% CI upper limit	P value
Pre vs. Post-test	19.7	16.9	17.3	22.2	<0.0001
Pre vs. retention test	11.1	17.5	7.2	15	<0.0001
Post vs. retention test	-9.8	17.6	-13.6	-5.9	<0.0001

SD, standard deviation; *CI*, confidence interval.

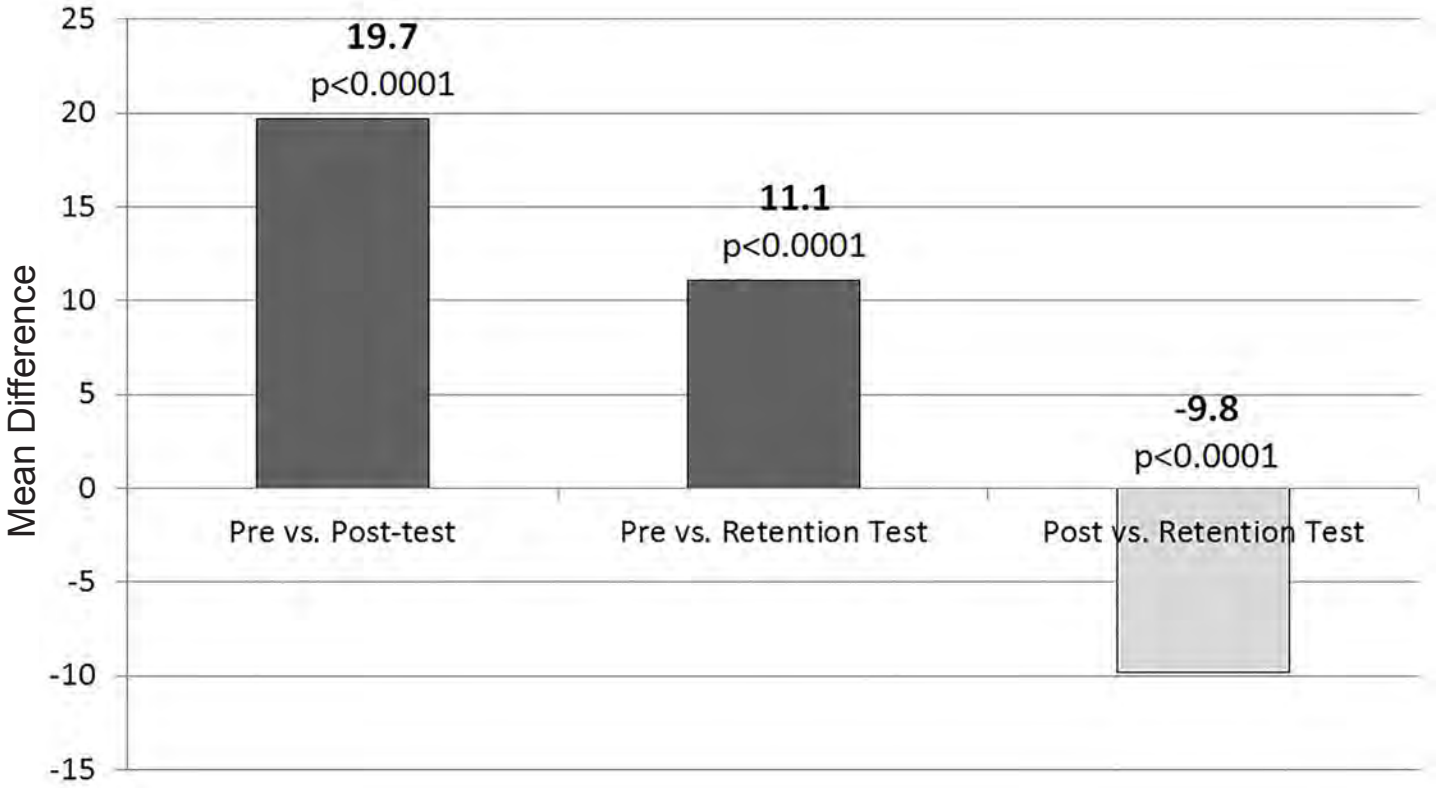

Figure 2. Difference in mean test performance between pre- and post-test, pre- and retention test, and post-test and retention test. Differences in performance all met statistical significance.

cardiac testing and therapies on the patients who are most likely to benefit, students can begin to understand the benefits of more efficient, value-based care. In addition, early education on this topic helps to disseminate information across the potential specialties that the students ultimately decide to pursue, helping to implement multidisciplinary care in a continuous fashion as patients move through initial evaluation and follow-up care.

LIMITATIONS

This study does have several limitations. First, our study included only a single institution where widespread training for clinical staff on the use of the HEART Pathway as a chest pain risk-stratification tool had already taken place. The implementation and success of a similar educational workshop to the one described here may not be as readily achieved in an institution without a similarly agreed-upon local standard of care. Second, many students did not complete all three tests. This is especially evident in the low completion rate of the retention test. While we believe that the improvements in knowledge are likely representative of the entire group, the possibility of students self-selecting based on how much they remembered of the information taught must be considered. Third, the data do not include a control group, so no comment can be made about whether this MD-PBW is more effective than the traditional teaching model. An argument could be made that a teaching model that more closely mimics the team-based care paradigm being adopted by many health systems to minimize fragmented care is likely still valuable, though further study would be needed to prove this point.

Other studies suggest that similar educational interventions are viewed positively by students.[4,5] No satisfaction data were collected for this MD-PBW. One consideration for future research would be a study that combines satisfaction and effectiveness of a similar intervention in order to better justify the resources required for such an undertaking. It would then be up to a particular institution to decide what amount of educational value would be required to take on an educational offering if it was not viewed positively by students and educators.

Finally, further study would be necessary to determine whether this information was retained long-term. Even more

important would be investigation on whether this workshop changed real-time clinical practice and patient outcomes.

CONCLUSION

A multidisciplinary, problem-based learning workshop increased the knowledge of cardiac risk stratification in patients who present with chest pain among third-year medical students. This builds on previous literature showing increased learner and educator satisfaction with similar educational interventions. Similar MD-PBWs on myriad conditions where a multidisciplinary team approach is beneficial could be used to prepare medical students to provide optimal patient care to improve patient outcomes.

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The Uphill Battle of Performing Education Scholarship: Barriers Educators and Education Researchers Face

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Introduction: Educators and education researchers report that their scholarship is limited by lack of time, funding, mentorship, expertise, and reward. This study aims to evaluate these groups' perceptions regarding barriers to scholarship and potential strategies for success.

Methods: Core emergency medicine (EM) educators and education researchers completed an online survey consisting of multiple-choice, 10-point Likert scale, and free-response items in 2015. Descriptive statistics were reported. We used qualitative analysis applying a thematic approach to free-response items.

Results: A total of 204 educators and 42 education researchers participated. Education researchers were highly productive: 19/42 reported more than 20 peer-reviewed education scholarship publications on their curricula vitae. In contrast, 68/197 educators reported no education publications within five years. Only a minority, 61/197 had formal research training compared to 25/42 education researchers. Barriers to performing research for both groups were lack of time, competing demands, lack of support, lack of funding, and challenges achieving scientifically rigorous methods and publication. The most common motivators identified were dissemination of knowledge, support of evidence-based practices, and promotion. Respondents advised those who seek greater education research involvement to pursue mentorship, formal research training, collaboration, and rigorous methodological standards.

Conclusion: The most commonly cited barriers were lack of time and competing demands. Stakeholders were motivated by the desire to disseminate knowledge, support evidence-based practices, and achieve promotion. Suggested strategies for success included formal training, mentorship, and collaboration. This information may inform interventions to support educators in their scholarly pursuits and improve the overall quality of education research in EM. [West J Emerg Med. 2018;19(3)619-629.]

INTRODUCTION

In recent years, educators have been increasingly challenged to apply evidence-based practice to their teaching. Despite increased production and dissemination of education scholarship, there is still a great need to improve the quality of medical education research and associate educational practices with patient care outcomes.[1-9] Medical educators have reported multiple challenges to their scholarly pursuits, including lack of time, expertise in research methodology, funding, mentorship, collaborators, research support, and reward for their efforts.[10-12] Limited data suggest that lack of time may be the greatest barrier.[11]

A recent workforce study of emergency medicine (EM) educators suggested that while education faculty make up a substantial proportion of a department's core faculty, departments often lack the full complement of education leadership positions.[13] Additionally, education faculty must frequently divide their non-clinical time among multiple academic roles.[13] It was also noted in this study that many departments lack personnel with education research expertise.[13] Potential interventions have been proposed to address these needs, including building communities of practice to enhance collaboration, increasing opportunities for funding, and devising strategies to gain protected time.[10] Despite these preliminary studies, how EM educators perceive these barriers and what interventions would be most beneficial in helping to overcome them is still not well understood.

The Council of Emergency Medicine Residency Directors (CORD) Education Scholarship Task Force and CORD Academy for Scholarship in Education in Emergency Medicine recommended that the EM education research community conduct a formal needs assessment to analyze the specific needs of EM educators in order to design and implement interventions to support educators and the field of education research. The objective of this study was to evaluate the perspectives of both core-faculty educators and successful education researchers with regard to the supporting factors and motivators to performing education research, as well as the barriers and their perceived impact, and proposed solutions to assist them in their scholarly endeavors.

Population Health Research Capsule

What do we already know about this issue?
Educators face multiple challenges in achieving their education scholarship goals. There is a need to illuminate effective ways to support them and to improve the quality of education research.

What was the research question?
What are educators' perceptions regarding barriers to performing scholarship and potential strategies for success?

What was the major finding of the study?
Common barriers were lack of time and competing demands. Suggested interventions were training, mentorship, and collaboration.

How does this improve population health?
This information may inform interventions to support educators in their scholarly pursuits and improve the overall quality of education research in emergency medicine.

METHODS

Study Setting and Participants

Core EM education faculty (defined as those individuals whose main academic role is dedicated to the educational mission of the department, including undergraduate medical education, graduate medical education, and faculty development), were identified through email inquiry of individual program leadership (program director and/or program coordinator), program websites, and personal knowledge. We identified successful EM education researchers in one of two ways: (1) by authorship on a manuscript included in *Academic Emergency Medicine*'s "Critical Appraisal of Emergency Medicine Education Research: The Best Publications of [years 2008-2014]"; or (2) designation of "Scholar" from the Association of American Medical Colleges Medical Education Research Certificate at CORD program.[14-21] When an individual belonged to both cohorts, s/he was enrolled in the education researcher arm of the study only. Data collection occurred between October 2015 and December 2015.

This study was deemed exempt by the institutional review board of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.

Study Design

This was a cross-sectional, mixed-methods needs assessment study, employing a standardized, survey instrument (with validity evidence previously collected) that allowed for free responses suitable for qualitative analysis. Subjects were invited to participate by email and provided with a link to an Internet-based survey, administered through SurveyMonkey®.[22] Two follow-up email invitations were sent at weekly intervals to non-responders. Informed consent was implied by those participants who chose to click on the survey link. To maximize response rate and include all possible relevant data, completion of all survey questions was not required.

Instrument Development

The authors developed two surveys, one for each stakeholder group, after literature review and input from members of the CORD Education Scholarship Taskforce to maximize content validity. Instrument development followed established guidelines for survey research.[23] The surveys consisted of multiple-choice, 10-point Likert scale, and free-response items. To optimize response process validity, items were read aloud among members of the study group and piloted with a small group of reference subjects. Based on results of piloting, we then revised survey

items for clarity and brevity. Final versions of the survey instruments are available in Appendix.

Statistical Analysis

We calculated and reported descriptive statistics for multiple-choice and rating-scale items. Two researchers experienced in qualitative methods, JJ and LY, independently analyzed data from free-response items using a thematic approach. They examined data line by line to identify recurring concepts and then assigned codes, which were further refined into themes using the constant comparative method.[24] After independent review, the two researchers met to establish a final coding scheme that was applied to all data. Inter-rater agreement was 93.9% and 89.4% for data from core educators and education researchers, respectively. Discrepancies were resolved by in-depth discussion and negotiated consensus.

RESULTS

General Results

A convenience sample of 204 core educators and 42 education researchers, from 118/164 (72%) EM training programs in the U.S. and Canada completed the surveys. Of the core educators responding, 159/197 (80.7%) reported performing research, of whom 111 (69.8%) performed research in medical education. Education researchers were highly productive: 19/42 (45.2%) reported more than 20 peer-reviewed education scholarship publications on their curricula vitae. In contrast, 68/197 (34.5%) of core educators had not published any education scholarship in the last five years. Characteristics of participants and scholarly productivity are shown in Table 1.

Motivators, Rewards, Career Satisfaction

Our qualitative analysis revealed a number of motivating factors for performing education research in both cohorts. The most prominent of these factors were the desire to disseminate knowledge, support evidence-based practices, meet academic promotion requirements, and personal interest. Results of qualitative analysis for education researchers and core educators are shown in Table 2 and Table 3, respectively. When asked to specifically rate various motivators, education researchers identified personal intellectual stimulation and to become a better teacher as most influential with mean ratings of 8.52 and 7.21 respectively on a 10-point scale (Figure 1). Core educators also rated these factors highest with mean ratings of 7.57 and 6.91 respectively (Figure 1).

The most common rewards education researchers reported include a sense of accomplishment by contributing to the body of knowledge of the field (39/42; 92.9%) and intellectual satisfaction from solving a problem (39/42; 92.9%) (Figure 2). Core educators also reported rewards of satisfaction of contributing to the body of knowledge of the field (123/147; 83.7%) and intellectual satisfaction of solving a problem (114/147; 77.6%) (Figure 2). Education researchers were satisfied with their achievements in education research and their overall careers, with mean ratings of 7.02 and 8.22 respectively, and felt that performing research contributed positively to their career (mean rating 7.14). Core educators were also satisfied with their careers with a mean rating of 7.62, but less satisfied with their achievements in education research with a mean rating of 4.54. Teaching was the most prominent contributor to career satisfaction for core educators (Table 3).

Barriers and Challenges

Lack of time was the greatest barrier for core educators, with mean rating of 8.61 on a 10-point scale (Figure 3). Core educators reported spending the majority of their time on clinical duties, with mean hours per week of 21.95 ± 10.90, followed by administrative duties 17.53 ± 10.38, teaching 7.58 ± 5.62, research 3.6 ±4.30, and other scholarly work 3.91 ± 3.51. Ideally, core educators would prefer to spend less time on clinical and administrative duties and more time on teaching, research, and other scholarly work. Desired mean hours/week include 18.42 ± 8.45 on clinical duties, 11 ± 7.38 on administrative duties, 9.61 ± 5.91 on teaching, 6.92 ± 5.16 on research, and 4.81 ± 3.41 on other scholarly work. The most prominent challenges for core educators and education researchers were lack of time and competing demands (Tables 2 and 3).

Core educators also cited lack of methodologic expertise as a major barrier. Approximately half of responding core educators (91/183; 49.7%) reported having a mentor. Major themes regarding the positive impact a mentor had on their ability to perform education scholarship for core educators included motivation and training. It should be noted, however, that a contrasting major theme identified was that the core educator's mentor did not impact this area at all (Table 3). The major theme regarding reasons educators did not have a mentor was lack of an identifiable candidate.

Strategies for Success

Education researchers and core educators felt that protected time, a collaborative community/research network, and mentorship would help them achieve their research goals (Tables 2 and 3). Core educators indicated they would like to acquire more skills in research study design (112/183; 61.2%), qualitative analysis (88/183; 48.1%), scientific writing (91/183; 49.7%), and quantitative analysis (77/183; (42.1%). The preferred formats for learning skills in medical education research were an online longitudinal course or a longitudinal faculty development course offered at their home institution with 65/181 (35.9%) and 61/181 (33.7%) selecting these options. Less-preferred formats included a daylong session at a professional society national meeting (25/181; 13.8%) or an advanced degree (21/181; 11.6%). Major themes regarding advice from both stakeholder groups to those wishing to become more involved in research included obtaining formal

Table 1. Characteristics of EM core educators and education researchers surveyed with regard to barriers and motivations to conduct research.

	Core educators	Education researchers
Gender		
Male	131/204 (64.2%)	ed27/42 (64.3%)
Female	73/204 (35.8%)	15/42 (35.7%)
Age		
<35 years old	26/204 (12.7%)	3/42 (7.1%)
35-50 years old	143/204 (70.1%)	26/42 (61.9%)
51-60 years old	35/204 (17.2%)	12/42 (28.6%)
>65 years old	0/204 (0%)	1/42 (2.4%)
Academic rank		
Instructor	8/204 (3.9%)	0/42 (0%)
Assistant professor	104/204 (51.0%)	15/42 (35.7%)
Associate professor	62/204 (30.4%)	13/42 (31.0%)
Professor	27/204 (13.2%)	11/42 (26.2%)
Other	3/204 (0.01%)	3/42 (7.1%)
Degrees held*		
MD	187/204 (91.7%)	39/42 (92.9%)
DO	16/204 (7.8%)	0/42 (0%)
MPH	12/204 (5.9%)	1/42 (2.4%)
EdD	2/204 (1.0%)	1/42 (2.4%)
PhD	4/204 (2.0%)	4/42 (9.5%)
Other Master's degree	28/204 (13.7%)	15/42 (35.7%)
Other	5/204 (2.5%)	3/42 (7.1%)
Current position(s)*		
Chair	3/200 (1.5%)	N/A
Vice chair for education	13/200 (6.5%)	N/A
Director of medical education	11/200 (5.5%)	N/A
Education fellowship director	7/200 (3.5%)	N/A
Program director	55/200 (27.5%)	N/A
Assist./associate program director	72/200 (36.0%)	N/A
Clerkship director	30/200 (15.0%)	N/A
Assistant clerkship director	4/200 (2.0%)	N/A
Simulation fellowship director	4/200 (2.0%)	N/A
Simulation director	16/200 (8.0%)	N/A
Other	36/200 (18.0%)	N/A
Fellowship training		
Yes	56/204 (27.5%)	14/41 (34.1%)
No	148/204 (72.5%)	27/41 (65.9%)
Types of peer reviewed medical education scholarship published*		
Research manuscript	91/197 (46.2%)	39/42 (92.9%)
Non research manuscript	49/197 (24.9%)	24/42 (57.1%)
Online curriculum	37/197 (18.8%)	14/42 (33.3%)
Online lecture/instructional video	25/197 (12.7%)	4/42 (9.5%)
None	68/197 (34.5%)	1/42 (2.4%)
Other	12/197 (6.1%)	5/42 (11.9%)
Number of peer-reviewed education scholarship publications listed on curriculum vitae		
0-5	162/196 (82.7%)	9/42 (21.4%)
6-10	21/196 (10.7%)	6/42 (14.3%)
11-15	5/196 (2.6%)	5/42 (11.9%)
16-20	5/196 (2.6%)	3/42 (7.1%)
>20	3/196 (1.5%)	19/42 (45.2%)
Formal training in research methodology		
Yes	61/197 (31.0%)	25/42 (59.5%)
No	136/197 (69.0%)	17/42 (40.5%)

*Participants were instructed to select all options that were applicable, and so results may total more than 100%.

Table 2. Results of qualitative analysis for education researchers.

Question	Major themes	Number of comments	Examples
What factors motivate you to perform research?	Dissemination of knowledge	21	"intellectual stimulation, promotion, contribution to the knowledge of the field"
	Support evidence-based practice	20	
	Personal interest	14	
	Intellectual stimulation	11	"1) I'm interested in advancing the field; 2) I like to share my knowledge; 3) I want to change the way we are doing stuff to be more evidence/theory based."
	Promotion	10	
What factors discourage you from spending time working on your research projects?	Administrative/education demands	22	"other admin/teaching responsibilities; less of a focus for promotion; less hope that grants will buy-down time"
	Clinical demands	17	
	Lack of time	16	
	Personal/family demands	7	"other competing interest; not enough local research infrastructure; little institutional support"
	Perceived futility	5	
	Lack of research support	5	
			"1) Finding blocks of time to design research projects and collaborate with other faculty; 2) Finding reliable, valid tools for assessing the impact of education interventions"
What challenges have you encountered in performing education research?	Lack of time	31	"1. Funding opportunities in med educ research often modest limiting ambition of research undertaken. 2. Med ed research tends to focus on problem description and diagnosis and less on development and robust evaluation of potential solutions to improve med education. 3. Linked to this there are often epistemiological battles and silos that hinder the development of interdisciplinary impactful research."
	Lack of funding	18	
	Work not valued/lack of leadership support	14	
	Lack of methodologic expertise	13	
	Lack of access to collaborators	11	
			"Significant time burden with residency administration, lack of formal training or great senior role models in education research, lack of departmental infrastructure to help execute nonclinical research"
			"Lack of departmental/institutional support, lack of monetary support, lack of recognition locally that education is important"
Overall, what do you feel would help you achieve your research goals?	Time	17	"Local recognition of its value, financial support, a community locally that supports this interest"
	Collaborative community/research network	11	
	Access to expertise	9	"Easier access to biostatisticians and study design experts"
	Funding	9	
	Mentorship	6	"Funding. Allowing for better interdisciplinary engagement between Med Ed research and other relevant disciplines/ fields."
	Research support	6	
			"National guidelines for reasonable clinical duties and protected time for education leadership roles"
What advice would you give an EM educator who wants to become more involved in education research?	Obtain formal training	17	"Cultivate mentors, gain a more formal education in education scholarship and don't go there unless you love it"
	Find collaborators	14	
	Secure mentorship	14	
	Practice patience and persistence	6	"find and cultivate relationships with collaborators outside of your department"
	Inform yourself of current practices/ literature	6	
			"1) Identify an area of interest; 2) Take the time to read the literature of what has been done in that area; 3) Seek a mentor in your department or school to provide constructive feedback during the design phase of your research"

Table 3. Results of qualitative analysis of core educators.

Question	Major themes	Number of comments	Examples
What are the major contributors to your career satisfaction?	Teaching	86	"When I witness my residents become a better clinician, educator, or researcher than I am."
	Mentorship	37	
	Professional relationships	35	
	Clinical work	35	"the people I work with, recognizing I am doing something that matters and is very important to the future of medicine"
	Sense of accomplishment	21	
	Variety	17	
			"Sense of accomplishment, benefit of seeing students/residents develop, excellent group that supports education"
			"autonomy for creation/innovation; multiple types of activities to do"
What challenges have you encountered in performing education research?	Lack of time	47	"Mentorship, methodology, time, lack of people interest in the same things…"
	Lack of methodologic expertise	41	
	Challenges with learners as study population	24	
			"lack of respect from chair and others as to importance or rigor of the research"
	Work not valued/lack of leadership support	22	
	Lack of funding	18	"mentorship in simulation education research with rigorous methods; interdepartmental and across college collaboration; lack of resources in the institution"
	Lack of mentorship	15	
	Lack of research resources	13	
			"difficult to assess outcomes. IRB hurdles. Lack of funding. Inadequate expert support."
What advice would you give to an EM educator who wants to become more involved in education research?	Obtain formal training	35	"Seek good mentorship. Consult someone with methodological expertise and someone with statistical expertise while your study is in the design phase."
	Secure mentorship	30	
	Find collaborators	20	
	Access expertise	11	
	Secure protected time	11	"Do a fellowship that emphasizes research methodology and an advanced degree."
	Gather leadership support	10	
			"find a department that supports and rewards education research"
			"partner with nationally active peers"
What factors motivate you to perform research?	Dissemination of knowledge	47	"demonstrate best practices and disseminate knowledge to help others"
	Promotion	46	
	Personal interest	41	
	Intellectual stimulation	31	"allows one to make evidence-based decisions regarding education."
	Job requirements	28	
	Support evidence based practice	23	
	Sense of accomplishment	11	"scientific knowledge advancement, improved patient care"
	Contribution to improvement of healthcare	11	
			"need to "publish or perish""
			"Job satisfaction; Required for RRC"
What factors discourage you from spending time working on your research?	Lack of time	74	"wanting to spend time with kids & friends which have greater value to me, desire to create new educational programs"
	Administrative/education demands	55	
	Clinical demands	36	
	Lack of research support	34	"stretched too thin, lack of mentorship/help with statistics, research support (personnel)"
	Perceived futility	16	
	Personal/family demands	13	
			"Almost anything else I do in my job is easier or more fun. Feeling like I'm pushing a big rock uphill trying to get a research process approved or paper published."
			"Publication rejections of projects I have spent countless hours on completing. Competing administrative and clinical duties that take time."

Table 3. Continued.

Question	Major themes	Number of comments	Examples
Overall, what do you feel would help you achieve your research goals?	Time Mentorship Expertise Research support Funding Collaborative community Leadership support	61 28 27 23 16 15 13	"Protected time for research. Evidence about successful infrastructures. A method of subdividing education research might enhance collaboration. " "greater mentorship, networking, accountability, funding (funding would at least tie me to a grant with deadlines, reports, deliverables, etc.)" "more formal education in medical education research beyond the few classes in my masters, having a statistician that I trust, having collaborators / mentors"
How has your mentor impacted your ability to perform education scholarship?	Positive impact No impact Motivation Training Resources Ideas/innovation	18 18 19 14 14 10	"Has helped me traverse some of the barriers, questioned my proposals in a thoughtful way and suggested strategies for improvement" "I have one mentor specifically trained as a social scientist in qualitative methodology who is actively impacting my ability to perform research by teaching me various skills (e.g. coding, study design, etc.); I have another mentor with EdD background that assisted me with faculty development and educational research/ scholarship, and I have two clinical mentors that connect me to large national networks and communities of practice" "My mentor has been instrumental in all aspects, by teaching me the necessary skills, providing me with opportunities, and continually reviewing my work and giving additional suggestions for improvement" "guidance, accountability, offering ideas I had not considered, motivating me to do the work"
How did you find your mentor?	In department During training Collaborative work	33 24 10	"Through a research conference, an education conference, one from my medical school long ago and one from my current department (my chair)"
Why don't you have a mentor?	Lack of identifiable candidate	46	"no one locally interested in what I am interested in with expertise more than I have" "Proximity, faculty interested in education at home institution early in careers needing mentorship themselves and more senior faculty have other research interests. Education research feels new, although it has been around for quite a while. Perhaps finally getting credit it deserves as a discipline for advancement in Medicine and Medical Schools?"

training, finding collaborators, and securing mentorship (Tables 2 and 3).

DISCUSSION

Critics of medical education research often cite a lack of researcher training and expertise as a key barrier to successful scholarship. While this was identified as a major barrier by our core educator stakeholder group, it is important to note that even formally trained, successful education researchers experienced challenges in this field similar to those who were untrained. In this study, both successful education researchers and core educators identified barriers consistent with prior literature.[10-12] These include barriers that are intrinsic to the researcher such as time constraints and lack of formal research training; extrinsic factors such as lack of funding, lack of research resources, collaborators, mentorship, and leadership support; and barriers inherent to this type of scholarship such as challenges with learners as a study population and perceived

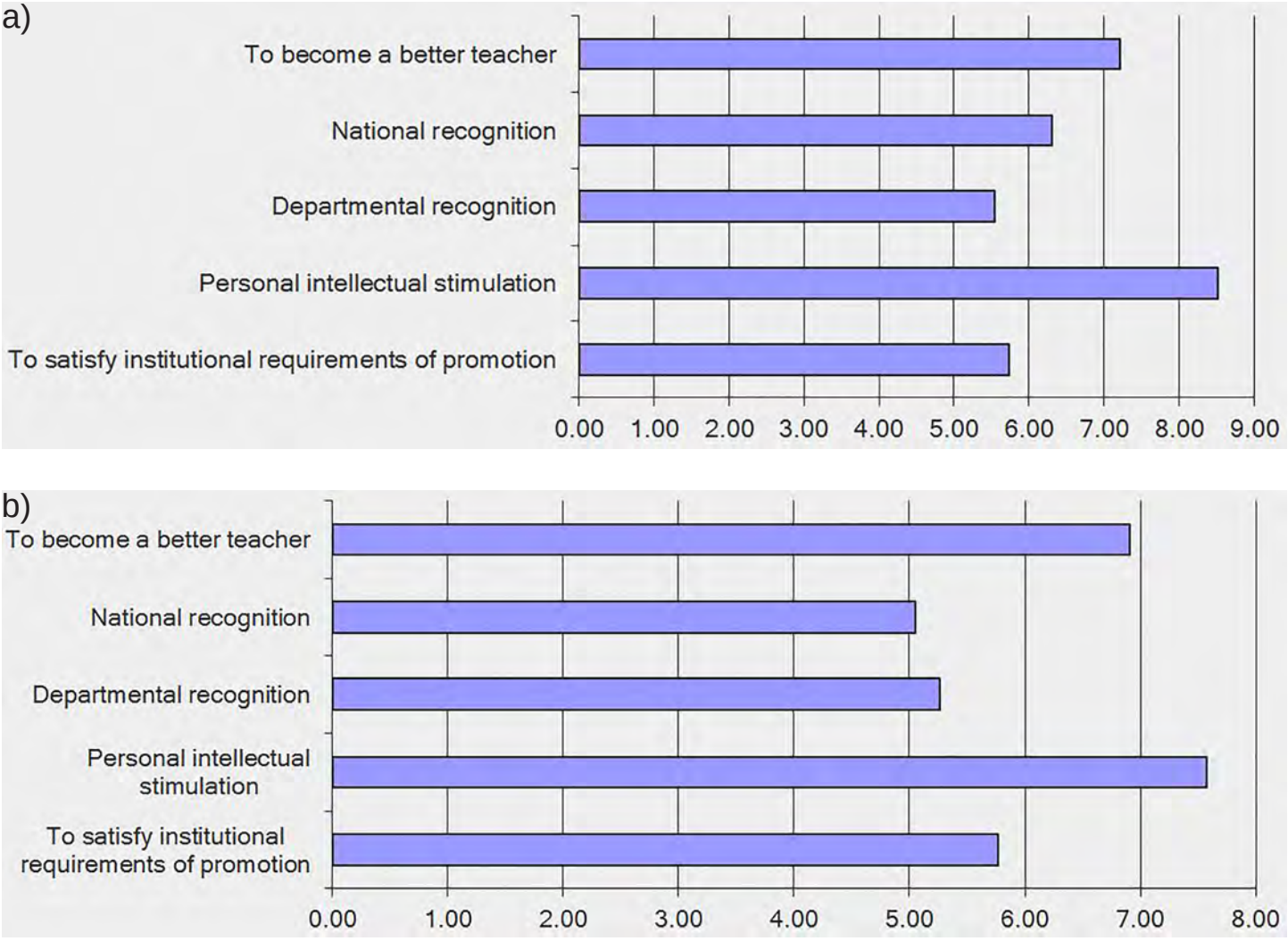

Figure 1. Mean ratings for motivating factors to perform research for a) education researchers and b) core educators (1= Does not motivate me at all; 10= Extremely motivates me).

futility. The fact that we saw a great deal of overlap between these two stakeholder groups suggests that these barriers may exist regardless of researcher experience or career stage.

The greatest barrier in this study seemed to relate to time constraints. This is not surprising given prior literature emphasizing the complexity and importance of this barrier as well as a prior EM workforce study demonstrating that educators often play multiple critical academic roles and have less time available for scholarly pursuits compared to other job requirements.[11,13] This previously identified mismatch between actual and ideal distribution of workload may not only negatively impact an educator's ability to perform scholarship but may also adversely affect career satisfaction and burnout.[13,25]

Mentorship was also identified as barrier for core educators: less than half of participants in this group reported having a mentor owing to lack of availability. This may indicate that currently few experts are available to meet the needs of education scholars and/or that those with expertise exist outside the field of EM.[13] Interestingly, successful education researchers were less likely to cite lack of mentorship as a barrier, but did recognize its importance to those looking to pursue education research. This may be because these individuals had available mentorship in their formative years, which may have contributed to their success. Those educators who did have mentorship identified multiple ways their mentorship positively contributed to their scholarly pursuits. It will be important to continue training interested educators in this area to build a cadre of medical education research experts who can meet the training and mentorship needs of future generations and for would-be scholars to look outside of their institution and/or specialty to find this expertise.

We also found a great deal of overlap between motivators to performing education scholarship between core educators and successful education researchers, which may reflect core

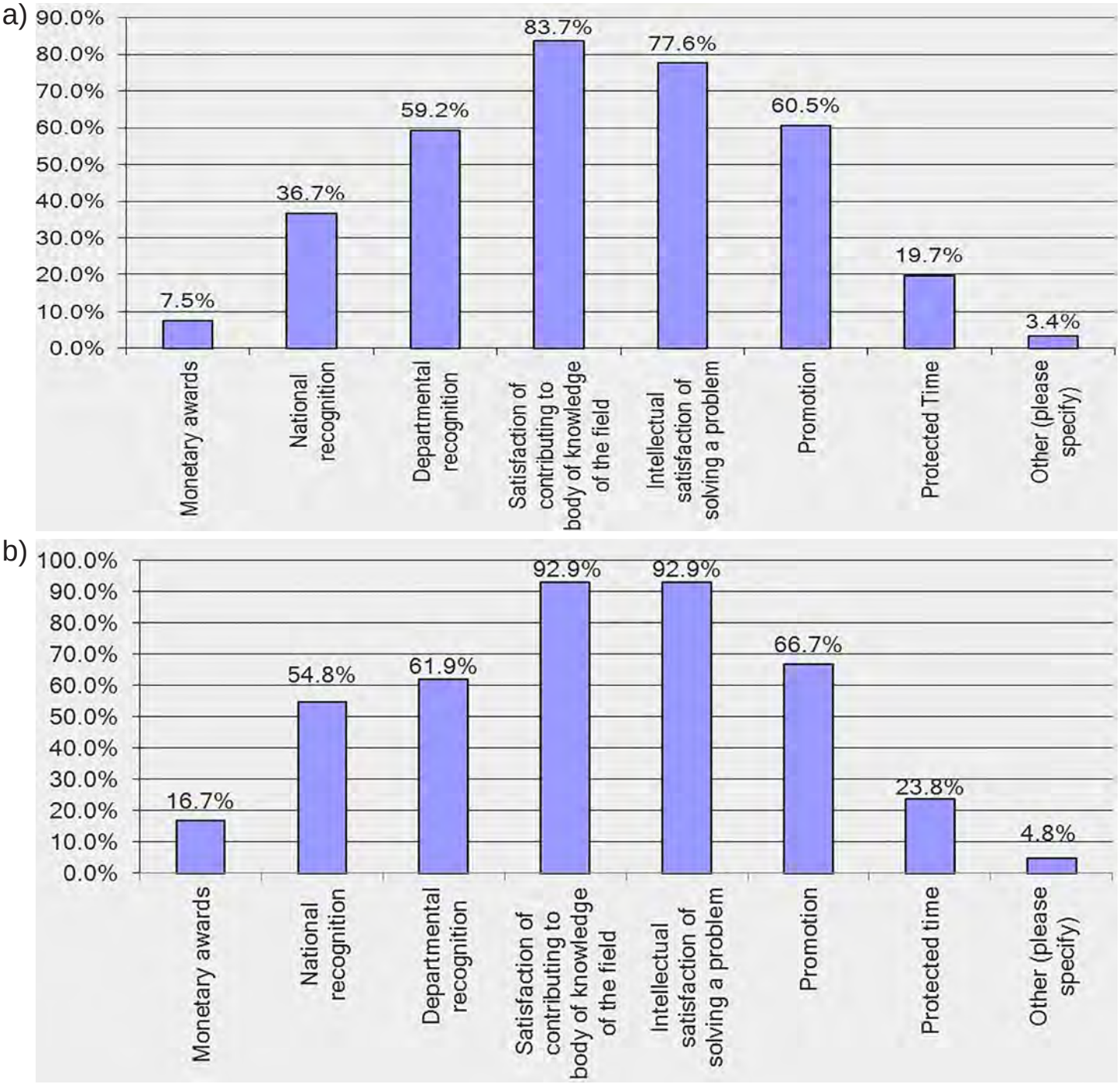

Figure 2. Response rates* for rewards of performing research for a) education researchers and b) core educators.
*Participants were instructed to select all options that were applicable, and so results may total more than 100%.

values such as an emphasis on life-long learning, creation of community of inquiry, desire to achieve success and contribute positively to the field, and to satisfy job requirements and achieve promotion. In this study educators and successful education researchers reported receiving more intrinsic than extrinsic rewards for performing education research. This is in line with prior literature identifying lack of reward as a barrier to performing education scholarship.[10]

Performing research positively contributed to career satisfaction for education researchers, which is not surprising if this is something that they chose to spend their time on despite identifying multiple barriers. Interestingly,

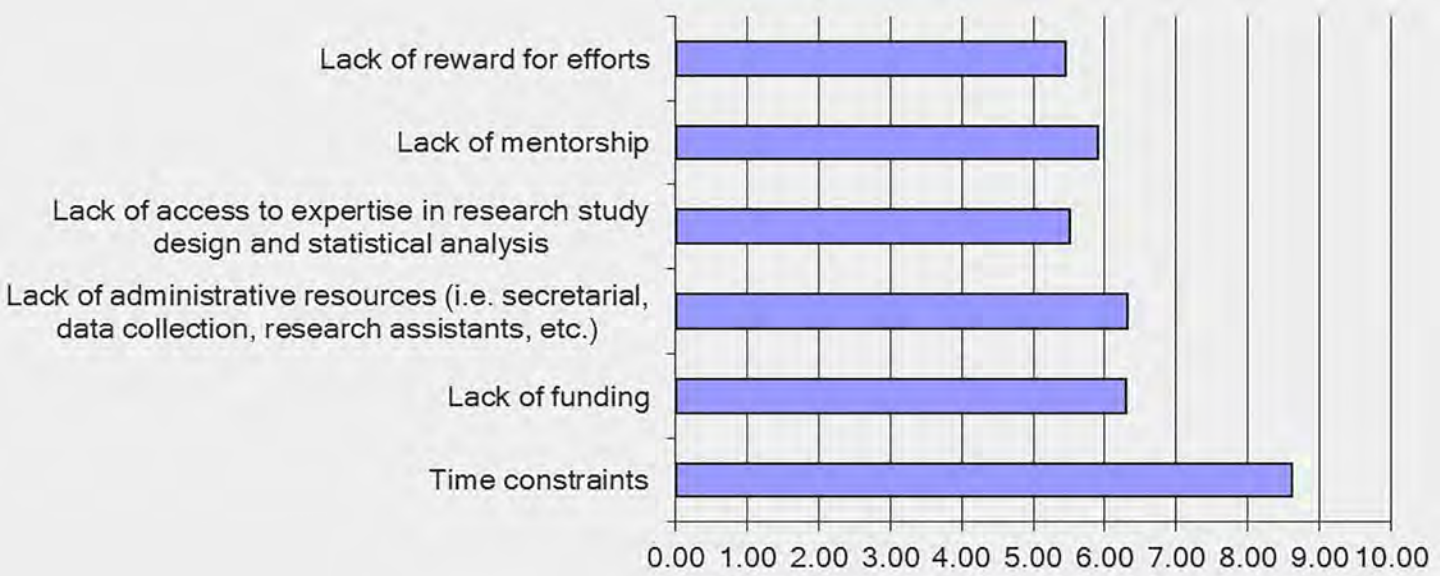

Figure 3. Mean impact ratings of barriers for core educators (1= Does not impact me at all; 10= Greatly impacts me).

despite being satisfied overall with their careers, core educators were less satisfied with their achievements in research. Since research may impact other factors that educators have identified as positively contributing to their satisfaction in this study, such as variety, sense of accomplishment and the potential to enhance teaching, it would be interesting to explore whether educator career satisfaction could be further enhanced by improving their satisfaction with their research achievements.

Advice from those with experience and success in the field is well aligned with the needs identified by participants in both stakeholder groups, further supporting that these are the areas where resources and support should be targeted. Suggested strategies span multiple levels including addressing needs both intrinsic and extrinsic to the would-be scholar, and barriers specific to the field of education research. The aspect of training and acquiring expertise is an expressed need and also recommended advice from those who have been successful. Core educators specifically seek more methodologic training and would prefer a longitudinal online course or one locally available at their institution. These formats are likely preferred because of accessibility since it has already been demonstrated in this study and others that time is an important issue and workload demands for educators are high.[10-11,13] To meet the expressed needs identified in this study and follow advice of those with experience and success in the field, future interventions should target an increase in training opportunities, access to expertise, creation of a cadre of trained medical education research experts to serve as mentors, increased funding opportunities and better research infrastructure, and emphasis on the value of this work to garner leadership support and assist in the development of mechanisms to ensure adequate protected time for educators to be successful in their scholarly endeavors.

LIMITATIONS

This was a convenience sample and completion of all items on the survey was not required as we desired to include all relevant data. It is possible that we may have failed to capture important information. However, this is a fairly large study and given the broad distribution of programs represented, we expect the perspectives expressed by participants to be representative of the group as a whole. Additionally, as this was a survey study, the results must be considered within the context of limitations inherent to this type of design. Despite these limitations, we still believe this study sheds further light on the barriers educators face in performing education research and illuminates motivators and potential strategies for improvement.

CONCLUSION

Our study identified multiple barriers, motivators/discouragers, as well as strategies for success in performing education scholarship, which were common to both core educators and successful education researchers. The most commonly cited barriers were lack of time and competing demands. Core educators were interested in attaining new skills in education research through faculty development. Key motivators to perform education research for both education researchers and core educators were the desire to disseminate knowledge, support evidence-based practices, and achieve promotion. Suggested strategies for success

included formal training, mentorship, and collaboration. This information may inform interventions to support educators in their scholarly pursuits and improve the overall quality of education research in EM.

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This Article Corrects: "Trends in Regionalization of Care for ST-Segment Elevation Myocardial Infarction"

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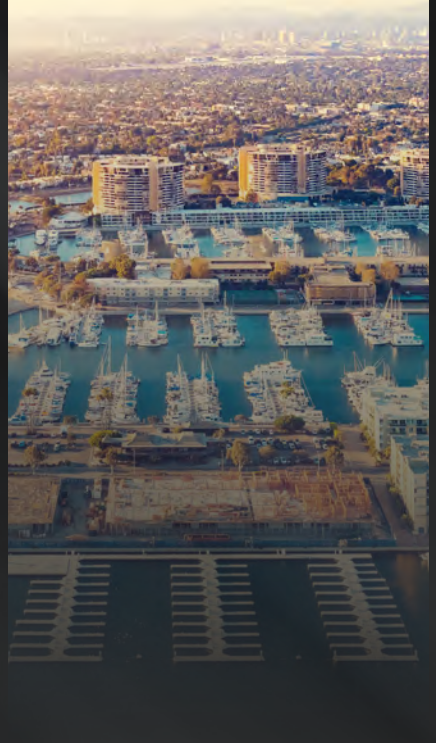

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