Received: 9 September 2020 | Revised: 7 March 2021 | Accepted: 7 July 2021

DOI: 10.1002/emp2.12522

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
WILEY

ORIGINAL RESEARCH

Evidence-Based Emergency Medicine

A clinical decision rule predicting outcomes of emergency department patients with altered mental status

Tyrell J Simkins DO, PhD[1] | David Bissig MD, PhD[1] | Gabriel Moreno MD[1,2] | Nimar Pal K Kahlon MD[1] | Fredric Gorin MD, PhD[1] | Alexandra Duffy DO[1]

[1] Department of Neurology, University of California, Davis, Sacramento, California, USA

[2] Touro University, Vallejo, California, USA

Correspondence
Tyrell Jonathan Simkins, DO, PhD, UC Davis Health, Department of Neurology, University of California, Davis, 3160 Folsom Blvd, Sacramento, CA 95816, USA.
Email: tsimkins@ucdavis.edu

Funding and support: By *JACEP Open* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

Study objective: Approximately 5% of emergency department patients present with altered mental status (AMS). AMS is diagnostically challenging because of the wide range of causes and is associated with high mortality. We sought to develop a clinical decision rule predicting admission risk among emergency department (ED) patients with AMS.

Methods: Using retrospective chart review of ED encounters for AMS over a 2-month period, we recorded causes of AMS and numerous clinical variables. Encounters were split into those admitted to the hospital ("cases") and those discharged from the ED ("controls"). Using the first month's data, variables correlated with hospital admission were identified and narrowed using univariate and multivariate statistics, including recursive partitioning. These variables were then organized into a clinical decision rule and validated on the second month's data. The decision rule results were also compared to 1-year mortality.

Results: We identified 351 encounters for AMS over a 2-month period. Significant contributors to AMS included intoxication and chronic disorder decompensation. ED data predicting hospital admission included vital sign abnormalities, select lab studies, and psychiatric/intoxicant history. The decision rule sorted patients into low, moderate, or high risk of admission (11.1%, 44.3%, and 89.1% admitted, respectively) and was predictive of 1-year mortality (low-risk group 1.8%, high-risk group 34.3%).

Conclusions: We catalogued common causes for AMS among patients presenting to the ED, and our data-driven decision tool triaged these patients for risk of admission with good predictive accuracy. These methods for creating clinical decision rules might be further studied and improved to optimize ED patient care.

Supervising Editor: Henry Wang, MD, MS

1 | INTRODUCTION

1.1 | Background

Altered mental status (AMS) can be defined as an acute change in thought content or level of arousal in the absence of focal neurological symptoms and signs. Health care workers frequently use AMS interchangeably with confusion, delirium, encephalopathy, altered level of consciousness, "found down," or unresponsive. AMS is present in ≈5%–10% of adult emergency department patients[1] with a high prevalence in elderly individuals and those with comorbid conditions.[2,3]

1.2 | Importance

The high mortality associated with acute mental status changes warrants treatment as a medical emergency.[4] Timely and focused care avoids diagnostic delays and reduces mortality.[5] However, the diagnostic challenge of AMS lies in the myriad of potential etiologies originating from virtually any organ system.[1,4,6] The clinical evaluation of AMS patients is variable because of the broad differential and lack of universally accepted guidelines. Workup in the emergency department (ED) can be extensive, leading to unnecessary costs and significant amounts of time needed to integrate test results into triage decisions.[7,8] Previous attempts to structure the diagnostic approach for AMS have focused on a narrow subset of causes or excluded important underdiagnosed conditions, such as dementia and schizophrenia.[4,9–12] An alternative approach is to identify the essential information needed to determine whether a patient with AMS is admitted or discharged from the ED.

1.3 | Goals of this investigation

Our objectives were to identify the causes of AMS in patients presenting to the ED and to create a clinical decision rule predicting patients' risk for hospital admission and mortality.

The Bottom Line

Altered mental status is a common reason for presentation to the emergency department (ED). In this study the authors applied recursive partitioning to clinical data from an academic medical center to derive a clinical decision rule identifying ED patients with altered mental status who may require hospital admission or who may be at increased risk for 1-year death. Although meriting independent validation, this study illustrates a potential approach to organizing risk stratification in this population.

2 | METHODS

2.1 | Study design and setting

This study was conducted at the University of California Davis Medical Center (UCDMC) in Sacramento, CA. UCDMC is an urban, high-volume, trauma, and referral teaching hospital serving the central valley of northern California. It has a large catchment area and serves as a primary center for medical treatment of the surrounding area. This research was approved by the UC Davis Internal Review Board (IRB # 873849). The electronic health record (EHR) system used at UCDMC was Epic (Epic Systems Corporation, Verona, WI).

The study was an observational retrospective cohort study on patients presenting to the UCDMC ED with a chief complaint of AMS in July and August of 2015. The goal of the study was to develop a clinical decision rule predicting admission of patients based upon statistical and hierarchical analysis of real-world data.

2.2 | Study population

We retrospectively analyzed adult patients (18 years old and up) who presented with a triage chief complaint of AMS to the UCDMC ED between July (5726 encounters, 4975 patients) and August 2015 (5892 encounters, 5074 patients). From these 11,618 encounters, we reviewed all patient encounters in which the initial ED chief complaint was listed as one of the following codes in the EHR: Altered Mental Status Acute, Altered Mental Status Stable Non-acute, Altered Mental Status with Fever, Delusional/Hallucinating, Psychiatric Problem, Confusion (Delirium), Memory Loss, Speaking Difficulty, Altered Level of Consciousness, Dementia, Found Down, and Neurologic Problem. Of these 352 patient encounters, one was excluded because of improper coding. The remaining 351 encounters were generated by 325 patients.

2.3 | Data collection

Each included encounter was manually reviewed to collect data. We recorded seven situation-related variables: hospital admission, ED triage level of acuity, time in the ED, number of ED visits in the past year, arrival by ambulance, independent living at baseline, and duration of hospitalization (if admitted) (Table 1). The final diagnosis for the etiology of AMS in each encounter was recorded as listed in the final document by the treating physician at discharge (ED or inpatient team; categorized in Table 2). After review of the 151 encounters from July 2015, the following final diagnostic categories were identified: intoxication, head trauma, chronic psychiatric condition, chronic medical condition, seizure, transient ischemic attack (TIA) or stroke, dehydration, hypoglycemia, infection, cardiac, other, and unknown. If multiple etiologies were listed as the final diagnosis for AMS, all the associated diagnoses were recorded. We also recorded initial vital signs and

TABLE 1 Summary statistics of AMS encounters. Encounter data and demographics for July and August 2015

Demographics	Derivation cohort (July 2015)	Validation cohort (August 2015)
Total # of ED encounters	5726	5892
Encounters for AMS	152 (2.7%)	199 (3.4%)
Male	83/152 (54.6%)	104/199 (52.3%)
Age (years)	52.3 (17.7)	51.6 (17.3)
Prior ED visit within 1 year prior to presentation	84/152 (55.3%)	103/199 (51.8%)
Average # of ED visits within 1 year prior to presentations	2.3 (3.5)	2.6 (4.5)
Encounters arriving by ambulance	89/152 (58.6%)	108/199 (54.3%)
Independent at baseline	125/152 (82.2%)	167/199 (83.9%)
Time spent in the ED (hours)	15.8 (36.9)	12.8 (17.6)
Number of encounters leading to admission	57/152 (37.5%)	86/199 (43.2%)
Duration of stay for those admitted (days)	8.3 (12.9)	9.5 (20.6)
Deaths within 1 year of AMS encounter	16/152 (10.5%)	32/199 (16.1%)
Age of patients who died within 1 year	67.2 (9.7)	65.4 (12.1)
Age of patients not known to die within 1 year	50.8 (17.6)	49.2 (16.9)

Abbreviations: AMS, altered mental status; ED, emergency department.
Data presented as N (%) or mean (SD).

TABLE 2 Causes of AMS in ED Patients from July and August 2015. The number of cases (%) in which each entity was a contributor to AMS of patients presenting to the UCDMC ED

Cause of AMS	July 2015	August 2015
Intoxication	64 (42.1)	73 (36.7)
Preexisting chronic psychiatric	36 (23.7)	53 (26.6)
Preexisting chronic non-psychiatric illness	48 (31.6)	57 (28.6)
Dehydration	6 (3.9)	24 (12.1)
Hypoglycemia	6 (3.9)	6 (3.0)
Infection	18 (11.8)	37 (18.6)
TIA or stroke	7 (4.6)	4 (2.0)
Seizure	6 (3.9)	5 (2.5)
Head trauma	2 (1.3)	0 (0)
Other	5 (3.3)	9 (4.5)
Cardiac	6 (3.9)	7 (3.5)
Unknown	18 (11.8)	13 (6.5)

Abbreviations: AMS, altered mental status; ED, emergency department; TIA, transient ischemic attack; UCDMC, University of California Davis Medical Center.
July: n = 152, August: n = 199.

lab values obtained within the first 24 hours of ED arrival (listed in Table 3). If present, data from urine drug screens, urinalyses, electrocardiograms, chest x-rays (CXRs), lumbar puncture, and head imaging also were recorded and classified (listed in Table 3). Prespecified rules for classification of select tests as "normal" versus "abnormal" were used. For radiologic studies, the final chart diagnosis by the reading radiologist was used for classification according to prespecified rules.

Data on mortality were assessed though manual chart review by determining if the AMS patient was documented in the EHR to have died within 1 year of their ED visit or entered hospice within 6 months of the ED visit.

2.4 | Outcomes

The primary outcome was hospital admission. The secondary outcome was 1-year mortality.

2.5 | Data analyses

2.5.1 | Handling of missing data

Absent clinical data were common. We deliberately excluded studies ordered more than 24 hours after ED arrival because they reflected inpatient evaluation rather than ED triage. Because data were missing not at random, excluding encounters that lacked a given diagnostic test would bias the sample population and multiple imputation was not thought to be valid.[13]

Acknowledging that missing lab values were deliberate, we thought it most accurate to use normal values in place of missing data using single imputation. For results with a binary outcome (eg, normal vs abnormal), missing values were presumed to be normal. This rule was applied to electrocardiogram (missing in 52%), CXR (missing in 47%), urinalysis (missing in 49%), computed tomography (CT) and magnetic resonance imaging (MRI) of the head (missing in 51% and 94% of cases, respectively), and urine drug screen (missing in 57% of cases). We made an exception for encounters with an abnormal CT in which case MRI

TABLE 3 List of collected clinical variables and univariate analysis

Variable	Admitted	Not admitted	*P*
Intoxicant exposure or known psychiatric history—n (%)	33 (23)	142 (69)	<0.001
Arrived by ambulance—n (%)	98 (68)	99 (48)	<0.001
High triage acuity ("Resuscitation or Crisis")—n (%)	134 (94)	144 (70)	<0.001
Oxygen saturation ≥ 92% on room air—n (%)	101 (70)	198 (86)	<0.001
Abnormal electrocardiogram—n (%)	23 (16)	7 (3)	<0.001
Abnormal chest x-ray—n (%)	45 (31)	8 (4)	<0.001
Abnormal urinalysis—n (%)	40 (28)	12 (6)	<0.001
Abnormal CT scan of the head—n (%)	20 (14)	1 (0.5)	<0.001
Abnormal brain MRI—n (%)	22 (15)	1 (0.5)	<0.001
Abnormal urine drug screen—n (%)	29 (20)	35 (17)	0.49
Sex, male—n (%)	80 (55)	107 (52)	0.59
Living unsupervised (eg, not from a nursing facility)—n (%)	120 (83)	172 (83)	0.89
Age, years—median (IQR)	61 (51–73)	47.5 (33–62)	<0.001
Number of ED visits in the preceding year—median (IQR)	1 (0–3)	1 (0–3)	0.66
HR, BPM—median (IQR)	89 (75–109)	88(77–99)	0.36
[a]HR difference (HR - 75 BPM)—median (IQR)	18 (10–36)	14 (8–24)	0.01
RR, BrPM—median (IQR)	18 (16–20)	16.5(16–18)	0.13
[a]RR difference (RR - 16 BrPM)—median (IQR)	2 (0–4)	2 (0–3)	<0.001
Body temperature, C—median (IQR)	36.7 (36.5–37.0)	36.7 (36.6–36.9)	0.66
[a]Body temperature difference (temperature - 37°C)—median (IQR)	0.4 (0.2–0.7)	0.3 (0.2–0.5)	<0.001
Systolic BP, mmHg—median (IQR)	123 (107–149)	127 (115–140)	0.39
[a]Systolic BP difference (SBP - 120 mmHg)—median (IQR)	16 (8–37)	13 (6–23.75)	0.003
Diastolic BP, mmHg—median (IQR)	73 (59–88)	75 (63.25–83)	0.69
[a]Diastolic BP difference (DBP - 75 mmHg)—median (IQR)	15 (6–25)	9.5 (4–18)	<0.001
WBC, thousands per mm3 – median (IQR)	8.9 (7.3–12.6)	7.9 (6.5–9.5)	<0.001
[a]WBC difference (WBC - 7.75 K/mm3)—median (IQR)	2.05 (0.95–4.95)	1.37 (0.64–2.55)	<0.001
Hgb, g/dL—median (IQR)	12.3 (10.3–13.9)	13.2 (12.3–14.4)	<0.001
[a]Hgb difference			
Women: (Hgb - 14 g/dL), men: (Hgb - 15.5 mg/dL)—median (IQR)	2.6 (1.3–4.6)	1.5 (0.9–2.6)	<0.001
Platelets K/mm3—median (IQR)	240 (167–305)	246 (202–299)	0.07
[a]Platelet difference (platelets – 265 K/mm3)—median (IQR)	67 (28–111)	52 (25–87)	0.01
Sodium, mmol/L—median (IQR)	138 (134–140)	139 (137–141)	<0.001
[a]Sodium difference (sodium - 140 mmol/L)—median (IQR)	3 (2–6)	2 (1–3)	<0.001
K mmol/L—median (IQR)	4.0 (3.5–4.5)	3.9 (3.5–4.1)	0.11
[a]K difference (potassium – 4.15 mmol/L)—median (IQR)	0.55 (0.25–0.95)	0.35 (0.15–0.65)	<0.001
Chloride mmol/L—median (IQR)	103 (97–106)	104 (102–106)	<0.001
[a]Chloride difference (chloride - 102.5 mmol/L) – median (IQR)	4.5 (1.5–7.5)	2.5 (1.5–4.5)	<0.001
Total CO2, mmol/L—median (IQR)	24 (21–27)	26 (24–28)	<0.001
[a]CO2 difference (total CO2 - 28 mmol/L)median (IQR)	4 (2–7)	2 (1–4)	<0.001
Blood urea nitrogen, mg/dL—median (IQR)	20 (11–36)	13 (9–18)	<0.001
Creatinine, mg/dL—median (IQR)	1.26 (0.80–2.27)	0.89 (0.72–1.07)	<0.001
Glucose, mg/dL—median (IQR)	129 (106–172)	105 (94–126)	<0.001
[a]Glucose difference (glucose - 119.5 mg/dL)—median (IQR)	27.5 (11.5–52.5)	21.5 (11.8–32.5)	0.005
Calcium, mg/dL—median (IQR)	8.9 (8.4–9.3)	9.1 (8.8–9.5)	<0.001
[a]Calcium difference (calcium - 9.55 mg/dL)—median (IQR)	0.65 (0.35–1.15)	0.47 (0.25–0.75)	<0.001

(Continues)

TABLE 3 (Continued)

Variable	Admitted	Not admitted	*P*
Magnesium, mg/dL—median (IQR)	2.0 (1.8–2.3)	2.0 (1.8–2.2)	0.56
[a]Magnesium difference (magnesium—2.05 mg/dL)—median (IQR)	0.25 (0.15–0.37)	0.18 (0.08–0.34)	0.005
Total protein, g/dL—median (IQR)	6.9 (6.4–7.5)	7.3 (6.8–7.6)	0.002
[a]Protein difference (total protein - 7.3 g/dL)—median (IQR)	0.7 (0.3–1.1)	0.4 (0.2–0.7)	<0.001
Albumin, g/dL—median (IQR)	3.4 (2.9–4.0)	4.0 (3.8–4.3)	<0.001
[a]Albumin difference (albumin - 4.1 g/dL)—median (IQR)	0.7 (0.3–1.2)	0.3 (0.1–0.5)	<0.001
Alkaline phosphatase, units/dL—median (IQR)	84 (65–113)	70 (57–86)	<0.001
Total bilirubin, mg/dL—median (IQR)	0.8 (0.6–1.1)	0.8 (0.6–1.0)	0.19
Direct bilirubin, mg/dL—median (IQR)	0.12 (0.10–0.20)	0.10 (0.09–0.16)	<0.001
AST, units/L—median (IQR)	32 (23–54)	30 (23–35)	0.007
ALT, units/L—median (IQR)	25 (17–42)	28 (17–38)	0.58
Ammonia, μmol/L—median (IQR)	21.3 (14.5–36.0)	17.3 (12.5–22.5)	<0.001
Lipase, units/L—median (IQR)	31 (22–40)	30 (24–36)	0.89
Ethanol, mg/dL—median (IQR; 90th%ile)	0 (0–0; 0)	0 (0–0; 125)	0.20
Troponin I, ng/mL—median (IQR)	0.014 (0.010–0.040)	0.010 (0.003–0.014)	<0.001
Lactate, mEq/L—median (IQR)	1.7 (1.2–2.4)	1.3 (1.0–1.6)	<0.001
TSH, microIU/mL– median (IQR)	1.71 (1.18–2.30)	1.83 (1.30–2.46)	0.18
[a]TSH difference (TSH- 1.825 microIU/mL)—median (IQR)	0.58 (0.24–1.02)	0.57 (0.28–0.98)	0.94
Free T4, ng/dL—median (IQR)	1.10 (0.90–1.25)	1.11 (0.92–1.28)	0.48
[a]T4 difference (free T4–1.1 ng/dL)—median (IQR)	0.18 (0.08–0.30)	0.18 (0.10–0.32)	0.50

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; BPM, beats per minute; BrPM, breaths per minute; CO2, carbon dioxide; CT, computed tomography; Hgb, hemoglobin; HR, heart rate; IQR, interquartile range; MRI, magnetic resonance imaging; K, potassium' RR, respiratory rate; T4,thyroxine; TSH, thyroid stimulating hormone.

[a]Difference from median normal lab value.

Combined imputed data from July and August 2015–there were no significant differences between the months.

was also presumed abnormal. Missing normally distributed continuous variables were imputed by random sampling of the hospital lab's normal distribution (mean ± two SDs defined by lab cutoff values). Two exceptions were troponin and ethanol. Troponin values are exponentially distributed; therefore, missing values were filled with a randomly selected value from a similar exponential distribution. Ethanol blood levels have a bimodal distribution and if absent presumed to be 0 mg/dL. These imputed values were used for all statistical analyses, unless otherwise noted. An exception to this was data from lumbar puncture. Only five of 351 encounters had a lumbar puncture; therefore, these data were neither imputed nor included in the analysis as they were felt to be so rare that they would not meaningfully contribute to the development of a clinical decision rule.

2.5.2 | Identification of statistically significant and unique clinical variables

All statistical analyses were performed in R (version 3.3.3; https://www.r-project.org).

Initially, each recorded laboratory or demographic value was tested to determine if it was associated with hospital admission from ED encounters during the month of July 2015 using univariate analysis (Table 3). We used a Fisher's exact test for categorical variables and a Wilcoxon rank-sum test for continuous variables. For continuous variables where either a high or a low value may be associated with ill health (eg, hyponatremia or hypernatremia), we assessed the absolute value of the lab after subtracting the median lab reference value. However, we found that the list of potentially useful variables ($P < 0.05$) was still too long to organize into a concise clinical decision rule, and thus we turned to multivariate approaches to narrow the list of critical clinical variables.

We next used non-parametric stepwise multiple regression, wherein the strongest single predictor of admission was identified and used as covariate to reassess the significance of all other variables. When two predictors are highly correlated (eg, systolic and diastolic blood pressure) using one as a covariate downplays the importance of the other. Thus, covariate analysis permits identification of the next-strongest *unique* predictor of admission. The process repeats, and, at each step, *P* values are recalculated to adjust for any non-zero correlation between predictors. After enough cycles, addition of another variable becomes redundant. Such a redundant variable does not improve the multiple regression model and weakens one or more of the initial unique predictors to the point that it falls above

a preselected threshold to enter the model ($P = 0.05$). This method helped identify the most salient predictive variables associated with hospital admission.

Given that stepwise multiple regression approaches often produce inefficient decision rules, *recursive partitioning analysis* can be used to generate meaningful decision rules from large and redundant variable sets.[14] Therefore, in addition to the previously described analyses, we separately analyzed the data using the recursive partitioning packages **rpart** and **ctree** packages in R.[15,16] These analyses helped further refine the list of important clinical variables predictive of hospital admission.

The outcome of performing the univariate, stepwise regression, and recursive partitioning analysis was the identification of a list of high-quality predictors for hospital admission that could then be arranged into a clinical decision rule.

2.5.3 | Clinical decision rule development

Multivariate methods narrowed the list of predictors to the following: known history of a significant psychiatric disorder (eg, schizophrenia) and/or a history of recent intoxication, serum creatinine, serum albumin (sometimes alongside aspartate aminotransferase), diastolic pressure, oxygenation on room air, ED triage assigned level of acuity, low hemoglobin, and abnormal brain imaging. For the development of a clinical decision rule, these variables were organized by the order of availability during a typical encounter. Responses to initial therapies (eg, glucose for hypoglycemia) were placed at the beginning of the decision rule because they often happen before hospital arrival, are high yield,[1] and were predictive using both univariate (Table 3) and multivariate analyses. Brain imaging was placed at the end of the decision rule given the order of availability in a typical encounter but was dropped after further refinements based on (1) review of July cases and (2) a desire to avoid sorting seriously ill patients into a "low-risk" category. We also found triage level of acuity performed best when moved later in the clinical decision rule. Cutoff values were manually adjusted to best sort patients into hospital admission versus discharge from the ED. This final clinical decision rule was used to sort patients into low, moderate, or high risk of admission. As an internal check on the performance of the clinical decision rule, we tested for an association between rule-assigned risk of admission and whether a patient was admitted on the July 2015 data using a chi-square test. The decision rule was not altered based on this internal check.

2.5.4 | Clinical decision rule validation

The developed clinical decision rule was validated by application to a novel set of ED cases with AMS (August 2015). We employed chi-square tests to determine if there was an association between the risk of admission determined with the clinical decision rule, and mortality risk within year of presentation. In all "moderate-risk" cases, and all cases for which the clinical decision rule was discrepant with clinical outcome, we performed a qualitative review.

3 | RESULTS

3.1 | Cohort characteristics

Summary statistics of the included encounters are presented in Table 1. Approximately half of the 325 patients were male. Ages were normally distributed with no differences between July and August cohorts. Excluding repeat visits occurring during the study period, 64% of patients had at least one prior ED visit in the past year.

Of the 351 encounters studied, 41.3% led to hospital admission (Table 1). Of those admitted, the mean (± SD) hospital length of stay was 9.0 ± 18.0 days (Table 1). The 48 patients who presented with AMS and died within one year of ED presentation were significantly older than those surviving (for each month $P < 0.001$; Table 1).

Of the identified cause(s) for a patient's AMS, 58.1% of encounters had only one identifiable cause (represented in Figure 1). These encounters were most often for intoxication and chronic psychiatric conditions. Less-common causes included stroke/TIA (8 cases) and hypoglycemia (7 cases). The remainder of AMS cases were multifactorial and frequently involved combinations of infection, dehydration, and chronic medical conditions (Table 2). Younger age was more associated with chronic psychiatric conditions and intoxication; whereas, older age was associated with dehydration, chronic medical conditions, and infection.

When infection was a contributor to AMS (55 cases), a CXR and urinalysis was reliably ordered. In those cases, 17 had an abnormal CXR, 31 had an abnormal urinalysis, and 10 had abnormalities in both. This left 14 cases without an abnormality on either test, most of which (8/14) still met at least two of four systemic inflammatory response syndrome criteria based on the first set of vital signs.[17,18]

3.2 | Development of the clinical decision rule

Using univariate analyses, we found that many variables were associated with hospital admission (Table 3). Stepwise regression analysis of July data then revealed that admission was more likely when there was no psychiatric history nor recent intoxication ($P < 0.001$), albumin was low ($P < 0.001$), brain MRI was abnormal ($P < 0.001$), creatinine was high ($P = 0.001$), the patient was not oxygenating well on room air ($P = 0.001$), and when aspartate aminotransferase was high ($P = 0.002$).

Recursive partitioning analysis using the **rpart** package in R prioritized splitting patients first by serum creatinine (high values favor admission) followed by the *absence* of a psychiatric/intoxicant history. This was followed by further splitting for anemia, hypotension, and low albumin. When using the **ctree** package, the most predictive information was the *absence* of a psychiatric or intoxication history ($P < 0.001$). For those with a psychiatric/intoxication history, elevated creatinine favored admission ($P = 0.007$). For those without a psychiatric/intoxication history, **ctree** identified low albumin as the strongest predictor ($P = 0.005$). When decision tree analysis was repeated without including interpolated missing laboratory data values, those

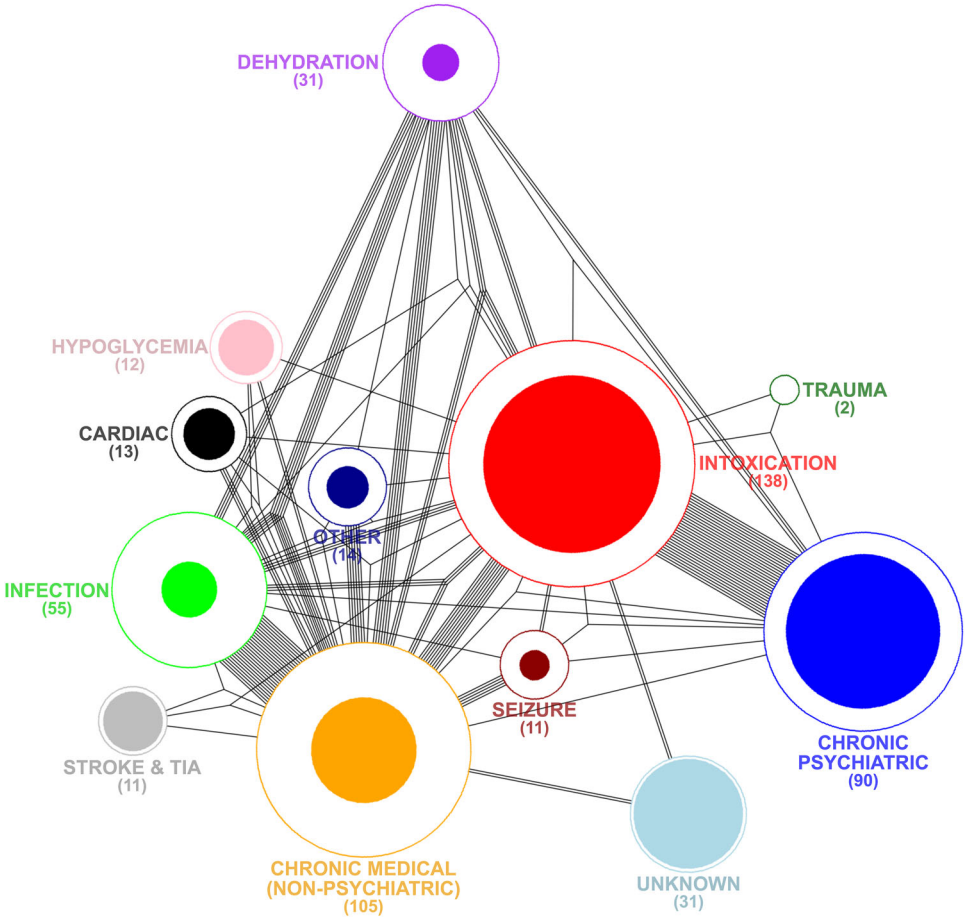

FIGURE 1 **Causes of altered mental status (AMS).** Modified Venn diagram: connecting lines denote shared cases, (n) = causes of AMS and are proportional to the area of the corresponding open circle, filled areas within circles are proportional to the number of pure cases, and non-filled areas represent mixed cases detailed by connecting lines. For example, eight of the 11 cases in the "Stroke and TIA" group had no other obvious cause of AMS (filled gray circle). The other three cases are represented by lines radiating outward. All three connect to chronic medical conditions, two of which are linked to a third cause (eg, a patient with a stroke *and* urosepsis *and* the baseline chronic medical condition of dementia). Abbreviation: TIA, transient ischemic stroke

without a psychiatric/intoxication history were best sorted by triage level of acuity (high acuity favoring admission, $P = 0.03$). Based on this analysis, we created a clinical decision rule for patients presenting to the ED with AMS (Figure 2). When the clinical decision rule was applied to July encounters as an internal check of performance, a patient's rule-assigned risk of admission was significantly related to the probability of admission ($P < 0.001$). Admissions occurred in 6% (5/78) from the low-risk group, 42% (14/33) in the moderate-risk group, and 93% (38/41) in the high-risk group.

3.3 | Evaluation of the clinical decision rule

The clinical decision rule's ability to predict admission was validated on a novel dataset acquired from August ED encounters. The clinical decision rule demonstrated a robust association between the decision rule assigned risk and admission ($P < 0.001$). Specifically, admission occurred in 15% (15/102) of the low-risk group, 46% (13/28) in the moderate-risk group, and 87% (60/69) in the high-risk group.

3.3.1 | High-risk for hospitalization

Summing data from both months, 110 encounters were stratified by the clinical decision rule as high risk. Of these, we identified 12 cases for which the clinical decision rule predicted admission, but the patient was discharged from the ED. We reviewed each of these discrepant cases individually. In four, the patient was ill enough to warrant admission, but admission was inconsistent with goals of care or illness severity was recognized later. Of the remaining eight cases, patients rapidly returned to their baseline without intervention.

3.3.2 | Low-risk for hospitalization

Combining data from both months, 20 patients categorized as low risk were admitted. In six cases, the single highest-priority diagnostic test based on clinical history—such as liver function tests for a patient running out of lactulose—was abnormal enough to warrant admission. Another nine low-risk patients were admitted for profound

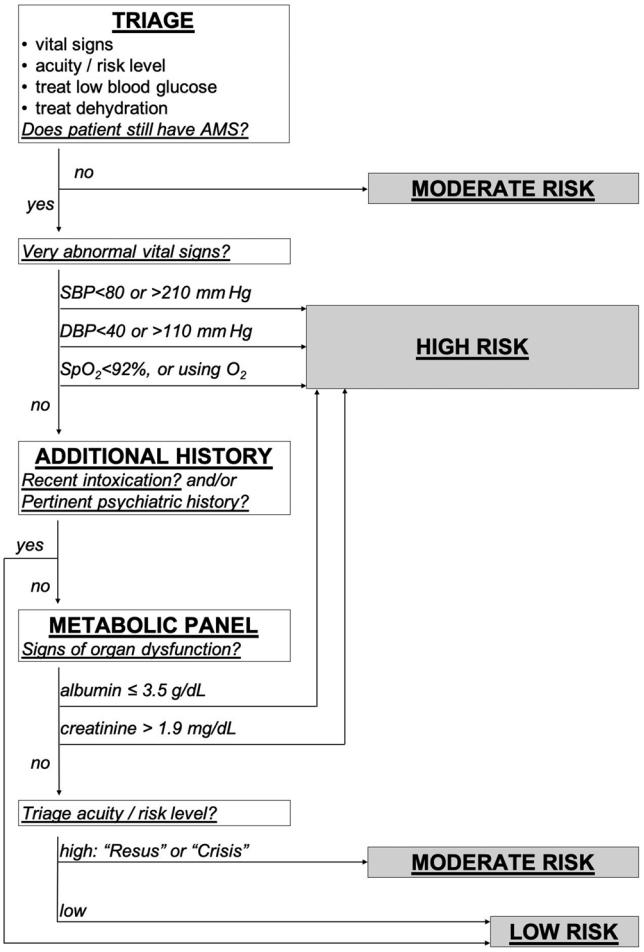

FIGURE 2 **Clinical decision rule for admission after ED presentation for AMS**. All grayscale elements of the flowsheet were developed using data from July 2015 and then validated against data from August 2015. Blood pressure cutoffs are listed in mmHg. Abbreviations: AMS, altered mental status; DBP, diastolic blood pressure; ED, emergency department; SBP, systolic blood pressure; SpO_2, oxygen saturation by pulse oximetry

intoxication. The remaining five cases were admitted because of inadequate home care.

3.3.3 | Moderate-risk for hospitalization

The clinical decision rule assigned 61 cases as moderate-risk. Patients who rapidly responded to treatment for hypoglycemia and dehydration were identified as moderate-risk (n = 13) and sometimes admitted because of other clinical concerns (eg, syncope workup). Review of the remaining 48 moderate-risk encounters revealed several things. Common AMS causes in this group included occult infection and intoxication denied on history. Of the 22 moderate-risk patients admitted, three had abnormal body temperature and two others had an elevated anion gap. Serum lactate was elevated in six. Of those not admitted, the most common cause of AMS was unknown (11 cases) because the patient left the ED before the physician had a chance to perform a complete workup. Several other trends were noted within moderate-risk group patients without dehydration or hypoglycemia: younger patients were most likely to have a positive drug screen, all patients with an abnormal CXR were over 55 years old, and most patients with an abnormal urinalysis were women. Based on these patterns, testing for the above (lactate, drug screen, CXR, urinalysis) in moderate-risk patients could be suggested to help further triage patients, but has not been validated against a novel dataset.

3.4 | Prediction of mortality

Mortality within one year of ED presentation was compared to the clinical decision rule's assigned risk of admission. As some encounters were repeat visits, only the first visit was considered in these analyses. For July, no low-risk patients died in the subsequent year compared to 30% of high-risk patients (Figure 3). The moderate-risk group had an intermediate mortality of 12.9% (Figure 3). This pattern was replicated in the August data (Figure 3). For each month, the rule-assigned risk was a significant predictor of mortality within one year (Figure 3). Combining the two months, roughly one-third of high-risk assigned patients died within a year, compared to 1.8% and 12.3% in the low- and moderate-risk groups, respectively (Figure 3).

3.5 | Study limitations

This study has several limitations. The dataset used in this study is relatively small but allowed for manual chart review. Manual chart review was deemed important for this initial analysis to (1) capture data not easily obtained through automated means (eg, rapid response of a hypoglycemic patient to glucose), (2) ensure accurate categorization of the causes of AMS, and (3) gauge the safety of labeling a patient as "low risk." The single-center retrospective design limits generalization to populations outside our hospital system. However, the methods used to develop this clinical decision rule are readily available at other health systems with an EHR from which data can be extracted. As such, customized AMS clinical decision rules could be created with relative ease. Streamlined data extraction using machine-learning techniques could accelerate/refine this process. Future studies may benefit from additional patient selection criteria (eg, Glasgow Coma Scale) to more fully capture all AMS patients. Another limitation of this study is that mortality was derived solely from EHR chart review rather than other methods (eg, coroner records). Thus, mortality associated with our clinical decision rule's assigned risk level may be underestimated. The retrospective nature of this study limits the ability to determine if the clinical decision rule can improve outcome measures such as mortality, morbidity, and cost-effectiveness.

4 | DISCUSSION

AMS is common in the ED with many etiologies and an associated high mortality rate.[4] Several authors note there is no consistent

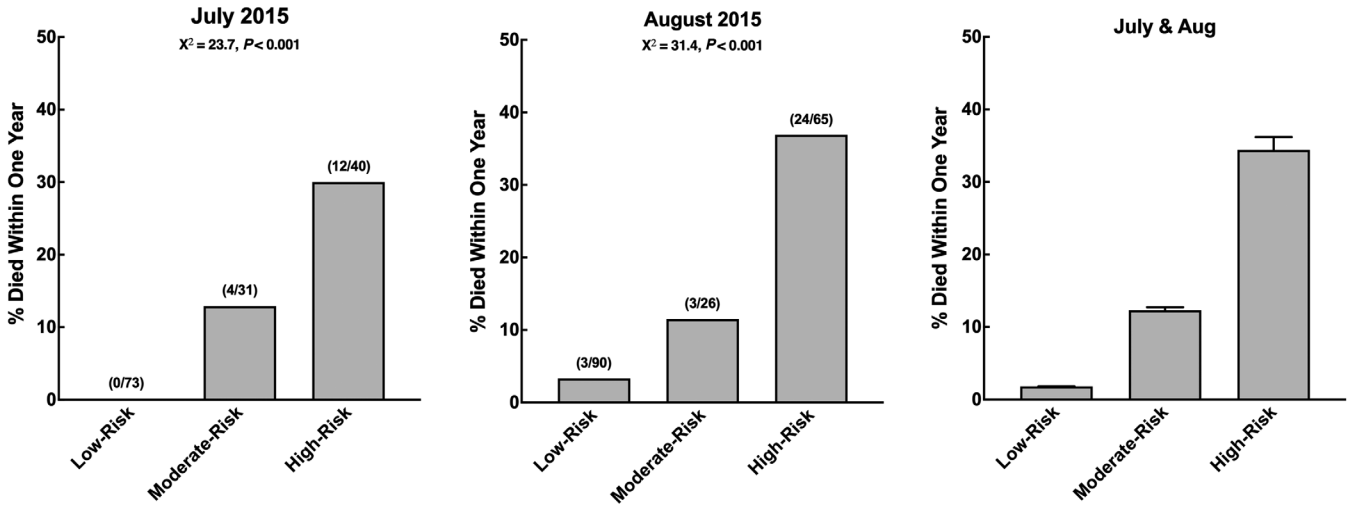

FIGURE 3 **Correlation between clinical decision rule outcome and 1-year mortality**. Mortality within one year is significantly correlated with clinical decision rule assigned risk of hospital admission in patients presenting to the ED with AMS. Left and middle: Bars represent the percentage of patients who died within one year. Numbers in parenthesis are the number of patients who died out of the total number of patients assigned to that group. Right: Bars represent the percentage of patients who died ±95% confidence interval

diagnostic approach to evaluate individuals presenting with AMS.[4–6,12] Our objective was to identify which data could most accurately and concisely predict the need for hospital admission. Using retrospective analysis, we identified a concise list of variables that accurately predicted admission of AMS patients. These factors guided our development of a clinical decision rule aiming for a data-driven, time-efficient approach to initial AMS workup by stratifying patients according to risk of admission. We also found that stratification of admission risk was predictive of 1-year mortality.

In our patient population, the most common etiologies of AMS included intoxication, chronic medical conditions, and psychiatric conditions (Figure 1). Multifactorial cases were common (151/351) with contributions from dehydration, infection, and/or chronic medical conditions (Figure 1; Table 2). Given the higher medical complexity and baseline disease burden in older patients, it is not surprising older age was associated with hospital admission and increased 1-year mortality. Surprisingly, age had a minimal contribution in multivariate analyses. Instead, the most critical information was obtained through clinical history, vital signs, and a few high-yield serum studies (Figure 2). This hierarchy of information matches prior work emphasizing the importance of clinical history-taking.[1]

In the present dataset, AMS most commonly represents neurological dysfunction secondary to the dysfunction of other organ systems. Our analysis indicates that presenting to an ED with AMS should be viewed as a critical life event. Patients with AMS presenting with a sufficiently large abnormality in any vital sign or select serum markers (Figure 2) should be viewed as having multiorgan dysfunction with a high likelihood of admission and 1-year mortality. The ~30% 1-year mortality observed in high-risk cases reflects the severity of multisystem disease underlying AMS presentations. Further studies on this concept are warranted, particularly whether mortality can be improved in AMS patients with earlier identification and treatment.

Given the lack of universally accepted approaches to AMS, published diagnostic algorithms support a broad initial workup.[1,5,6] Our algorithm implies many diagnostic tests are not necessary to determine the need for admission. Therefore, this represents an opportunity to limit testing and speed ED triage. As an example, CT of the head was ordered for 37% (88/220 cases) of low- and moderate-risk patients and was abnormal in five cases. Four of those abnormalities would have been captured by restricting CT imaging to those with (1) prior intracranial malignancy, (2) new head trauma, or (3) focal neurological signs. The fifth case was an incidental subdural hematoma that did not change clinical management. Had the CT head been ordered for all the decision rule high-risk patients (n = 120) and restricted to low-risk cases with the aforementioned indications, CT orders could be reduced by nearly 50%. However, it is recognized that some ED imaging for low-risk cases is warranted to fully rule out potential serious processes. Although expanded laboratory testing and brain imaging are expected for high-risk AMS patients, some of these studies might be safely deferred until hospital admission.

In summary, AMS is an emergency clinical presentation representing underlying organ dysfunction of variable etiology and an associated high mortality. We have created a method by which real world clinical data were used to generate a clinical decision rule for patients presenting to the ED with AMS. This method could be easily implemented in any hospital setting with an EHR. Further refinement of this method and the resultant clinical decision rule could be aided by modern machine learning techniques. Additional validation and refinement of this method may also be used to assist providers in arriving at decision points along the diagnostic journey more quickly and effectively.

CONFLICT OF INTEREST

The authors report no conflict of interest.

PRESENTATIONS

A portion of this work was presented at the American Academy of Neurology Annual Meeting, Boston, MA, April 2017.

AUTHOR CONTRIBUTIONS

GM, FG, and AD devised the project. DB, TJS, GM, and NPKK collected the data and developed the triage algorithm. DB performed the statistical analysis. DB, TJS, and AD wrote the manuscript with input from all authors.

ORCID

Tyrell J Simkins DO, PhD https://orcid.org/0000-0002-6063-174X
David Bissig MD, PhD https://orcid.org/0000-0001-9664-5433

REFERENCES

1. Kanich W, Brady WJ, Huff JS, et al. Altered mental status: evaluation and etiology in the ED. *Am J Emerg Med*. 2002;20(7): 613-617.
2. Hustey FM, Meldon SW. The prevalence and documentation of impaired mental status in elderly emergency department patients. *Ann Emerg Med*. 2002; 39(3): 248-253.
3. Wilding L, Eagles D, Molnar F, et al. Prospective validation of the ottawa 3DY scale by geriatric emergency management nurses to identify impaired cognition in older emergency department patients. *Ann Emerge Med*. 2016; 67(2): 157-163.
4. Xiao HY, Wang YX, Xu TD, et al. Evaluation and treatment of altered mental status patients in the emergency department: life in the fast lane. *World J Emerg Med*. 2012; 3(4): 270-277.
5. Sanello A, Gausche-Hill M, Mulkerin W, et al. Altered mental status: current evidence-based recommendations for prehospital care. *West J Emerg Med*. 2018; 19(3): 527-541.
6. Douglas VC, Josephson SA. Altered mental status. *Continuum (Minneap Minn)*. 2011; 17(5 Neurologic Consultation in the Hospital): 967-983.
7. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1996–2013. *JAMA*. 2016; 316(24): 2627-2646.
8. Papanicolas I, Woskie LR, Jha AK. Health care spending in the United States and other high-income countries. *JAMA*. 2018; 319(10): 1024-1039.
9. Boise L, Neal MB, Kaye J. Dementia assessment in primary care: results from a study in three managed care systems. *J Gerontol A Biol Sci Med Sci*. 2004; 59(6): M621-6.
10. Cradock J, Young AS, Sullivan G. The accuracy of medical record documentation in schizophrenia. *J Behav Health Serv Res*. 2001; 28(4): 456-465.
11. Camilleri R. Development of a prediction model for diagnosis of acute poisoning in patients with altered mental status and absent history of alcohol/drug ingestion. *J Emerg Med*. 2017; 53(5): 680-684.
12. Martel ML, Klein LR, Lichtenheld AJ, Kerandi AM, Driver BE, Cole JB. Etiologies of altered mental status in patients with presumed ethanol intoxication. *Am J Emerg Med*. 2018; 36(6): 1057-1059.
13. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. *BMC MedRes Methodol*. 2017; 17(1).
14. Strobl C, Malley J, Tutz G. An introduction to recursive partitioning: rationale, application, and characteristics of classification and regression trees, bagging, and random forests. *Psychol Methods*. 2009; 14(4): 323-348.
15. Terry Therneau BA. *rpart: Recursive Partitioning and Regression Trees*. 2019.
16. Hothorn T, Hornik K, Zeileis A. Unbiased recursive partitioning: a conditional inference framework. *J Computation Graph Statis*. 2006; 15(3): 651-674.
17. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest*. 1992; 101(6): 1644-1655.
18. Gando S, Shiraishi A, Abe T, et al>. The SIRS criteria have better performance for predicting infection than qSOFA scores in the emergency department. *Sci Rep*. 2020; 10(1): 8095.

AUTHOR BIOGRAPHY

Tyrell J. Simkins, DO, PhD, is an Assistant Professor of Neurology at UC Davis Health in Sacramento, California.

How to cite this article: Simkins TJ, Bissig D, Moreno G, Kahlon NPK, Gorin F, Duffy A. A clinical decision rule predicting outcomes of emergency department patients with altered mental status. *JACEP Open*. 2021;2:e12522. https://doi.org/10.1002/emp2.12522