Analyzing risk factors, resource utilization, and health outcomes of hospital-acquired delirium in elderly emergency department patients

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Thesis

ANALYZING RISK FACTORS, RESOURCE UTILIZATION, AND HEALTH OUTCOMES OF HOSPITAL-ACQUIRED DELIRIUM IN ELDERLY EMERGENCY DEPARTMENT PATIENTS

by

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ANALYZING RISK FACTORS, RESOURCE UTILIZATION, AND HEALTH OUTCOMES OF HOSPITAL-ACQUIRED DELIRIUM IN ELDERLY EMERGENCY DEPARTMENT PATIENTS

SARAH PERNICE TADIRI

ABSTRACT

Background

Delirium is a disorder that is characterized by an acute change in cognitive functioning including inattention, and disordered thinking. Delirium disproportionately affects the population over the age of 65, and is associated with increased costs, worse outcomes and longer lengths of stay. Although delirium is estimated to affect approximately 10% of elderly patients in the emergency department (ED) and 42% of elderly inpatients, it often goes unrecognized by the clinical staff. There is evidence that delirium can be prevented through non-pharmacologic prevention strategies, however it is less clear which patients should be targeted for these measures.

Objectives

The objective of this study is to identify risk factors for development of hospital-acquired delirium during the most proximal aspect of a patient’s hospital course, namely the ED. Secondary objectives of this study are to analyze resource utilization and outcomes associated with the development of hospital-acquired delirium.

Methods
This study is a secondary analysis of a prospective observational study conducted over 3 years at a single urban university hospital. Patients over the age of 65, who could complete a structured cognitive assessment interview, were screened for delirium by a trained research assistant. Patients that were judged to be not delirious in the ED, and who were then admitted to an inpatient unit were included in the final cohort. A validated chart review method was used to determine if patients developed delirium during the course of their hospitalization. Potential predictors of hospital-acquired delirium, including demographics, laboratory values, comorbidities and outcomes, were also abstracted from the medical chart. We performed a univariate analysis of these predictors and included those covariates with a p values ≤0.2 in multivariate analysis. We allowed 1 predictor per 10 outcomes in the final model to avoid over-fitting and evaluated the discriminatory ability and calibration of the model using the c-statistic and Hosmer-Lemeshow goodness-of-fit test.

Results

Of the 520 patients included in our cohort, 77 developed delirium over the course of their inpatient visit. Multivariate analysis identified 7 risk factors to predict delirium in elderly emergency department patients admitted to the hospital. Patients were more likely to develop delirium during their stay if they were age 80 or older, had a history of dementia, had a history of stroke or transient ischemic attack, were hypoxic or hyponatremic in the ED, or had an ED admitting diagnosis of acute stroke/transient ischemic attack or fall. The model
had a c-statistic of 0.73 and a non-significant p-value of 0.7 in the Hosmer-Lemeshow goodness-of-fit test.

**Conclusion**

The predictive model that we created may help identify a population to target for delirium prevention strategies in elderly emergency department patients, thereby reducing delirium incidence in hospitalized patients, and the associated morbidity, mortality, and healthcare utilization.
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LIST OF ABBREVIATIONS

ADLs .......................................................... Activities of Daily Living
APACHE II ........................................ Acute Physiology and Chronic Health Evaluation
BUN .......................................................... Blood Urea Nitrogen
CAM ........................................................ Confusion Assessment Method
CCI .......................................................... Charlson Comorbidity Index
CDC ........................................................ Centers for Disease Control
DSD .......................................................... Delirium Superimposed on Dementia
DSI .......................................................... Delirium Symptom Interview
DSM-IV ............................................. Diagnostic and Statistical Manual of Mental Disorders-4th edition
DSM-5 ............................................. Diagnostic and Statistical Manual of Mental Disorders-5th edition
ED .......................................................... Emergency Department
HELP ....................................................... Hospital Elder Life Program
ICD .......................................................... International Classification of Diseases
ICU .......................................................... Intensive Care Unit
IQR .......................................................... Interquartile Range
NCD ........................................................ Neurocognitive Disease
NICE ................................................. National Institute for Health and Clinical Excellence
MDAS .................................................... Memorial Delirium Assessment Scale
MMSE ..................................................... Mini Mental State Examination
SAS ......................................................... Statistical Analysis Software
SD .......................................................... Standard Deviation
SNF ................................................................. Skilled Nursing Facility
TIA ................................................................. Transient Ischemic Attack
WBC ...................................................... White Blood Cell
INTRODUCTION

Delirium is a neurocognitive disorder characterized by inattention and a disturbance of cognition such as disorientation, memory loss, or visuospatial deficits (American Psychiatric Association, 2013). These symptoms are acute in onset, and tend to fluctuate in severity throughout the course of the day. Delirium can be induced by substance intoxication or withdrawal, medications, or underlying medical conditions (American Psychiatric Association, 2013). There are three psychomotor subtypes of delirium: hypoactive, characterized by lethargy and somnolence, hyperactive, characterized by restlessness or agitation, and mixed, in which patients display both hypoactive and hyperactive traits (American Psychiatric Association, 2013).

Delirium and the Aging Population

The elderly population in the United States is growing rapidly. The Centers for Disease Control and Prevention (CDC) predicts that over the next 25 years the population of individuals age 65 and older will double, and that by the year 2030, “older adults will account for roughly 20% of the U.S. population” (Centers for Disease Control and Prevention, 2013,p.iii). Delirium impacts the elderly population to the greatest extent. While this condition affects an overall small percentage (1-2%) of the general population, it is estimated to affect up to 14% of those over the age of 85 (Inouye, 2006).
In elderly populations delirium is usually multi-factorial, caused by a combination of predisposing and precipitating factors (Inouye, Westendorp, & Saczynski, 2014). Predisposing risk factors of delirium have been well studied, and include older age, prior history of a stroke, and history of dementia (Cole, 2004) (Inouye et al., 2014) (Ahmed, Leurent, & Sampson, 2014). Precipitating factors that have been identified in elderly inpatients include use of physical restraints, malnutrition, polypharmacy, use of bladder catheter and iatrogenic events (Inouye SK & Charpentier PA, 1996). Patients with many predisposing risk factors are more vulnerable to development of delirium, and may develop delirium after exposure to a benign precipitating factor. However, a patient with no, or fewer predisposing factors may be more resilient to precipitating insults, and require a larger precipitating factor to develop delirium (Inouye et al., 2014). Although many published studies have identified risk factors of delirium in the elderly population, most focus on either precipitating factors in an inpatient setting, or patients who are already delirious in the emergency department (ED). It is therefore important to identify risk factors for a population that is not delirious in the ED, but may become delirious after hospital admission.

Delirium in elderly patients is associated with worse outcomes, longer lengths of stay, increased hospital costs, and higher rates of admission to a long-term care facility (Cole, 2004). The American Psychiatric Association estimates that elderly patients affected by delirium, “have three times the risk of nursing home placement and about three times the functional decline as hospitalized
patients without delirium at both discharge and 3 months post-discharge" (American Psychiatric Association, 2013). Delirium is also associated with increased costs and hospital resources. A study of delirium in inpatient settings found that total cost were significantly higher in patients with delirium, and estimated that the national burden of delirium on the health care system ranges from $38 billion to $152 billion each year (Leslie, Marcantonio, Zhang, Leo-Summers, & Inouye, 2008). Delirium is also associated with mortality estimates ranging from 22-76% among inpatients, and has been shown to be associated with 13% shorter lifespan at one-year post hospitalization (Inouye, 2006) (Leslie DL et al., 2005). In critically ill intensive care unit (ICU) patients, it has been estimated that 7.2% of deaths are attributable to delirium (Klein Klouwenberg et al., 2014). Furthermore, in elderly ED patients, delirium has been demonstrated to be an independent predictor of mortality within 30 days, and within 6 months of discharge (Kennedy et al., 2014) (Han et al., 2010).

**Role of the Emergency Department**

As the elderly population increases, EDs are playing an increased role in the healthcare of these patients. A review published by the American Geriatrics Society found that from 2001 to 2009, annual emergency department visits by patients over the age of 65 increased 24.5%, from 15.9 million to 19.8 million, outpacing the population growth of this demographic (Pines, Mullins, Cooper, Feng, & Roth, 2013). The rates of hospital admissions from the ED and of ICU admissions also increased during this time period, suggesting that resource
utilization for the geriatric patient population is increasing through both frequency and severity of visits (Pines et al., 2013). A separate systematic review of over 190 studies also found that the frequency of acute illness was higher in this population that in younger adults, suggesting that, “the visit increase in older age groups is not explained by more trivial or non-urgent visits” (Gruneir, Silver, & Rochon, 2011, p.143). This indicates that shifting visits to non-emergent, or outpatient care settings may not be possible, and further solidifies the importance of the role of EDs in caring for this population in the future. Delirium is estimated to affect approximately 10% of patients over the age of 65 in the ED and up to 42% of hospitalized patients (Kennedy et al., 2014) (LaMantia, Messina, Hobgood, & Miller, 2014) (Siddiqi, House, & Holmes, 2006). The ED, therefore, also assumes a gateway role in early diagnosis and prediction of delirium for hospitalized patients. As formal screening of every patient over the age of 65 who is admitted to the hospital may not be feasible, it is important to identify those who have the highest risk of developing delirium throughout their hospital course.

**Recognition of Delirium**

Poor recognition of delirium in clinical settings is well documented. The American Geriatrics Society estimates that over half of delirious patients are not diagnosed, “Largely because hypoactive delirium is typically unrecognized or misattributed to dementia,” (The American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015, p.142). Since the hypoactive
motoric subtype of delirium is characterized by decreased psychomotor activity and somnolence, it is often overlooked in clinical settings (Inouye et al., 2015). This is particularly concerning because the hypoactive subtype is far more common than the hyperactive or mixed subtypes, and accounts for the majority of delirious patients in the ED (Han et al., 2009).

Another barrier to recognition is the fluctuating course of delirium. Severity of symptoms tends to fluctuate over the course of the day, and so without frequent contact, it may be difficult to recognize. The current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), which has replaced the term “dementia” with “major or mild neurocognitive disorders (NCD)” outlines diagnostic features of both delirium and NCD (American Psychiatric Association, 2013). Clinical features of NCDs can be similar in presentation to delirium, and include a decline from baseline functioning in areas such as attention, learning, memory, and social cognition (American Psychiatric Association, 2013). The greatest distinction between delirium and NCD is therefore the onset of symptoms. Whereas delirium is acute in onset, NCDs develop more gradually over time. However, this is not always easy to discern clinically, and “Is particularly difficult in those elderly individuals who had a prior NCD that may not have been recognized, or who develop persistent cognitive impairment following an episode of delirium” (American Psychiatric Association, 2013). Delirium can also be superimposed on dementia (DSD), further complicating recognition of the condition (Morandi et al., 2012).
Diagnosis of delirium becomes even more challenging in the ED. A systematic review of delirium studies specific to the ED, estimates that emergency providers positively identify delirium in only 16-35% of cases (LaMantia et al., 2014). Lewis et al found that, “almost half of the patients with delirium were discharged from the ED without this diagnosis being entertained” (Lewis, Miller, Morley, Nork, & Lasater, 1995, p.144). This highlights the need for implementation of a standardized screening method to identify patients in the ED and inpatient wards who are delirious, or at risk of becoming delirious.

**Screening and Diagnostic Tools**

Over 24 delirium screening tools have been used in published studies to identify patients who may be at risk for delirium (Inouye et al., 2014). The American Geriatrics Society recently published guidelines for best practice in managing postoperative delirium, that recommends healthcare professionals should perform a preoperative assessment of delirium risk factors, and may consider instituting daily postoperative screening for the duration of their stay (Inouye et al., 2015). Among their recommendations, the panel stressed the importance of educating health care professionals in the use of a validated delirium screening instrument (Inouye et al., 2015). Similarly, a geriatric taskforce assembled by the Society for Academic Emergency Medicine created a list of quality metrics for geriatric patients specifically in the ED (Terrell et al., 2009). This list includes six quality indicators for cognitive assessment, and suggests among the six, that all older persons be screened for cognitive impairment, and
assessed to determine whether any impairment is acute in onset (Terrell et al., 2009). The National Institute for Health and Clinical Excellence (NICE) recommends screening admitted patients based on the following four risk factors: age, cognitive impairment, hip fracture, and severity of illness, for indicators of delirium (Young, Murthy, Westby, Akunne, & O'Mahony, 2010). NICE categorizes indicators into four categories, and recommends that qualifying patients be screened daily as inpatients. Patients who exhibit deficits in cognitive function, perception, physical function, or social behavior should undergo diagnostic assessment (Young et al., 2010).

Currently, the most widely used diagnostic tool in assessing delirium is the Confusion Assessment Method (CAM) (Inouye et al., 2014). The CAM was developed in 1990 in an effort to create a standardized method for non-psychiatric clinicians to assess and diagnose delirium in hospitalized patients (Inouye et al., 1990). It has since been adapted for use in at least 12 languages, and specialized for use in the ED, ICU, and nursing homes (Inouye et al., 2014). The CAM algorithm is based on the diagnostic criteria for delirium from the Diagnostic and Statistical Manual of Mental Disorders III-R, which was the current version at the time of its development (Inouye et al., 1990). It has been validated to determine delirium based on observations taken during a structured interview with the patient to assess cognitive functioning (Monette et al., 2001). The algorithm relies on the evaluation of four key elements of delirium: 1) acute onset and fluctuating course, 2) inattention, 3) disordered thinking, and 4) altered
levels of consciousness. An individual is determined to be delirious if they exhibit features one, two and either three or four (Inouye et al., 1990). It has been shown to have high specificity (90-95%), high sensitivity (94-100%), and high inter-rater reliability (κ=0.81) in assessment of the four features of the CAM algorithm (Inouye et al., 1990).

Table 1. The Confusion Assessment Method (CAM) Diagnostic Algorithm.
The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4. Adapted from (Inouye et al., 1990)

<table>
<thead>
<tr>
<th>Feature 1.</th>
<th>Acute Onset and Fluctuating Course</th>
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<tr>
<td>This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions: Is there evidence of an acute change in mental status from the patient’s baseline? Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?</td>
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<th>Feature 2.</th>
<th>Inattention</th>
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<td>This feature is shown by a positive response to the following question: Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?</td>
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<th>Feature 3.</th>
<th>Disorganized Thinking</th>
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<tr>
<td>This feature is shown by a positive response to the following question: Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?</td>
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<tr>
<th>Feature 4.</th>
<th>Altered Level of Consciousness</th>
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<td>This feature is shown by an answer other than “alert” to the following question: Overall, how would you rate this patient’s level of consciousness? (alert [normal], vigilant [hyperalert], lethargic [drowsy, easily aroused], stupor [difficult to arouse], or coma [unarousable])</td>
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Prevention and Interventions

The most effective strategy to decreasing the morbidity and mortality associated with delirium is through delirium prevention, however it is unclear which patients would most benefit from the implementation of delirium prevention and when delirium prevention should be initiated. It is logical that implementation of delirium prevention strategies from the most proximal aspect of a patient’s hospitalization, namely admission from the ED, would have the most impact.

The American Geriatrics Society recently assembled an expert panel to publish guidelines on delirium prevention strategies in post-operative older adults (The American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015). Prevention strategies include eliminating precipitating factors of delirium. The mostly widely used prevention strategy technique is the Hospital Elder Life Program (HELP) (Inouye et al., 2014). Developed in 1999, HELP targets specific risk factors of delirium in order to accommodate multifactorial origins of the condition. Specifically, HELP targets cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment, and dehydration (Inouye et al., 1999). Examples of interventions include orientation aids, such as white boards with the names of the clinical staff in patient rooms, noise reduction and schedule adjustments to promote normal sleep hours, and visual and hearing aids (Inouye et al., 1999). The intervention showed a significant decrease in both the incidence of delirium and the number of days patients experienced delirium (Inouye et al., 1999). It has also shown
high fidelity in improving outcomes and preventing delirium across multiple clinical sites (Inouye, Baker, Fugal, Bradley, & for the HELP Dissemination Project, 2006). It is important to note, that although implementation of HELP has shown statistically significant decreases in initial development of delirium, and of number of delirious days, the interventions had no statistically significant effects on severity once a patient became delirious (Inouye et al., 1999). This further underlines the importance of prevention and recognition of risk factors.
OBJECTIVES

This study aims to identify what predisposing and precipitating factors present during a patient's ED evaluation can predict his or her risk of developing delirium during a hospital admission. Delirium has been widely demonstrated in previous studies to be under-diagnosed in the hospitalized elderly population, but there is very little literature regarding prediction of delirium after hospital admission using ED data. The specific aims of this study are:

- To identify ED based risk factors of hospital-acquired delirium in patients over the age of 65
- To analyze resource utilization attributed to hospital-acquired delirium
- To compare health outcomes, including length of stay, 30-day return visits, and death, of patients who develop delirium during their admission to those who don’t develop delirium

Through this study we hope to identify a population of elderly patients in the ED who are at risk for developing delirium, and who would benefit from delirium prevention strategies.
METHODS

Study Design and Selection of Participants

In order to determine ED based risk factors for hospital-acquired delirium, we conducted a secondary analysis of a prospective observational study of delirium in the emergency department of a single, urban, academic, tertiary care hospital with 55,000 visits per year. One thousand subjects were enrolled between 2009 and 2012. Subjects were screened and enrolled by trained research assistants, typically between the hours of noon and 8pm. Patients who were over the age of 65, and able to complete a structured delirium assessment in English were considered eligible for delirium screening and cognitive assessment. Patients were considered ineligible if the treating physician believed the study protocol would interfere with their clinical care, if informed consent could not be obtained from either the patient or a surrogate, if the patient did not speak English, or if they had presented to the ED more than 4 hours prior to enrollment in the study. This time limit reflects the criteria of the initial study, which analyzed delirium upon presentation to the ED, and therefore wanted to avoid including patients who might have developed delirium while in the ED. Subjects who completed the delirium assessment and were determined to be non-delirious in the emergency department, and who were admitted to an inpatient unit were included in our final cohort.
**Delirium Screening by Interview**

After obtaining informed consent from the subject or a surrogate, a trained research assistant conducted an interview to assess the subject’s mental status. Training consisted of review of a manual detailing administration and scoring of all assessments, review of videotaped interviews with patients, as well as completion of supervised interviews with patients in the ED.

The interview consisted of a Mini-Mental State Examination (MMSE), Delirium Symptom Interview (DSI), and the Memorial Delirium Assessment Scale (MDAS). The MMSE consists of questions testing orientation, registration, attention, recall, and language (Folstein, Folstein, & McHugh, 1975). The DSI consists of questions about the symptoms which the patient is experiencing that might indicate delirium (Albert et al., 1992). The MDAS is a scoring system, which rates the severity of each of 10 assessment points based on the diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) (Breitbart et al., 1997). Interviewers used information from the entire interview to rate each of the criteria on a 4-point scale (none, mild, moderate, severe) in order to determine the overall severity of a patient’s delirium (Breitbart et al., 1997). This combination of the MMSE, DSI, and MDAS, coupled with the CAM algorithm has been validated for use by non-clinicians in identifying cases of delirium in elderly patients, and shown high inter-rater reliability ($\kappa=0.95$) for diagnosis (Simon et al., 2006). These assessments were then used to determine if the patient was delirious according to the CAM algorithm (Table 1).
Due to the difficulty in assessing fluctuation of a patient’s mental status in an ED setting, due to the brief visit durations, we used a modified version of the CAM. According to this version of the CAM, a subject is likely to be delirious if they exhibited an acute change in mental status or fluctuating course, with inattention and either disordered thinking or an altered level of consciousness. This method has been used in other studies set in the ED and has been found to be consistent with the original CAM algorithm in identifying probable cases of delirium (Lewis et al., 1995).

**Delirium Screening by Chart Reviews**

Trained research assistants used a validated chart review method to determine if the patient became delirious at any point during their inpatient hospital course. This method was validated against the CAM with 74% sensitivity and 83% specificity (Inouye et al., 2005). The chart-based instrument relies on searching for key terms in the medical record that suggest evidence of acute change in mental status. Terms include, but are not limited to delirium, mental status change, inattention, disorientation, hallucinations, agitation, and inappropriate behavior (Inouye et al., 2005). Trained research assistants reviewed inpatient nursing and physician notes to determine each subject’s baseline mental status, and to determine if there was indication that the patient experienced changes in mental status, inattention, disordered thinking, and level of consciousness. Any evidence determined to indicate delirium was recorded verbatim, and the source (nurse, physician etc.) was noted. Training consisted of
review of delirium symptoms and delirium assessment tools, as well as chart reviews supervised by clinicians and researchers with prior experience evaluating delirious patients. At least 40% of charts, selected at random, underwent a second, independent review to ensure consistency of review between research assistants, and to calculate a kappa statistic of inter-rater reliability.

Other Measures

We also collected data on the types of variables that had been shown to be associated with delirium risk in prior studies of elderly inpatients. We collected information about demographics, initial vital signs, laboratory results, comorbidities, medications, and ED physician admitting diagnosis from subjects’ charts. We calculated the Charlson Comorbidity Index (CCI), an estimate of overall risk of morbidity (Charlson, Pompei, Ales, & MacKenzie, 1987), for each patient. Recognizing that age and certain laboratory variables may not be predictive as continuous variables, we also analyzed these covariates as dichotomous variables, with cut-off values based on accepted clinical values. We examined hyperglycemia, hypoglycemia, hypoxia, hypernatremia, hyponatremia, elevated white blood cell (WBC) count, low WBC count, hyperkalemia, hypokalemia, hyperchloremia, hypochloremia, elevated blood urea nitrogen (BUN), and low and elevated bicarbonate. We examined age as a dichotomous variable with different cut-offs.
We also calculated the Acute Physiological and Chronic Health Evaluation II (APACHE II) score for each patient. APACHE II was developed in 1985 as a method of determining overall severity of illness (Knaus, Draper, Wagner, & Zimmerman, 1985). It involves scoring patients from 0-71 on health metrics including age, past medical history, laboratory values, and physiological metrics (Knaus et al., 1985). Elevated APACHE II score has been shown to be significantly correlated with delirium in multiple studies of inpatient settings, as well as the ED (Ahmed et al., 2014) (Kennedy et al., 2014).

For our secondary objective, we collected information about resource utilization, including admission to an ICU, length of stay, total hospital charges, discharge to a new skilled nursing facility (SNF) or new acute rehabilitation facility, and 30-day mortality. Follow-up telephone calls and chart reviews were conducted 30 days after original presentation to the emergency department, to collect information about rehospitalization, rehabilitation, and mortality.

**Statistical Analysis**

The data was calculated and analyzed using Statistical Analysis System (SAS) software. We performed a univariate analysis to identify emergency department-based factors associated with acquisition of delirium during an inpatient admission. For dichotomous variables, proportions were reported, and p-values were calculated using Fishers Exact Test. For continuous variables with normal distribution, means with standard deviation (SD) were reported, and p-values were calculated using a t-test. For continuous, non-normal variables,
medians with 25-75% interquartile ranges (IQR) were reported, and p-values were calculated using the Wilcoxon rank test. Variables with a p≤0.2 were included in a multivariate logistic regression model. Forward selection was used to create a final model of covariates with p≤ 0.05. We allowed 1 predictor per 10 outcomes to avoid overfitting. We used the c-statsistic and Hosmer-Lemeshow test to assess model accuracy. Internal validation of the c-statistic was performed using a bootstrap method with 500 iterations. The odds ratio of each predictor was used to create a scoring model to assess risk for delirium in this patient population, and identify a subset of patients in the ED who should undergo formal delirium screening. To evaluate resource utilization, we compared ICU admission, 30-day mortality, discharge to a new SNF or rehabilitation facility, and rehospitalization rates of patients with and without hospital-acquired delirium using a Fishers Exact test. Median lengths of stay and hospital charges were also reported along with 25-75% IQR and compared using the Wilcoxon rank-sum test. Length of stay was log-transformed to achieve normality and controlled for age, dementia, CCI Score, nursing home residence and APACHE II score.
RESULTS

Description of Study Population

Of the 1000 subjects who were consented and enrolled in the primary study, 8 were withdrawn or excluded for incomplete cognitive testing, and 38 were excluded because they were unable to be classified definitively as delirious or non-delirious using the CAM. Of the 954 subjects who completed minimum cognitive assessments, 99 were found to be delirious in the ED by the CAM algorithm. A further 335 were not admitted to an inpatient unit. For our final analysis, we analyzed the medical records of 520 subjects to determine whether subjects became delirious during their hospital course (Figure 1). Our cohort was 90% Caucasian, 50% male, with a mean age of 77.5, and 90% living independently. The median CCI score of our cohort was 2, and the median APACHE II score was 9. Review of inpatient medical records identified 77 patients who developed delirium in the hospital. The chart review method for delirium identification showed good inter-rater reliability with a kappa statistic of 0.80 (95% CI 0.72-0.89).
Figure 1: Summary of Subject Enrollment

1000 Enrolled

- 38 Unable to be classified by Confusion Assessment Method
- 8 Withdrawn from study/ Unable to complete minimum interview

954 Completed Assessments and Classified

- 99 Patients Delirious by CAM in the ED
- 335 Not admitted to inpatient unit

520 included in final analysis

- 443 Patients Non-Delirious throughout Hospital course

77 Patients with evidence of delirium in medical

Figure 1: Summary of Subject Enrollment
Univariate Analysis

Univariate analysis was used to identify possible predisposing and precipitating risk factors for hospital-acquired delirium (Table 2, Table 3). The following 14 variables had a p-value ≤0.2 and were included in the multivariate analysis: age, Caucasian race, African American race, independent living, history of dementia, history of a stroke or transient ischemic attack (TIA), CCI score, antidepressant medications, opioid medications, abnormal temperature, abnormal hemoglobin levels, ED physician diagnosis of chest pain, ED physician diagnosis of fall, and ED physician diagnosis of a stroke or TIA. Additionally, the following continuous covariates were found to have a p-value ≤0.2 when dichotomized and were also included in the multivariate analysis: hypoxia (oxygen saturation <90%) (p=0.03), hyponatremia (<130 mEq/L) (p=0.05), elevated WBC count (>12.0 *10^9 /L) (p=0.16), low WBC count (< 4.0 *10^9 /L) (p=0.20), hypokalemia (K<3.5 mEq/L) (p=0.15), hypochloremia (<90 mEq/L) (p=0.09), and elevated bicarbonate (>30 mEq/L) (p=0.09).

Table 2: Demographics and Comorbidities of Subject Population. Univariate analysis of demographics, past medical history and medications of delirious and non-delirious subjects. Proportions and percents are reported for dichotomous variables, means and SD are reported for normal continuous variables, and medians and 25-75% IQR are reported for non-normal continuous variables.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire Cohort (N=520)</th>
<th>Delirious (N=77)</th>
<th>Non-Delirious (N=443)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – year, mean (SD)</td>
<td>77.5 (7.7)</td>
<td>80.0 (7.4)</td>
<td>77.1 (7.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>260 (50%)</td>
<td>39 (51%)</td>
<td>221 (50%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Race</td>
<td>White, n (%)</td>
<td>Black or African American, n (%)</td>
<td>Latino, n (%)</td>
<td>Independent Living, n (%)</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------</td>
<td>----------------------------------</td>
<td>---------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Race</td>
<td>470 (90%)</td>
<td>47 (9 %)</td>
<td>2 (0.4%)</td>
<td>465 (90%)</td>
</tr>
<tr>
<td>White</td>
<td>74 (96%)</td>
<td>3 (4%)</td>
<td>0 (0%)</td>
<td>63 (83%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>396 (89%)</td>
<td>44 (10%)</td>
<td>2 (0.4%)</td>
<td>402 (92%)</td>
</tr>
<tr>
<td>Latino</td>
<td>0.09</td>
<td>0.13</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety, n (%)</td>
<td>40 (8%)</td>
<td>4 (5%)</td>
<td>36 (8%)</td>
<td></td>
<td>0.49</td>
</tr>
<tr>
<td>Afib/Aflutter, n (%)</td>
<td>134 (26%)</td>
<td>23 (30%)</td>
<td>111 (25%)</td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Chronic Lung Disease, n (%)</td>
<td>116 (22%)</td>
<td>21 (27%)</td>
<td>95 (21%)</td>
<td></td>
<td>0.30</td>
</tr>
<tr>
<td>Renal Disease, n (%)</td>
<td>129 (25%)</td>
<td>16 (21%)</td>
<td>113 (25%)</td>
<td></td>
<td>0.47</td>
</tr>
<tr>
<td>Coronary Artery Disease, n (%)</td>
<td>223 (43%)</td>
<td>35 (45%)</td>
<td>188 (42%)</td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Dementia, n (%)</td>
<td>32 (6%)</td>
<td>16 (21%)</td>
<td>16 (4%)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Depression, n (%)</td>
<td>77 (15%)</td>
<td>12 (16%)</td>
<td>65 (15%)</td>
<td></td>
<td>0.86</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>156 (30%)</td>
<td>27 (35%)</td>
<td>129 (29%)</td>
<td></td>
<td>0.35</td>
</tr>
<tr>
<td>Seizure Disorder, n (%)</td>
<td>5 (1%)</td>
<td>0 (0%)</td>
<td>5 (1%)</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke or TIA, n (%)</td>
<td>43 (8%)</td>
<td>12 (16%)</td>
<td>31 (7%)</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>CCI score, median (IQR)</td>
<td>2 (1-3)</td>
<td>2 (1-4)</td>
<td>2 (1-3)</td>
<td></td>
<td>0.13</td>
</tr>
</tbody>
</table>

| Outpatient medications      |              |                                  |               |                           |         |
| Number of medications, median (IQR) | 9 (6-12) | 9 (7-15)                          | 9 (6-12)      |                           | 0.43    |
| Antidepressants, n (%)      | 38 (7%)      | 10 (13%)                          | 28 (6%)       |                           | 0.05    |
| Opioid, n (%)               | 35 (7%)      | 9 (12%)                           | 26 (6%)       |                           | 0.08    |
| Antipsychotic, n (%)        | 6 (1%)       | 2 (3%)                            | 4 (1%)        |                           | 0.22    |
| Sedatives, n (%)            | 39 (7%)      | 7 (9%)                            | 32 (7%)       |                           | 0.64    |

| Table 3: Clinical Presentation of Study Population. Univariate analysis of presenting illness, vital signs, and laboratory values in delirious and non-delirious |
subjects. Proportions and percents are reported for dichotomous variables, and medians and 25-75% IQR are reported for non-normal continuous variables.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire Cohort (N=520)</th>
<th>Delirious (N=77)</th>
<th>Non-Delirious (N=443)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triage vitals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature, (Fahrenheit), median (IQR)</td>
<td>98.1 (97.6-98.6)</td>
<td>98.0 (97.3-98.5)</td>
<td>98.1 (97.6-98.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Heart Rate, (beats/min), median (IQR)</td>
<td>77 (65-88)</td>
<td>77 (67-87)</td>
<td>77 (67-87)</td>
<td>0.79</td>
</tr>
<tr>
<td>Respiratory Rate, (breaths/min), median (IQR)</td>
<td>18 (16-20)</td>
<td>18 (16-18)</td>
<td>18 (16-20)</td>
<td>0.85</td>
</tr>
<tr>
<td>Systolic Blood Pressure,(mmHg), median (IQR)</td>
<td>133 (118-152)</td>
<td>132 (118-152)</td>
<td>133 (118-152)</td>
<td>0.97</td>
</tr>
<tr>
<td>Diastolic Blood Pressure, (mmHg), median (IQR)</td>
<td>67 (59-78)</td>
<td>68 (60-82)</td>
<td>67 (59-78)</td>
<td>0.63</td>
</tr>
<tr>
<td>Oxygen Saturation, (%), median (IQR)</td>
<td>98 (97-100)</td>
<td>98 (96-100)</td>
<td>98 (97-100)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>ED Laboratory Results</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Blood Cell, (*10^9 /L), median (IQR)</td>
<td>8.0 (6.5-10.3)</td>
<td>7.9 (6.4-10.3)</td>
<td>8.5 (6.7-10.5)</td>
<td>0.43</td>
</tr>
<tr>
<td>Hemoglobin, (g/dL), median (IQR)</td>
<td>12.3 (10.8-13.6)</td>
<td>12.4 (10.8-13.6)</td>
<td>12.2 (10.5-13.5)</td>
<td>0.19</td>
</tr>
<tr>
<td>Sodium, (mEq/L), median (IQR)</td>
<td>139 (136-141)</td>
<td>139 (136-141)</td>
<td>139 (137-141)</td>
<td>0.87</td>
</tr>
<tr>
<td>Potassium, (mEq/L), median (IQR)</td>
<td>4.2 (3.9-4.6)</td>
<td>4.2 (3.9-4.6)</td>
<td>4.3 (3.9-4.7)</td>
<td>0.67</td>
</tr>
<tr>
<td>Chloride, (mEq/L), median (IQR)</td>
<td>102 (99-105)</td>
<td>102 (99-105)</td>
<td>102 (100-105)</td>
<td>0.70</td>
</tr>
<tr>
<td>Bicarbonate, (mEq/L), median</td>
<td>26 (24-28)</td>
<td>26 (24-28)</td>
<td>27 (24-29)</td>
<td>0.36</td>
</tr>
<tr>
<td>(IQR)</td>
<td>BUN, (mEq/L), median (IQR)</td>
<td>Creatinine, (mEq/L), median (IQR)</td>
<td>Glucose, (mg/dL), median (IQR)</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------</td>
<td>-----------------------------------</td>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22 (24-28)</td>
<td>1.1 (0.9-1.5)</td>
<td>114 (97-143)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22 (17-33)</td>
<td>1.1 (0.9-1.5)</td>
<td>112 (97-142)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>23 (17-36)</td>
<td>1.1 (0.8-1.5)</td>
<td>118 (101-146)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.76</td>
<td>0.81</td>
<td>0.30</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ED Physician Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain, n (%)</td>
</tr>
<tr>
<td>Congestive Heart Failure, n (%)</td>
</tr>
<tr>
<td>Fall, n (%)</td>
</tr>
<tr>
<td>Gastrointestinal Hemorrhage, n (%)</td>
</tr>
<tr>
<td>Cerebral Vascular Accident or Transient Ischemic Attack, n (%)</td>
</tr>
<tr>
<td>Infection (any), n (%)</td>
</tr>
<tr>
<td>Pneumonia, n (%)</td>
</tr>
<tr>
<td>Urinary Tract Infection, n (%)</td>
</tr>
<tr>
<td>Seizure, n (%)</td>
</tr>
<tr>
<td>APACHE II score, median (IQR)</td>
</tr>
</tbody>
</table>

Multivariate Analysis

Of the 21 variables that were significant in univariate analysis, multivariate analysis identified 9 covariates that were predictive in the ED for delirium in elderly hospitalized patients: age, history of dementia, history of stroke/TIA, opioid medications, hypoxia (O2 saturation<90%), hyponatremia (<130 mEq/L),
hypokalemia (<3.5 mEq/L), ED diagnosis of fall, and ED diagnosis of stroke/TIA. As there were 77 delirious patients in our cohort, we limited our final model to 7 predictors to avoid over-fitting. In univariate analyses, age was significantly associated with hospital-acquired delirium as both a continuous, and dichotomized variable, however it is clinically more practical to use a dichotomous variable in a risk prediction model. We compared the c-statistic for age as a continuous variable and dichotomized at various cut points in univariate modeling. As the c-statistics were the same for age as a continuous variable and age ≥ 80 years (0.62 [95%CI 0.55-0.68] and 0.60 [95%CI 0.54-0.66] respectively, p=0.29), we used this dichotomized threshold in our multivariate model. The c-statistics for other dichotomized age cut-offs were significantly smaller than age as a continuous variable. We used forward selection, to create the model with the strongest independent predictive correlations. Our final predictive model consists of age 80 or greater, history of dementia, history of a stroke/TIA, hypoxia, hyponatremia, ED physician diagnosis of fall, and ED physician diagnosis of stroke/TIA (Table 4). The model demonstrated had a c-statistic of 0.73 and a non-significant p-value of 0.7 in the Hosmer-Lemeshow goodness-of-fit test. Internal validation was performed through bootstrap analysis of 500 iterations, and demonstrated retention of the model’s discriminatory ability, with an average c-statistic of 0.74 (SD=0.03).

Table 4: Multivariate Analysis of Delirium Risk. Multivariate analysis of predictive variables of hospital-acquired delirium in elderly ED patients.

<table>
<thead>
<tr>
<th>Predictive Variable</th>
<th>Odds</th>
<th>95% Confidence</th>
</tr>
</thead>
</table>

24
Delirium Prediction Model

Using the predictive covariates from the multivariate model, a score system was designed to predict risk of hospital-acquired delirium in elderly ED patients (Table 5). Point values were assigned to each covariate and were weighted based on the relative odds ratios of each factor. Sensitivity and specificity of the model were assessed at different cut-off scores (Table 6). The percent of patients that would require screening based on each cut-off was also determined. A cut-off score of at least one point based on our model would identify delirious patients with good sensitivity (0.82) and specificity (0.54), and require 58% of patients in this population, to be formally screened.

Table 5: Delirium Score Model. Points are assigned based on relative odds ratios.
Table 6: Sensitivity and Specificity of Delirium Score Model. Sensitivity and specificity of different cut-off scores to undergo formal delirium screening based on our delirium score model. For each cut off, the percentage of patients that would be positive is reported.

<table>
<thead>
<tr>
<th>Score Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Percent Patients Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>0.82</td>
<td>0.54</td>
<td>58%</td>
</tr>
<tr>
<td>≥2</td>
<td>0.55</td>
<td>0.85</td>
<td>21%</td>
</tr>
<tr>
<td>≥3</td>
<td>0.30</td>
<td>0.93</td>
<td>10%</td>
</tr>
<tr>
<td>≥4</td>
<td>0.19</td>
<td>0.96</td>
<td>6%</td>
</tr>
</tbody>
</table>

Outcomes and Healthcare Utilization

Compared to non-delirious patients in our cohort, delirious patients generally experienced worse outcomes (Table 7). Delirious patients exhibited a 5.2% 30-day mortality rate, compared to 0.9% in non-delirious patients (p=0.02). The association between 30-day mortality and hospital-acquired delirium remained significant (p=0.003) after controlling for age, dementia, CCI Score, nursing home residence and APACHE II score. The median length of stay for delirious patients was 4 days, compared with 2 days for the non-delirious group (p<0.0001). Hospital-acquired delirium remained predictive of longer length of stay (p<0.0001) in a log-transformed model of length adjusted for age, dementia, CCI Score, nursing home residence and APACHE II score. Delirious patients were more likely to be admitted to a long-term care facility upon discharge from the hospital. The proportion of delirious patients who were discharged to a new SNF or acute rehabilitation facility was 30%, compared to only 13% in the non-delirious group (p<0.0004). Delirious patients also accumulated greater total
hospital charges that non-delirious patients (p<0.0001); however there was no
difference in hospital charges when adjusted for length of stay (p=0.15). There
was also no significant difference in the rates of ICU admission (p=1.0), or 30-
day rehospitalizations (p= 0.8) between the delirious group, and the non-delirious
group.

Table 7: Outcomes of Hospital-Acquired Delirium. Analysis of outcomes in
patients with and without hospital-acquired delirium. Proportions are reported for
dichotomous variables, and medians with 25-75% IQR are reported for non-
normal, continuous variables.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Entire Cohort (N=520)</th>
<th>Delirious (N=77)</th>
<th>Non-Delirious (N=443)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day Mortality, n (%</td>
<td>8 (1.5%)</td>
<td>4 (5.2%)</td>
<td>4 (0.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>30-day Rehospitalization</td>
<td>80 (15%)</td>
<td>11 (14%)</td>
<td>69 (16%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Discharge to a new SNF or acute rehabilitation, n (%)</td>
<td>79 (15%)</td>
<td>23 (30%)</td>
<td>56 (13%)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Admission to ICU, n (%)</td>
<td>6 (1.2%)</td>
<td>5 (1.3%)</td>
<td>5 (1.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Total Length of Stay, days, median (IQR)</td>
<td>2 (1-4)</td>
<td>4 (2-7)</td>
<td>2 (1-4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospital Charges, median (IQR)</td>
<td>$14,063 (9,774-22,375)</td>
<td>$18,212 (12,756-35,928)</td>
<td>$13,015 (9,222-20,640)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
DISCUSSION

Risk Prediction Model

Through validated chart review methods, we identified 77 (15%) patients who were non-delirious at ED presentation, and developed delirium throughout their hospital admission. Although this is lower than other estimates of inpatient delirium, our cohort excluded 65 admitted patients who were already delirious in the ED. Accordingly, 24% of the 585 admitted patients were delirious on admission or developed delirium while hospitalized, which is consistent with prior studies of delirium occurrence (11-64%) among inpatients (Inouye et al., 2014) (Siddiqi et al., 2006).

The predictive model we developed had good discrimination with a c-statistic of 0.73 and good calibration, as demonstrated by a non-significant p-value on the Hosmer-Lemeshow goodness-of-fit test. The covariates identified to be predictive of hospital-acquired delirium by our multivariate analysis were age greater than 80, previous history of dementia, previous history of stroke/TIA, hypoxia, hyponatremia, ED diagnosis of a stroke/TIA, and ED diagnosis of a fall. The fact that our model includes a combination of predisposing and precipitating factors is consistent with the multivariate model of delirium causes that is has been previously described in elderly patients (Inouye et al., 2014).

Many of the individual risk factors that we identified are also supported by prior reviews and cohort studies examining delirium in inpatient settings. Among these common covariates are older age, history of dementia, abnormal sodium...
levels, hypoxia, and history of a stroke (Cole, 2004) (Inouye et al., 2014) (Inouye et al., 2015) (Ahmed et al., 2014). Abnormal sodium levels could also indicate underlying dehydration which has also been identified as a risk factor for postoperative delirium (Chow, Rosenthal, Merkow, Ko, & Esnaola, 2012). While ED physician diagnosis of a fall is not widely supported by previous studies as an independent risk factor, immobilization has been linked to delirium (Chow et al., 2012). It is possible that diagnosis of a fall may be linked to immobilization due to injury or implementation of fall precautions. This demonstrates consistency of our results with prior research and further suggests some consistency between inpatient risk factors and ED risk factors of delirium in elderly patients. Elements of our multivariate model including age, history of dementia, and history of a stroke are also consistent with risk factors that have been identified in other studies specific to ED cohorts (Kennedy et al., 2014) (Han et al., 2009). Of note, our primary study didn’t find a diagnosis of stroke/TIA to be significantly correlated with delirium in the ED, but our secondary analysis found it to be significantly associated with hospital-acquired delirium (Kennedy et al., 2014). This could represent differences in the patient population, or it could reflect physiological delay in delirium onset post stroke.

Other risk factors that we didn’t find to be significant, but have been identified in ED populations through other studies include reduced competency with Activities of Daily Living (ADLs), infection, and hearing impairment, and severity of illness (Kennedy et al., 2014) (Han et al., 2009). For this analysis we
did not collect information on either ADLs or hearing impairment, as they were not routinely assessed in our ED at the time of this study. Our study did not find infection or APACHE II score to be significantly associated with delirium, which could again reflect the difference in study populations or, as both were significantly associated with ED delirium in our primary study (Kennedy et al., 2014), may represent a temporal relationship between these measures and delirium onset. For instance, if a patient is susceptible to develop delirium from a high severity of illness, they will already be delirious on presentation to the ED.

This model has the potential to inform inpatient delirium screening approaches, hence impacting health systems and the care provided to elderly patients. As a prediction rule, our model could help identify a subset of these patients in the ED who should undergo formal screening for delirium. If formal screening was completed on all patients with a score of at least 1, the model would successfully identify delirious patients with a high sensitivity of 0.82. The limited specificity of 0.54 at this cut off, however, would require daily inpatient screening of 58% of admitted older patients. However, as prior publications have recommended formal screening of all admitted elderly patients, this would still represent a reduction in the number of patients who need screening (Young et al., 2010).

If instead, a cutoff score of at least 2 points is used, it would only require 20% of the patients to be formally screened, however the sensitivity of the model is substantially reduced to 55% (Table 7); accordingly we would miss 45% of
hospital-acquired delirium. However, this still may represent an overall decrease in rates of missed delirium, as Spronk et al found that only 28% of delirious days experienced by ICU patients were identified by attendings (Spronk, Riekerk, Hofhuis, & Rommes, 2009). A cut-off above 2 points would reduce sensitivity too much to be useful as a tool.

Alternatively, this model could be used to implement a two-tiered approach to stratification of delirium risk. A cut-off score of one could be used to identify patients who should undergo formal screening, while a cut-off of two would indicate patients who may warrant implementation of multifactorial delirium prevention measures such as the HELP program. Delirium screening is less time consuming and more cost effective than implementation of delirium precautions, so this approach could optimize hospital resource use while maximizing identification of delirium.

Importantly, this model is a simple tool that is easy to use, and can be implemented by any care provider, or potentially be automated by electronic systems to identify at-risk admitted patients who might benefit from routine screening and delirium prevention strategies. As previously discussed, delirium often goes undiagnosed both in the ED and in inpatient settings. If this model can be used to identify a subset of high risk patients, who will need delirium prevention measures, before they are even admitted, it may help reduce the rates of undiagnosed delirium, increase targeted implementation of delirium prevention measures, and decrease overall incidence of delirium. The
implications of this are particularly important as our results, along with those of prior studies have demonstrated the increased mortality, length of stay, and costs associated with delirium. Since prevention methods are currently the most effective way to reduce the mortality associated with delirium, this population (those that are not delirious in the ED but become delirious after hospital admission) may be the best target for reducing overall mortality and healthcare resources attributed to delirium.

**Delirium Outcomes and Utilization Metrics**

Delirious patients in our cohort experienced higher rates of mortality, longer lengths of stay, greater hospital charges, and higher rates of admission to a SNF than the non-delirious patients. This is consistent with other studies of delirium, both in the inpatient setting as well as the ED (Siddiqi et al., 2006) (Leslie DL et al., 2005) (Han et al., 2010). The greater hospital charges however, are driven by the fact that delirious patients had longer lengths of stay, as there was no difference in hospital charges when we controlled for length of hospitalization.

While prior studies have found correlation between delirium and rates of ICU admissions and rehospitalizations we found no significant difference in rehospitalizations or ICU admissions between delirious and non-delirious study populations. This could also be a reflection of our unique study cohort, particularly exclusion of any patients who were already delirious in the ED. In our primary study we found that ED delirium was associated with ICU admission and
rehospitalization rates. Therefore these differences may be because patients who are delirious on arrival to the ED may be a generally sicker population, or be due to differences in delays to treatment, or malnutrition. Further research is necessary to determine the reasons for these differences.

Limitations

This study was completed entirely at a single urban university tertiary care center. Patients included in our cohort therefore tend to be of a higher acuity than patients at smaller community hospitals. It is possible that elements of our model such as diagnosis of a stroke/TIA would not be a useful metric in those settings where patients tend to be of generally lower acuity. Given the process of informed consent and delirium assessment, we were also unable to enroll patients of limited English proficiency. It is possible that the risk prediction model created using this patient population is not applicable to all populations, or all types of hospitals.

Furthermore, two of the covariates included in our final model, physician diagnosis of a stroke and physician diagnosis of fall, rely on assessment from the clinical care team. Therefore the model can’t necessarily be applied until the patient has already been seen by a physician in the ED. However, as this model is designed for patients that will ultimately be admitted to an inpatient unit, this would still represent an early time point in the course of care, and still allow for calculation prior to admission.
Another limitation of this study is the use of the CAM. The CAM is unable to assess 100% of patients in the ED, since a positive diagnosis of delirium relies on a sudden onset or fluctuation of symptoms. If the interviewer and care team did not witness fluctuation of symptoms, or if the patient’s baseline was unknown, the CAM was unable to classify the patient as delirious even if inattention with disordered thinking or altered level of consciousness had been identified. These patients, however, were excluded from our analysis.

The results were further limited by necessity for informed consent. If a patient was not able to consent, and a healthcare proxy was not present, they could not be included in the study. This excluded population could include patients with multiple risk factors of delirium, including dementia, cognitive impairments, or visual or hearing impairments. Furthermore, our study only assessed patients cognitive functioning at a single time point, early in their ED course. For these reasons it is possible that our estimates underestimate the incidence of delirium in the ED, or overestimate the proportion of patients that acquired delirium as an inpatient.

We were also limited by the information that we were able to collect. Specifically, while we documented home medications for each patient, we didn’t collect information on medications that were prescribed in the ED, or during the hospital course. Certain medications have been reported to be associated with onset of delirium in previous studies, so it is possible that inclusion of hospital medications could alter our model. Lastly, our risk prediction model demonstrates
correlation, but not necessarily causation. We were able to identify covariates that may indicate a likelihood of developing delirium, but that do not necessarily cause delirium.

**Suggestions for Future Research**

As previously mentioned, this model demonstrates good discrimination in our patient population, but further research is necessary before it can be implemented clinically. External validation of the model is necessary to ensure that it is applicable to diverse patient populations, and different types of hospitals. Further research is also required to better understand causes of delirium, and create interventions to successfully reduce morbidity and mortality after a diagnosis has been made.

In conclusion, we created a predictive scoring model that can be used to identify at the most proximal point of care, a subset of patients who are at higher risk for development of delirium over the course of their hospital admission. Once externally validated, this model can hopefully be useful in targeting prevention strategies to the most at-risk populations.


CURRICULUM VITAE

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EDUCATION
Boston University School of Medicine; Boston, MA, Expected May 2016
Master of Science in Medical Sciences
Boston University, Sargent College; Boston, MA, January 2014
Bachelor of Science in Human Physiology
Minor in Public Health

EMPLOYMENT
BETH ISRAEL DEACONESS MEDICAL CENTER; Boston, MA, 2011-Present
Clinical Research Assistant, Emergency Department (2011-Present)
Responsibilities include recruitment, screening and enrollment of research patients, interacting with patients/family members, phlebotomy and specimen processing, data collection, entry and database maintenance, and completion follow-up phone calls. Lead Clinical Research Assistant for a study researching the epidemiology of delirium in emergency room patients.

Laboratory Technician, Center for Vascular Biology Research at Harvard Medical School (2011)
Research involving biomarkers in sepsis patients. Responsibilities included running Enzyme-Linked Immunosorbant Assays (ELISA) on blood samples obtained through clinical research initiatives.

BRIGHAM AND WOMEN’S HOSPITAL; Boston, MA, Fall 2013
Intern, Non-Invasive Cardiovascular Imaging, Department of Radiology
Responsibilities included interviewing patients to collect past medical history and information about their presenting illness, explaining procedures to patients, and monitoring blood pressure and ECGs during various procedures including cardiovascular stress tests, cardiopulmonary stress tests, stress echocardiograms and nuclear imaging.

MASSACHUSETTS GENERAL HOSPITAL & BOSTON UNIVERSITY; Boston, MA, Summer 2013
Clinical Research Assistant, Bionic Pancreas Summer Camp Study
Collaborative research initiative between BU and MGH for the clinical trial of an automated bihormonal, closed-loop artificial pancreas in adolescents with Type 1 diabetes. Responsibilities included monitoring subjects’ data and troubleshooting device errors.

BOSTON UNIVERSITY; Boston, MA, Summer 2012
Front Desk Attendant, Department of Events and Conferences
Guest service for visiting conferences. Responsibilities included facilitating
the arrival and departure of conference housing guests, providing
assistance to guests while in residence, and interacting with guests both in
person and by telephone.

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL; Worcester, MA,
Summer 2008-2010
Laboratory Technician, Pathology Research Department (2009-2010)
Researching miRNAs in prediction of thyroid cancer progression. Isolated
RNAs from LCM tumor samples and FFPE blocks; ran miRNA arrays;
performed various other lab tasks, including Western Blots,
electrophoresis, maintenance of cell lines, end-point PCR, real-time PCR
miRNA assays. Manuscript accepted for publication.

Laboratory Technician, Cancer Biology (2008)
Assisted in breast cancer research. Cloned miRNA target into plasmid
vector and created retrovirus containing the plasmid; performed end-point
PCR and gel electrophoresis, grew cell cultures, maintained cell lines,
isolated DNA from cells.

PUBLICATIONS AND PRESENTATIONS
Shapiro, Edward R. Marcantonio. How Accurate Are Emergency
Physicians And Nurses In Assessing Delirium Motoric Subtypes And
Delirium Superimposed On Dementia? Presented at Society of Academic
Kennedy, M., Enander, R. A., Tadiri, S. P., Wolfe, R. E., Shapiro, N. I., &
Marcantonio, E. R. (2014). Delirium risk prediction, healthcare use and
mortality of elderly adults in the emergency department. Journal of the
American Geriatrics Society, 62(3), 462–469.
http://doi.org/10.1111/jgs.12692

VOLUNTEER EXPERIENCE
SQUASHBUSTERS; Boston, MA, March 2015-Present
SquashBusters is an after-school program that combines athletics and
academic elements for adolescents in grades 7-12 in Boston city schools.
I volunteer as a tutor for homework and special enrichment programs such as
SAT preparation.

SARGENT SERVICE LEARNING; San Jose, Costa Rica, March 2013
Traveled with Sargent College staff and medical professionals to volunteer
in temporary clinics aimed at providing health care to underserved
populations. Clinics provided medical consults, nutrition consults, dentistry
and pharmaceuticals. Trip also included volunteer work at homes for the
elderly, and leading nutrition workshops at a local day care center.

BOSTON UNIVERSITY GLOBAL MEDICAL BRIGADES; Tegucigalpa,
Honduras, May 2012
Traveled with medical professionals, medications and supplies to provide healthcare to underserved communities. Brigade services included general medicine, gynecology, dentistry, pharmacy and public health lectures for both children and adults.