

SCREENING FOR DELIRIUM USING THE ELECTRONIC MEDICAL RECORD

by

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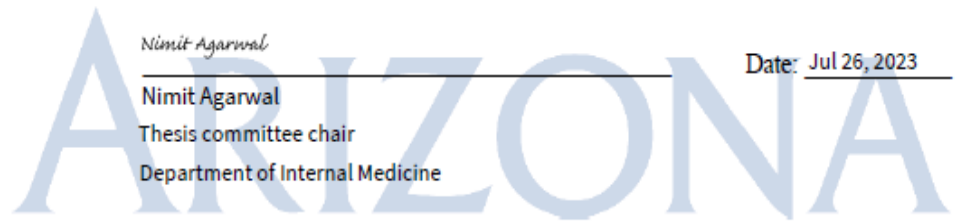
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Final approval and acceptance of this thesis is contingent upon the candidate's submission of the final copies of the thesis to the Graduate College.

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Screening for Delirium using the Electronic Medical Record

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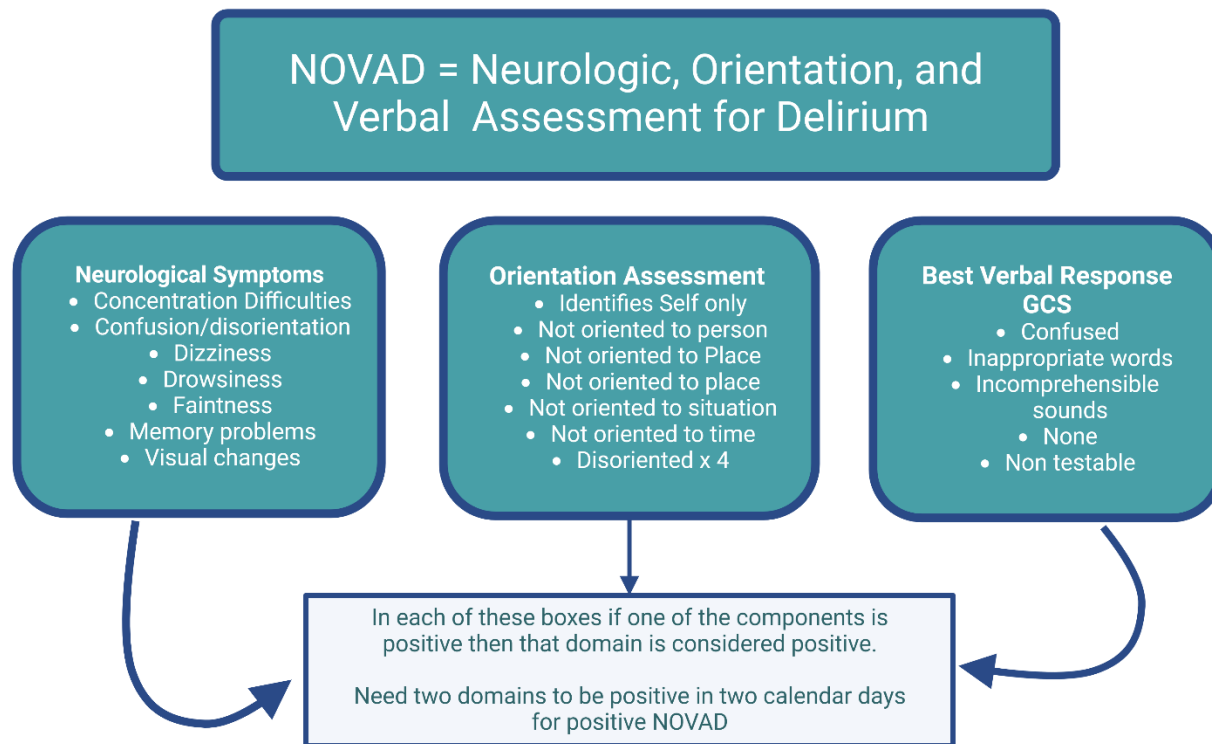
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TABLE OF CONTENTS

I.	Tables and Figures	5
II.	Abstract.....	11
III.	Conflict of Interest Statement	12
IV.	Forward.....	12
V.	Introduction	
	a. Delirium Overview	15
	b. Risk Factors and Diagnosis.....	15
	c. Pathophysiology.....	16
	d. Electronic Medical Record Screening Tools.....	19
	e. NOVAD Study	20
VI.	Methods	
	a. Participant Information	21
	b. Data Collection.....	21
	c. Data Interpretation/Scoring	22
	d. Statistical Analysis.....	23
VII.	Results.....	23
VIII.	Discussion	24
IX.	Conclusions	28
X.	Appendix	28
XI.	References	31

TABLES AND FIGURES

Figure 1: A graphic depicting the NOVAD tool. Each box in the middle lists a nursing assessment, domain, taken from the EMR to screen for delirium. For each domain (neurologic symptoms, orientation assessment, and best verbal response on GCS) nurses can document any of the following choices that are listed under the domain title. The test is considered positive if two domains are positive in two calendar days. Created with BioRender.com



Abbreviations: GCS (Glasgow coma score)

Screening for Delirium using the Electronic Medical Record

Table 1: Overall participant characteristics including age, sex, race, and length of hospital stay.

Characteristics	Overall (N= 464,395)
Age mean (sd)	56.18 (20.82)
<65 n (%)	274, 374 (59.08)
65-74	83,732 (18.03)
75-84	70,536 (15.19)
85+	35, 753 (7.70)
Sex n (%)	
Male	203,442 (43.81)
Female	260,856 (56.17)
Unknown (missing)	97 (0.02)
Race n (%)	
Asian/Pacific Islander	5,298 (1.14)
Black	27,847 (6.00)
Hispanic	100,314 (21.60)
Native American/Alaskan	15,921 (3.43)
Other/Multiple	7,968 (1.72)
Unknown	3,576 (0.77)
White	303,471 (65.35)
LOS (days) Med(IQR)	3.37 (1.97, 6.21)

Abbreviations: interquartile range (IQR), length of stay (LOS), median (med), standard deviation (sd)

Screening for Delirium using the Electronic Medical Record

Table 2: Positive and negative sample size for each test broken down and further characterized by age, age group, sex, and length of stay.

Characteristics	NOVAD Neg (n=328,619)	NOVAD Pos (n=135,776)	CAM Neg (n=453,212)	CAM Pos (n= 11,183)	ICD-10 Code Neg (n=411,890)	ICD-10 Code Pos (n=52,505)
Age mean (sd)	51.78 (20.38)	66.84 (17.79)	55.89 (20.82)	69.66 (15.89)	54.73 (20.84)	67.54 (16.72)
Age group n (%)						
<65	222,068 (80.94)	52,306 (19.06)	270,795 (59.75)	3,579 (32.00)	254,809 (92.87)	19,565 (7.13)
65-74	52,893 (63.17)	30,839 (36.83)	80,974 (17.87)	2,758 (24.66)	71,103 (84.92)	12,629 (15.08)
75-84	39,019 (55.32)	31,517 (44.68)	67,640,273 (14.92)	2,896 (25.90)	57,988 (82.21)	12,548 (17.79)
85+	14,639 (40.94)	21,114 (59.06)	33,803 (7.46)	1,950 (17.44)	27,990 (78.29)	7,763 (21.71)
Sex n (%)						
Male	132,969 (65.36)	70,473 (34.64)	197,552 (97.10)	5,890 (2.90)	175,767 (86.40)	27,675 (13.60)
Female	195,581 (74.98)	65,275 (25.02)	255,564 (97.97)	5,292 (2.03)	236,035 (90.48)	24,821 (9.52)
Unknown (missing)	69 (71.13)	28 (28.87)	96 (98.97)	1 (1.03)	88 (90.72)	9 (9.28)
LOS (days) Med(IQR)	2.82 (1.78, 4.83)	5.94 (3.21, 10.82)	3.33 (1.90, 6.05)	9.08 (5.15, 16.09)	3.11 (1.90, 5.72)	6.77 (3.68, 12.67)

Abbreviations: Modified confusion assessment method (CAM), International classification of diseases version 10 (ICD-10), Interquartile range (IQR), length of stay (LOS), median (med); Negative (neg) Neurologic, orientation, and verbal assessment for delirium (NOVAD); Positive (pos), standard deviation (sd)

Screening for Delirium using the Electronic Medical Record

Table 3: Sensitivity, specificity, positive predictive value and negative predictive value of NOVAD and CAM in predicting delirium among the present study sample using ICD-10 codes for delirium and encephalopathy as true positive for delirium

Parameters	NOVAD vs ICD-10 code	CAM Vs ICD-10 code
Sensitivity % (95% CI)	86.63 (86.53, 86.73)	13.74 (13.64, 13.83)
Specificity % (95% CI)	78.08 (77.96, 78.20)	99.04 (99.01, 99.06)
Positive Predictive Value % (95% CI)	33.50 (33.36, 33.64)	64.53 (64.35, 64.63)
Negative Predictive Value % (95% CI)	97.86 (97.82, 97.91)	90.01 (89.92, 90.09)
Chi square p-value	<0.0001	<0.0001
Likelihood Ratio	<0.0001	<0.0001

Abbreviations: Modified confusion assessment method (CAM), International classification of diseases version 10 (ICD-10), Interquartile range (IQR), length of stay (LOS), median (med); Negative (neg) Neurologic, orientation, and verbal assessment for delirium (NOVAD); Positive (pos), standard deviation (sd)

Screening for Delirium using the Electronic Medical Record

Table 4: Reported race of participants and break down of positive and negative NOVAD and CAM scores by race.

Race	n (%)	NOVAD Neg (n=328,619)	NOVAD Pos (n=135,776)	CAM Neg (n=453,212)	CAM Pos (n= 11,183)
Asian/Pacific Islander	5,298 (1.14)	3,934 (1.20)	1,364 (1.00)	5,220 (1.15)	78 (0.70)
Black	27,847 (6.00)	20,386 (6.20)	7,461 (5.50)	27,285 (6.02)	562 (5.03)
Hispanic	100,314 (21.60)	75,418 (22.95)	24,896 (18.34)	98,364 (21.70)	1,950 (17.44)
Native American/Alaskan	15,921 (3.43)	10,748 (3.27)	5,173 (3.81)	15,541 (3.43)	380 (3.40)
Other/Multiple	7,968 (1.72)	5,683 (1.73)	2,285 (1.68)	7,769 (1.71)	199 (1.78)
Unknown	3,576 (0.77)	2,884 (0.88)	692 (0.51)	3,531 (0.78)	45 (0.40)
White	303,471 (65.35)	209,566 (63.77)	93,905 (69.16)	295,502 (65.20)	7,969 (71.26)

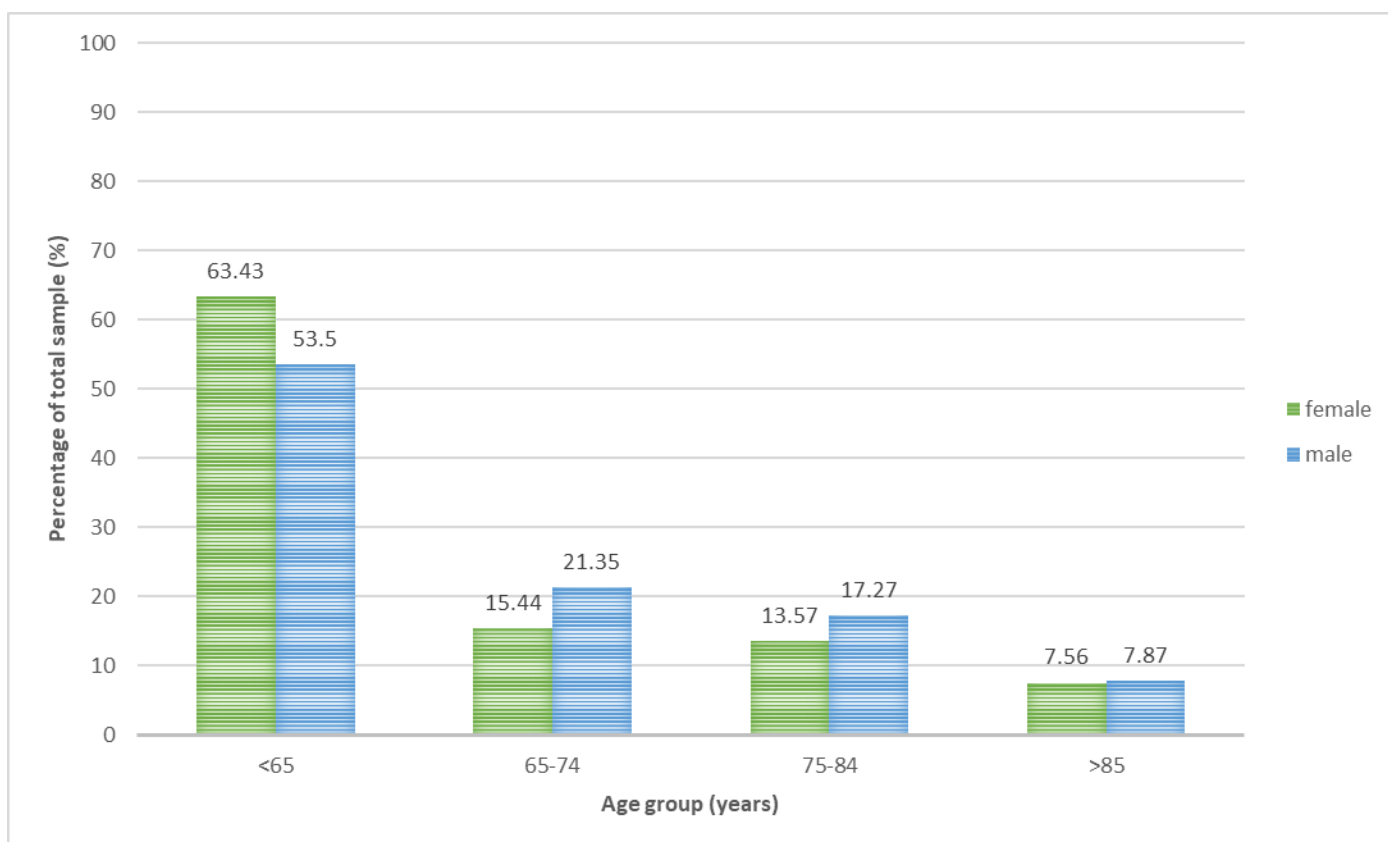
Abbreviations: Modified confusion assessment method (CAM), Negative (neg) Neurologic, orientation, and verbal assessment for delirium (NOVAD); Positive (pos)

Screening for Delirium using the Electronic Medical Record

Table 5: Percentage and total number of male and female participants for each age group

Age group	Female (n=260,856)	Male (n=203,442)
n (%)		
<65	165,449 (63.43)	108,849 (53.50)
65-74	40,282 (15.44)	43,443 (21.35)
75-84	35,393 (13.57)	35,133 (17.27)
>85	19,732 (7.56)	16,017 (7.87)

Figure 2: Bar graph depicting percentage of male and female participants for each age group



Screening for Delirium using the Electronic Medical Record

ABSTRACT

Background: Delirium is characterized by an acute disturbance in cognition and attention. It is common and disproportionately affects elderly hospitalized adults. It is associated with increased risk of dementia, increased mortality, and increased healthcare costs. Early detection and identification of those at highest risk for delirium is crucial to mitigate these adverse effects. The current study seeks to determine the validity of a novel screening tool: the Neurological Orientation, Verbal response Assessment of Delirium (NOVAD) to detect delirium utilizing Electronic Medical Record (EMR) data.

Methods: This is a retrospective observational study of EMR data extracted from hospitalized patients at a large multi-state hospital system. Data for the NOVAD score was documented by nurses as part of routine assessments and extracted from the patient's EMR. This was then compared to the patient's Confusion Assessment Method (CAM) score as recorded by nursing as well as whether a physician had documented the patient as having Delirium or Encephalopathy by International Classification of Disease version 10 (ICD-10) code. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated by comparing NOVAD detection of delirium to CAM and delirium or encephalopathy ICD-10 code.

Results: 464,395 participants were included in this study. The mean age of study participants was 56.18 years (SD 20.82) and the sample was 56.17% female (n = 260,856). The prevalence of participants in the study with a positive NOVAD score was 29.23% (n = 135,776; 95% CI: 0.2911, 0.2937). Nursing administered modified CAM score was documented positive in 2.41% (n = 11,183; 95% CI: 2.31%, 2.45%) of participants. NOVAD was found to be 86.63% sensitive (95% CI 86.53, 86.73) and 78.08% specific (95% CI: 77.96, 78.20) based on ICD-10 code diagnosis of delirium or encephalopathy as being truly positive for delirium.

Screening for Delirium using the Electronic Medical Record

Conclusion: The current study's results suggest that NOVAD is a sensitive early warning screening tool for delirium in hospitalized adults. Given poor specificity the tool is best suited for identifying patients who would benefit most from specialist care teams.

CONFLICT OF INTEREST STATEMENT

Kyle Angus Hendrie, DO has no conflicts of interest to disclose.

FORWARD

Perspective as a Psychiatry Resident

I was first given the opportunity to be involved in delirium research by Dr. Babar Khan, while in medical school at Marian University College of Osteopathic Medicine. I am fortunate to be the grandson of renowned geriatric psychiatrist and clinician researcher, Dr. Hugh Hendrie, who convinced his intensivist friend and research colleague that training me in the ways of clinical research was worthwhile. At that time, I was a second-year medical student and had little if any clinical experience with delirium but some combination of the enigma surrounding the condition and Dr. Khan's incredible enthusiasm reeled me in. When I have spare time, much like my grandfather before me, I am an avid reader of crime fiction. Unlike a great crime fiction novel, the answer to our questions about delirium are not found at the end of any text currently written. In continuing to involve myself in delirium research I realized the opportunity exists to help write the conclusion; to potentially solve a mystery.

I found a mention of the opportunity, on the program's website, to complete a graduate degree program in clinical translational sciences while in residency, during my application process and this heavily influenced my decision to rank the program as my top choice. In coming to the University of Arizona Phoenix College of Medicine for psychiatry residency I found another enthusiastic clinician scientist mentor in Dr. Nimit Agarwal. Dr. Agarwal was gracious enough to invite me to help him test and develop an improved screening method for delirium in hospitalized patients.

Screening for Delirium using the Electronic Medical Record

As a psychiatry resident, the value of improving early identification of those patients at highest risk for delirium is obvious. On the psychiatry consultation service, we take care of patients admitted to the hospital for reasons other than psychiatric conditions but who are also in need of a psychiatrist's opinion or management. When the psychiatry consultation team is asked to see a patient with delirium, it is too late. The patient has already become agitated; perhaps they physically assaulted a nurse or attempted to leave the hospital when it was clear they lacked capacity to soundly make such a decision. Physical and chemical restraints have often already been ordered. In other instances, the patient is profoundly withdrawn, and staff are concerned for a depressive syndrome. It is grotesque to see a frail, geriatric patient restrained to a hospital bed, too sedated to answer simple questions.

I completed my psychiatry residency during the COVID-19 pandemic. For a large portion of my program, patients in the hospital were not allowed visitors. This left them without their greatest potential advocates: family and friends. Every unit in the hospital was short-staffed meaning nurses and technicians were taking care of a higher volume of complex patients; not to mention the immense stress these individuals were dealing with outside of the work environment related to the pandemic.

It is too late when the psychiatry consultation team is called in these instances because we have no effective medications to cure delirium. Even non-pharmacologic strategies proven to help prevent the condition do not have consistent clinical trial data to support their efficacy in curing the condition or shortening the course. The best we can do is advocate for the patient. We recommend all the known interventions to prevent delirium often knowing that nursing staff are aware of these interventions but don't have time to complete all of them on every patient. When we are doing our job correctly, we are also advocating for nurses and other hospital staff; listening and providing support in any way we can. The management and prevention of a patient with delirium requires a team effort. It is difficult, demoralizing at times, but this condition has the potential to cause too many adverse effects to be ignored.

Screening for Delirium using the Electronic Medical Record

As discussed in this thesis, delirium is associated with numerous adverse consequences including increased mortality and risk of dementia. With no curative treatment, detecting the condition in early stages or preventing it all together by intervening in those patients at highest risk is imperative. An electronic medical record tool to identify these patients that utilizes nursing assessments already being completed with high compliance could be paramount in helping specialty teams, such as psychiatry or geriatric medicine, prioritize the patients who are in most need of symptom management or preventative care.

I do not view this thesis submission as the ending; I see it as a status update. I will continue to work to help solve the enigma that is delirium and to improve the medical care of hospitalized adults in the process.

Screening for Delirium using the Electronic Medical Record

INTRODUCTION

Delirium Overview

Delirium is a common and dangerous condition with significant cost impact on public health.¹

Prevalence estimates vary but are as high as 35% in all patients on general medical hospital floors and as high as 82% in patients on intensive care units.¹ A meta-analysis from 2020 of hospitalized patients in 33 studies found a pooled prevalence of 23%.² Delirium is shown to increase mortality, risk of future cognitive impairment, hospital length of stay, and institutionalization among other adverse outcomes.¹

It is underrecognized and underdiagnosed.³⁻⁵ This is despite the existence of multiple sensitive and specific diagnostic assessments and measurement tools.⁶ Furthermore, many cases of the syndrome are preventable.^{7,8} Currently, there are no evidence based curative treatments for the condition, and medications often administered to delirious patients are largely used to mitigate associated agitation.⁹

Leslie and colleague's 2008 article published in Archives of Internal Medicine estimated yearly cost of delirium in the United States based is as much as \$152 billion. In comparison, estimated yearly costs for other major medical conditions include \$327 billion per year in 2017 for diabetes, \$216 billion per year in 2018 for heart disease and stroke, \$183 billion per year in 2015 for cancer, and \$62 billion per year in 2019 for sepsis.¹⁰⁻¹⁴

With associations to multiple adverse consequences for patients, no curative treatment and high healthcare costs, it is imperative to detect the condition early and identify those at highest risk for developing the condition early, to optimize prevention strategies.

Risk Factors and Diagnosis

The most widely recognized definition of delirium is from the Diagnostic and Statistical Manual for Disease version 5 Text Revision (DSM-5-TR) where it characterized as a neurocognitive disorder and defined by a disturbance in attention and cognition as well as reduced environmental awareness that is

Screening for Delirium using the Electronic Medical Record

acute, fluctuating and a change from a person's baseline attention and awareness. The DSM-5-TR definition further states the condition must have an identified physiologic cause and not be better explained by another neurocognitive condition.¹⁵ The confusion assessment method, a groundbreaking screening tool developed by delirium research pioneer Sharon Inouye M.D., has been adapted to fit a variety of different environments (IE. CAM-ICU, bCAM). Other tools relying on behavioral checklists have also been developed such as the Delirium Observation Screening (DOS), the Nursing Delirium Screening Scale (NuDESC), and the NEECHAM confusion tool. Severity scales also exist such as the Delirium Rating Scale (DRS) and the Memorial Delirium Assessment Scale (MDAS).⁶ While these tools are validated in research environments, their validation often does not hold up when implemented in other healthcare settings.¹⁶

Delirium most commonly affects older, hospitalized adults. A systematic review and meta-analysis reported a mean difference for old age and delirium as 2.74 (95% CI 0.11, 5.38), when compared with those not considered to be of old age. Old age was defined to be above the age of 60 for three studies included in this analysis and above the age of 65 for one study.¹⁷ Other established risk factors for delirium include dementia, co-morbid medical conditions, sensory impairment, limited mobility, use of mechanical ventilation, urinary catheterization, use of deliriogenic medications (namely anti-cholinergic medications, GABAergic sedatives and opiate pain medications), and electrolyte abnormalities.^{1,17,18}

Pathophysiology

Simplistically, delirium arises when the brain is unable to maintain its baseline functioning in the presence of physiologic stressors. In 1980, Zibigniew Jerzy Lipowski (ZJ Lipowski) published *Delirium: Acute Brain Failure in Man*; a comprehensive text on current understanding of the condition. In reference to the pathophysiology of delirium he states "Our knowledge of this area is very incomplete." He draws parallel to a text written in 1936: "In discussing at the present time the possible pathogenesis of delirium we have therefore to leave the sphere of knowledge and enter that of hypothesis and

Screening for Delirium using the Electronic Medical Record

speculation." Today, numerous studies have been conducted to improve our understanding of delirium pathophysiology and attempts to summarize key mechanistic pathways diagrammatically continue to resemble a spider web.

Two review articles published since 2017 are widely cited and referenced for their thorough yet succinct compilation of the current evidence-based hypotheses of delirium pathophysiology: José Madonado's article "Delirium pathophysiology: An updated hypothesis of the etiology of acute brain failure" published in the *International Journal of Geriatric Psychiatry* in 2018 and Wilson et al.'s article "Delirium" published in *Nature Reviews Disease Primers* in 2020. Both discuss health related factors that put patients at highest risk for the syndrome and use what is known about these factors to synthesize proposed pathophysiologic mechanisms.

Predisposing factors for delirium include long standing characteristics that have been shown to place a person at higher risk for the condition. These include older age, dementia and other cognitive impairments, psychiatric illness, frailty, having multiple chronic medical conditions, sensory impairment (hearing or vision impairment), alcohol use and poor nutritional status.⁹ Precipitating factors are acute attributes that when occurring in the presence of predisposing factors put a person at highest risk for developing delirium. These include acute medical conditions (acute kidney injury, infection, dehydration etc.), surgery, falls and other forms of traumatic injuries, insufficiently managed pain, substance withdrawal, and use of deliriogenic medications (anticholinergic medications, benzodiazepines, opiate pain medications, etc.) among others.^{9,18}

Maldonado reports the mnemonic "End Acute Brain Failure" in his 2020 article to help readers remember 20 clinically relevant predisposing and precipitant risk factors: Electrolyte abnormalities and fluid imbalance, neurological disorders and injuries, deficiencies (nutritional), age and gender, cognitive functioning, urine tox (referring to acute substance intoxication and withdrawal states), trauma, endocrinopathies, behavioral-psychiatric disorders, rx (referring to medication use and other

Screening for Delirium using the Electronic Medical Record

toxidromes), anemia, anoxia, hypoxia and low perfusion/oxygenation states; infections, noxious stimuli (referring to pain), failure (referring to organ failure), Apache score (referring to illness severity), isolation and sensory deprivation, light, sleep and circadian rhythm; uremia and other metabolic disorders, restraints and immobility, and emergence delirium (referring to delirium arising when patients awake from iatrogenic sedation, coma or other states of decreased conscious awareness).

In some instances, one or a few precipitating factors is enough to trigger delirium in someone without predisposing factors though most cases of delirium are in persons with multiple predisposing and precipitating factors.⁹

Authors in both articles hypothesize that delirium pathophysiology involves a combination of multiple processes. Dr. Maldonado refers to his conceptualization of delirium pathophysiology as “the systems integration failure hypothesis.” He describes predisposing and precipitant factors as causing neuronal aging, neuroinflammation, oxidative stress, neuroendocrine dysregulation, and circadian dysregulation. These processes in turn lead to neurotransmitter dysregulation and neural network dysconnectivity and phenotypic delirium symptoms.¹⁹

Wilson et al., describe their synthesis as an “evidence-based conceptual framework of delirium pathophysiology” by compiling data from animal models and clinical research studies in the field.⁹ Like Maldonado, Wilson and colleagues conclude that delirium arises from some combination of dysfunction in brain energy metabolism (both through energy substrates such as ATP and glucose and decreased cerebral oxygen supply), inflammation (both system and central nervous system processes), and imbalances of “drugs, stress and neurotransmitters.”⁹

While Wilson et al. 2020, mention the plausibility of blood brain barrier dysfunction as playing a role in delirium pathophysiology they opine that evidence to support this is lacking. Maldonado in his 2017 article listed active transport across the blood brain barrier and blood brain barrier disruption as possible pathways for the neuroinflammatory response seen in delirium. Devinney and colleagues in

Screening for Delirium using the Electronic Medical Record

2023 released a pre-print version of an article detailing a research study that assessed CSF fluid to plasma albumin ratio (CPAR) as a measure of blood brain barrier dysfunction before and after surgery to investigate the role of BBB dysfunction in delirium. Authors of this study report, change in CPAR was greater in study participants who developed delirium compared to those who did not suggesting an association between increased blood brain barrier permeability following surgery and delirium. ²⁰ An author on this article, Niccolo Terrando has investigated and demonstrated this association in several studies using an orthopedic surgery animal model of delirium. ²¹

Electronic Medical Record Screening Tools

There are many tools that utilize electronic medical record data to screen for or assess severity of different medical conditions. They can aid in identifying patients at high risk for developing these conditions and early detection when the conditions are present. ^{22,23}

Delirium is often considered to be a diagnosis of exclusion and as such it is commonly suggested that other possible neurologic and psychiatric explanations for symptoms appearing to be delirium should be ruled out. Considering the incredible diversity of pathologic conditions that can cause delirium, this idea could be considered counterintuitive. Delirium is a difficult condition to rule out. Many hospitalized patients have at least one precipitating and predisposing factor for delirium. Many studies use EEG findings as a marker of delirium. For decades it has been recognized that patients with delirium show characteristic findings on EEG of generalized cortical slowing. ²⁴ While this can aid in diagnosis, and more recently has shown promise in early screening for the condition, it is not considered to be of medical necessity in diagnosing the condition. ^{9,25}

In 2008, the National Quality Forum (NQF), in contract with the United States Department of Health and Human Services (HHS) endorsed the Severe Sepsis and Septic Shock: Management Bundle (SEP-1): a measure aimed to promote “efficient, effective and timely delivery of high-quality sepsis care.” A key

Screening for Delirium using the Electronic Medical Record

component to this bundle was early identification of patients at highest risk for sepsis using electronic medical record data. This measure continues to be endorsed by NQF even after the most recent measure review in 2022. Multiple early warning systems using EMR exist for identifying sepsis including Systematic Inflammatory Response Syndrome (SIRS) and “q SOFA” assessing for Sequential Organ Failure Assessment (SOFA). Both have been widely adapted into an EMR tools.^{26,27} Despite a greater portion of yearly United States Health Care costs being spent on delirium, no similar government organization backing exists to promote the development of a similar early warning system tool for delirium. While not specific to delirium, the NQF in contract with the Centers for Medicare and Medicaid Services, published a recommendation report titled *Leveraging Electronic Health Record (EHR)-Sourced Measures to Improve Care Communication and Coordination*. Among recommendations is that “stakeholders should develop new, standardized EHR [Electronic health record] data elements to document and assess care communication and coordination.”²⁸ The waxing and waning nature of delirium often leads to discrepancies in assessment between clinicians and nursing staff who see the patient at different times throughout the day. A patient with delirium may be fully oriented and talkative at 2 PM, agitated and only oriented to self at 7 PM and somnolent and oriented to self and place the following morning. It is therefore an ideal condition to use this recommendation related to EMR data elements to potentially improve care coordination in instances where discrepancies exists.

NOVAD Study

Hospitals using EMR adapted versions of well validated delirium assessments still under-diagnose the condition. Data from a pilot investigation into the detection rate of delirium using a version of CAM, modified for input into the electronic medical record by nurses in a large hospital system, showed delirium prevalence using this tool was 2.7% among all non-surgical hospitalized patients between the ages of 65 and 99 years old. The low prevalence of positive scores suggests this method misses several

Screening for Delirium using the Electronic Medical Record

cases of delirium. This is despite 99% adherence to policy that nurses are to perform this assessment once per shift. Because of the recognized and increasing shortage of healthcare workers in the United States, there is growing pressure to create ways to make assessment of each individual patient more efficient.²⁹

In this study we present a novel smart-EMR based screening tool for delirium called NOVAD: the neurologic, orientation and verbal assessment of delirium. The aim of the current study is to determine the sensitivity, specificity, and predictive value of this tool in detecting delirium in hospitalized adults. In creating this tool we utilize assessments that nurses are already performing and documenting consistently and accurately. With delirium being common and dangerous in older hospitalized adults and contributing a substantial amount to the yearly cost of healthcare, improving early identification of those with the condition and those at highest risk has the potential to have a significant positive impact on population health.

METHODS

Participant Information

This is a retrospective observational study of consecutive admissions to hospitals in the Banner Health System between the dates of January 1, 2020 and December 31, 2020. The Banner Health System includes 30 hospitals spread across Arizona, California, Colorado, Nebraska, Nevada, and Wyoming including 3 academic medical centers in Arizona.³⁰ Participants included all in-patient admissions of individuals 18 years and older that fell within the aforementioned dates.

Data Collection

At Banner Health hospitals, expectations of nursing staff include evaluating each patient using a version of the Confusion Assessment Method (CAM) modified for direct input into the electronic health record.

Screening for Delirium using the Electronic Medical Record

Nurses also document other patient characteristics including a neurologic assessment, a Glasgow Coma Score and an assessment of patient's orientation each shift into the EHR. In a preliminary review it was concluded that nurses complete these assessments with high frequency and accuracy. The following data were extracted from the EHR based on nursing documentation: the presence of neurologic symptoms on the neurologic assessment, a patient's "best verbal response" from the Glasgow Coma Score, completed "orientation assessment" and their modified CAM scores during their hospital stay. Figure 1 shows the possible options for each element included in the patient's NOVAD score. A participant was recorded as one hospitalization (one single medical record number). For each participant the presence of physician documentation of International Classification of Diseases Version 10 (ICD-10) codes delirium for encephalopathy. The use of encephalopathy codes as well as those associated with delirium was used as literature suggests that only using physician documentation of delirium would miss a large proportion of patients with delirium.^{31,32} Specific codes were chosen based on current literature related to coding trends for delirium.^{3,4,31,33} Fifty-four individual codes were selected (Appendix 1). Patient's demographic information and length of hospital stay were also recorded from the EHR.

Data Interpretation/Scoring

The NOVAD test was considered positive if two domains were positive in two calendar days. The negative answers for each domain were "none" for neurologic symptoms, an "oriented" best verbal response and "oriented x4" on orientation assessment. Anything other than these answers for a given domain was considered positive (Figure 1). The NOVAD score was compared to the patient's modified CAM score as recorded by nursing as well as whether a physician documented diagnoses of Encephalopathy or other ICD-10 code listed above for evaluating the validity of the NOVAD tool.

Screening for Delirium using the Electronic Medical Record

Statistical Analysis

Baseline demographics data and clinical characteristics were compared across the test groups using a one-way Analysis of Variance for continuous variables and chi-square tests for categorical variables. The median length of stay was compared among the test groups using the Wilcoxon rank-sum test. The group comparison of the proportions of patients in different Banner facilities was done using Fisher's exact test. The sensitivity, specificity, positive predictive value and negative predictive value results were obtained by computing the diagnostic test with a chi-square p-value. Three groups of the validation statistic measures were performed: NOVAD positive score compared to CAM positive score where CAM positive score was assumed to be truly diagnostic for delirium, NOVAD positive score compared to physician diagnosis of delirium or encephalopathy where diagnosis of delirium or encephalopathy was assumed to be truly diagnostic for delirium, and CAM positive score compared to physician diagnosis of delirium or encephalopathy where diagnosis of delirium or encephalopathy was assumed to be truly diagnostic for delirium. All analyses were performed in StataSE 17 (64-bit) and a 2-sided type 1 error rate of .05 was used as the threshold for statistical significance.

RESULTS

464,395 participants were included in this study. The mean age of study participants was 56.18 years (SD 20.82) and the sample was 56.17% female (n = 260,856). When dividing the sample into groups based on age, 59.08% were less than 65 years (n=274,374), 18.03% were between 65 and 74 years (n=83,732), 15.19% were between 75 and 84 years (n=70,536) and 7.7% were older than 85 years (n=35,753). 65.35% (n=303,471) of participants identified as White, with 21.60% (n=100,314) identifying as Hispanic, 6.00% (n=27,847) as Black, 3.43% (n=15,921) as Native American/Alaskan, and 1.14% (n=5,298) as Asian/Pacific Islander (Table 1).

Screening for Delirium using the Electronic Medical Record

The prevalence of participants in the study with a positive NOVAD score was 29.23% (n = 135,776; 95% CI: 29.11, 29.37). Nursing administered modified CAM score was documented positive in 2.41% (n = 11,183; 95% CI: 2.31%, 2.45%) of participants. 11.31% (n = 52,505; 95% CI: 11.22% , 11.40%) of participants had a physician documented ICD-10 code of delirium or encephalopathy. Further description of data for NOVAD, modified CAM and ICD-10 code in study participants is shown in Table 2. Length of stay (LOS) in median number of hospital days is shown in Table 2. The median LOS for the entire sample was 3.37 (IQR 1.97, 6.21) compared to 5.94 (IQR 3.21, 10.82) for the NOVAD positive group, 9.08 (IQR 5.15, 16.09) for the CAM positive group and 6.77 (IQR 3.68, 12.67) for the ICD-10 code diagnosed group.

NOVAD was found to be 86.63% sensitive (95% CI 86.53, 86.73 p-value < 0.0001) and 78.08% specific (95% CI: 77.96 ,78.20 p-value < 0.0001) based on ICD-10 code diagnosis of delirium or encephalopathy as being truly positive for delirium. The positive predictive value for NOVAD was 33.50% (95% CI 33.36, 33.64, p-value < 0.0001) and the negative predictive value was 97.86% (95% CI 97.82, 97.91, p-value <0.0001). (Table 3)

Modified CAM administered by nursing was found to be 13.74% sensitive (95% CI 13.64, 13.83; p-value < 0.0001) and 99.04% specific (95% CI 99.01, 99.06, p-value < 0.0001) based on ICD-10 code diagnosis of delirium or encephalopathy as being truly positive for delirium. The positive predictive value for nursing administered modified CAM was 64.49% (95% CI 64.35, 64.63, p-value < 0.0001) and the negative predictive value was 90.01% (95% CI 89.92, 09.09, p-value <0.0001) (Table 4).

DISCUSSION

The current study aimed to determine the sensitivity, specificity, positive predictive value, and negative predictive value of a novel screening tool for delirium that utilizes nursing assessments documented in the EMR.

Screening for Delirium using the Electronic Medical Record

Results from the current study suggest that NOVAD is highly sensitive (86.63% 95% CI 86.53, 86.73) in screening for delirium as diagnosed by ICD-10 code. The negative Predictive value (97.86%, 95% CI 97.82, 97.91) further suggests the tool is effective in identifying true positive cases. Additional findings in our study support the use of the NOVAD tool in screening for delirium as they show that factors known to be associated with delirium are also strongly correlated with NOVAD positivity. Higher age groups showed a statistically significant increase in NOVAD positivity (Table 1). The prevalence of NOVAD positivity was 29.23% for all participants which is in line with estimates of delirium in hospitalized adults.^{1,18} A statistically significant difference was seen in this study between sex and likelihood of NOVAD positivity. The likely cause of this finding is that the sample of males in this study had a lower percentage of participants under 65 years old (108,849 of 203,442; 53.50%) compared to females (165,449 of 260,856; 63.43%) (Table 5 and Figure 2). Our study sample was diverse with certain minority groups represented at higher percentages than in other similar studies (Table 4). In addition, there was no significant difference between NOVAD positivity by race. Many similar studies do not report on participant race so having this info is a strength in and of itself.

While the specificity and positive predictive value of the test are low, this is expected given the NOVAD variables do not perfectly match with DSM-V-TR criteria for delirium. There are variables that if added to NOVAD would more than likely increase the specificity and PPV of the tool. However, a goal in developing the NOVAD tool was to avoid increasing the workload of hospital staff. In alignment with this goal, we identified nursing assessments that were being performed and documented with high consistency.

Our results further suggest that the sensitivity of the current method of screening for delirium for many hospital systems, an EMR modified version of CAM, is about 2%. This is in stark contrast with the literature reported validity of CAM where reports are up to 100% sensitive and 94% specific which

Screening for Delirium using the Electronic Medical Record

suggests the assessment is not being administered properly. This is despite health system wide training exercises aimed to train staff to properly administer these assessments.

Other research teams have investigated using EMR data to screen for or identify delirium. Rudolph et al. 2016 reported on the validation of a delirium rule (e-NICE) that uses electronic medical record data to predict delirium. The e-NICE tool generates a delirium risk score and authors demonstrated that the higher risk scores were associated with higher delirium prevalence and incidence.³⁴ Chen et al. 2022 reported on a natural language processing instrument that uses detection of keywords in participant's EMR to screen for delirium. They demonstrated varied sensitivity and specificity of this tool based on different thresholds with the lowest cutoff score reported to be 90% sensitive (82.4, 94.7) and 29.9% specific (26.5, 33.5) and the highest cut off score reported to be 55.5% sensitive (45.7-64.8) and 90.0% specific (87.4, 92.1).³⁵

Liu et al., 2022 used EMR data to develop a combined Long short-term memory (LSTM) model (described as "a state-of-the-art deep learning model designed to analyze sequential data") and a machine learning model that improved prediction of new onset delirium in their study. Some of the features included in this complex model were age, heart rate, Richmond Agitation-Sedation Score (RASS score), and number of CAM assessments.³⁶ Bishara et al., 2022 also reported on two novel machine learning models using EMR data, in their case to predict postoperative delirium. They reported that both models showed improved prediction of postoperative delirium compared with multivariable logistic regression models.³⁷

Other methods are being developed to improve screening for delirium that do not utilize EMR data. Kamdar and colleagues have used video simulations to improve nursing staff proficiency in using the CAM-ICU tool.³⁸ Other research groups have developed shorter assessment methods, such as the Ultra Brief Confusion Assessment Method (UB-CAM) and the Single Question in Delirium (SQiD), to improve efficiency of delirium screening.^{16,39} Gen Shinozaki and colleagues have reported that they have

Screening for Delirium using the Electronic Medical Record

developed a bispectral EEG (BSEEG) tool that is effective in detecting delirium, can correlate EEG slowing to delirium severity, and more recently that the tool can predict patient's comparative mortality risk.²⁵

Therefore, implementation of a tool like NOVAD is one of many examples of how hospital systems can improve screening for the condition.

One limitation of our study is that documentation of ICD-10 code diagnosis for delirium and encephalopathy is an imperfect measure of delirium prevalence. The prevalence of documented delirium and encephalopathy diagnosis based on ICD-10 code in our study was 11.31%. This is lower than most literature reports of prevalence of delirium in hospitalized adults and suggests that delirium is uncommonly coded for by physicians. This notion has been documented elsewhere in the literature.

3,4,31,33

The study being retrospective in nature is also a limitation. To compliment the results of the present study, a prospective validation study is on-going. In the prospective study, the NOVAD score will be compared with trained research team diagnosis of delirium to determine sensitivity, specificity, PPV and NPV.

NOVAD was developed as a tool to screen for delirium as opposed to a diagnostic assessment. A secondary objective of the tool's development team was to identify patients who would be most appropriate for management by a geriatric hospitalist group as opposed to a non-geriatric hospitalist group. In this way, it is likely most useful in populations for which positive screens will receive additional assessment and support by an appropriate medical team. In the setting where the NOVAD tool was developed, it serves as one of multiple EMR based tools the geriatric medicine interdisciplinary team uses to identify patients that may benefit from consultation by their service.

Screening for Delirium using the Electronic Medical Record

CONCLUSIONS

This retrospective validation study demonstrates that a novel electronic medical record tool making use of documented nursing assessments is sensitive for screening for delirium in hospitalized adults. Further validation of the tool is on-going with a prospective design.

APPENDICES**Appendix 1: Displays the ICD-10 codes used to identify participants with physician diagnosis of delirium/encephalopathy**

ICD-10 Codes for Delirium	
F05	Delirium due to known physiological condition
F05.9	delirium, unspecified
F05.1	delirium superimposed on dementia
F05.8	other delirium
F10.4	mental and behavioral disorders due to use of alcohol, withdrawal state with delirium
F10121	Alcohol abuse with intoxication delirium
F10221	Alcohol dependence with intoxication delirium
F10231	Alcohol dependence with withdrawal delirium
F10921	Alcohol use, unspecified with intoxication delirium
F11121	Opioid abuse with intoxication delirium
F11221	Opioid dependence with intoxication delirium
F11921	Opioid use, unspecified with intoxication delirium
F12121	Cannabis abuse with intoxication delirium
F12221	Cannabis dependence with intoxication delirium
F12921	Cannabis use, unspecified with intoxication delirium
F13121	Sedative, hypnotic or anxiolytic abuse with intoxication delirium

Screening for Delirium using the Electronic Medical Record

F13221	Sedative, hypnotic or anxiolytic dependence with intoxication delirium
F13231	Sedative, hypnotic or anxiolytic dependence with withdrawal delirium
F13921	Sedative, hypnotic or anxiolytic use, unspecified with intoxication delirium
F13931	Sedative, hypnotic or anxiolytic use, unspecified with withdrawal delirium
F14121	Cocaine abuse with intoxication with delirium
F14221	Cocaine dependence with intoxication delirium
F14921	Cocaine use, unspecified with intoxication delirium
F15121	Other stimulant abuse with intoxication delirium
F15221	Other stimulant dependence with intoxication delirium
F15921	Other stimulant use, unspecified with intoxication delirium
F16121	Hallucinogen abuse with intoxication with delirium
F16221	Hallucinogen dependence with intoxication with delirium
F16921	Hallucinogen use, unspecified with intoxication with delirium
F18121	Inhalant abuse with intoxication delirium
F18221	Inhalant dependence with intoxication delirium
F18921	Inhalant use, unspecified with intoxication with delirium
F19121	Other psychoactive substance abuse with intoxication delirium
F19221	Other psychoactive substance dependence with intoxication delirium
F19231	Other psychoactive substance dependence with withdrawal delirium

Screening for Delirium using the Electronic Medical Record

F19921	Other psychoactive substance use, unspecified with intoxication with delirium
F19931	Other psychoactive substance use, unspecified with withdrawal delirium

ICD-10 Codes for Encephalopathy	
A812	Progressive multifocal leukoencephalopathy
E512	Wernicke's encephalopathy
G0430	Acute necrotizing hemorrhagic encephalopathy, unspecified
G0431	Post-infectious acute necrotizing hemorrhagic encephalopathy
G0432	Post-immunization acute necrotizing hemorrhagic encephalopathy
G0439	Other acute necrotizing hemorrhagic encephalopathy
G92	Toxic encephalopathy
G9340	Encephalopathy, unspecified
G9341	Metabolic encephalopathy
G9349	Other encephalopathy
I673	Progressive vascular leukoencephalopathy
I674	Hypertensive encephalopathy
I6783	Posterior reversible encephalopathy syndrome
J1081	Influenza due to other identified influenza virus with encephalopathy
J1181	Influenza due to unidentified influenza virus with encephalopathy
P9160	Hypoxic ischemic encephalopathy, unspecified
P9161	Mild hypoxic ischemic encephalopathy
P9162	Moderate hypoxic ischemic encephalopathy
P9163	Severe hypoxic ischemic encephalopathy

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