UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM MEDICINA: CIÊNCIAS MÉDICAS

# IDENTIFICAÇÃO DE PACIENTES IDOSOS COM MAIOR RISCO PARA DELIRIUM NO DEPARTAMENTO DE EMERGÊNCIA

LUCAS OLIVEIRA JUNQUEIRA E SILVA

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“The best interest of the patient
is the only interest to be considered,
and in order that the sick may have
the benefit of advancing knowledge,
union of forces is necessary.”

William J. Mayo

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## RESUMO

O delirium é uma disfunção cerebral aguda associada a um aumento na mortalidade, hospitalização prolongada e diminuição dos resultados funcionais. O diagnóstico de delirium no departamento de emergência (DE) é frequentemente perdido, e a triagem para delirium tem sido proposta como uma solução para aumentar seu diagnóstico. Nesta tese de doutorado, foi realizada uma revisão sistemática para identificar potenciais fatores de risco para delirium e implementado um protocolo de triagem utilizando o Delirium Triage Screen (DTS) seguido do Brief Confusion Assessment Method (bCAM) para pacientes do DE. Além disso, foi desenvolvido um escore de estratificação de risco utilizando variáveis clínicas disponíveis no momento da visita ao DE para identificar pacientes de alto risco para delirium. Também foi avaliado se intervenções realizadas no DE, como cateterização vesical ou administração de opioides ou benzodiazepínicos, aumentaram o risco de desenvolver delirium durante a internação hospitalar. Por fim, a associação entre delirium e aumento da mortalidade foi investigada para entender melhor o prognóstico desses pacientes. Os resultados desta tese demonstraram que é possível identificar subgrupos de idosos com maior risco para delirium na emergência, o que pode ser utilizado para otimizar a identificação precoce desses pacientes. É importante destacar que o delirium está associado a um prognóstico ruim, com aumento da mortalidade e piora dos resultados funcionais. Portanto, é fundamental que os profissionais de saúde coloquem mais esforços na triagem de pacientes de alto risco para delirium, a fim de melhorar o prognóstico desses pacientes.



**Palavras chave**: delirium; geriatria; emergência; estratificação de risco; fatores de risco; prognóstico.

## ABSTRACT

Delirium is an acute brain dysfunction associated with increased mortality, prolonged hospitalization, and decreased functional outcomes. The diagnosis of delirium in the emergency department (ED) is often missed, and screening for delirium has been proposed as a solution to increase its diagnosis. In this doctoral thesis, a systematic review was conducted to identify potential risk factors for delirium, and a screening protocol was implemented using the Delirium Triage Screen (DTS) followed by the Brief Confusion Assessment Method (bCAM) for ED patients. Additionally, a risk stratification score was developed using clinical variables available at the time of the ED visit to identify high-risk patients for delirium. The study also evaluated whether interventions performed in the ED, such as bladder catheterization or administration of opioids or benzodiazepines, increased the risk of developing delirium during hospitalization. Finally, the association between delirium and increased mortality was investigated to better understand the prognosis of these patients. The results of this thesis demonstrated that it is possible to identify subgroups of older adults with a higher risk of delirium in the ED, which can be used to optimize early identification of these patients. It is important to highlight that delirium is associated with a poor prognosis, including increased mortality and worsening functional outcomes. Therefore, healthcare professionals should put more efforts into screening high-risk patients for delirium.



**Key Words**: delirium, geriatrics, emergency department, risk stratification, risk factors.

## LISTA DE FIGURAS

## LISTA DE ABREVIATURAS E SIGLAS

AVC: acidente vascular cerebral

b-CAM: brief Confusion Assessment Method

DTS: Delirium Triage Scale

DE: Departamento de Emergência

REDEEM: REcognizing DElirium in Emergency Medicine

UTI: unidade de terapia intensiva

# SUMÁRIO

## 1. INTRODUÇÃO

Delirium é uma emergência neuropsiquiátrica caracterizada por uma perturbação na atenção e consciência. É acompanhado por uma perda aguda de cognição em um curto período de tempo, que não pode ser explicada por um transtorno neurocognitivo pré-existente ou em evolução, como demência. (WILSON et al., 2020) Como a apresentação clínica do delirium em pacientes geriátricos pode ser sutil, a triagem ativa para essa condição é necessária. A falta de detecção do delirium no Departamento de Emergência (DE) tem sido descrita como um problema de qualidade de atendimento. (SANDERS, 2002) Por esse motivo, as Diretrizes Americanas de Emergências Geriátricas (AMERICAN COLLEGE OF EMERGENCY PHYSICIANS et al., 2014) recomendam que a triagem para delirium na emergência deva ser um padrão de atendimento. Apesar da ocorrência frequente de delirium em pacientes geriátricos e das consequências negativas, há vários desafios práticos por trás da implementação de tal estratégia e a triagem de *todo* idoso que se apresenta na sala de emergência não é viável. A identificação de um subgrupo de pacientes de alto risco é fundamental para otimizar o processo de triagem no ambiente frequentemente caótico do DE.

Embora os fatores de risco para delirium possam ser semelhantes em diferentes ambientes, é necessário entender se existem diferenças importantes no ambiente de emergência. O ambiente de emergência tem características únicas quando comparado com as enfermarias hospitalares ou unidades de terapia intensiva (UTIs). Estudos hospitalares geralmente incluem pacientes até 48 horas após a admissão. (BUURMAN et al., 2011; GONZÁLEZ et al., 2009; INOUYE et al., 1998; MURRAY et al., 1993) Dada a natureza flutuante do delirium, o status de delirium de um paciente após 48 horas de admissão pode ser completamente diferente do status de delirium na chegada à emergência ou durante o tempo de permanência na emergência, o que dificulta a generalização desses estudos para o paciente idoso na emergência. Além disso, os prestadores de cuidados de saúde no DE podem ter

informações limitadas sobre o paciente (por exemplo, se o paciente não puder fornecer um histórico confiável e/ou não houver membros da família presentes). Portanto, os fatores de risco identificados em outros ambientes podem ser menos relevantes ou não aplicáveis no contexto da emergência.

Nesta tese, procurou-se identificar os principais fatores de risco para delirium em pacientes idosos na emergência e explorar a possibilidade de uma triagem direcionada em indivíduos de maior risco. Além disso, foi avaliado o impacto prognóstico da presença de delirium em pacientes idosos na emergência. Para tanto, foram realizados **quatro** trabalhos, atualmente já publicados. O primeiro trabalho apresenta uma revisão sistemática com meta-análise para identificar fatores de risco para delirium (tanto prevalente quanto incidente) na emergência. O segundo trabalho descreve o desenvolvimento de um escore de estratificação de risco para identificar idosos com alto risco de delirium na apresentação na emergência. O terceiro investiga os fatores modificáveis na emergência que impactam a incidência de delirium durante a hospitalização. Por fim, o quarto trabalho investiga se a presença de delirium na emergência está associada a uma maior mortalidade no curto e médio prazo.

## 2. REVISÃO DA LITERATURA

Delirium é uma condição aguda caracterizada por uma mudança rápida na função cerebral e que afeta principalmente a capacidade de concentração e atenção, frequentemente se apresentando com flutuação de sintomas, pensamento desorganizado e alteração do nível de consciência. (WILSON et al., 2020) O risco de desenvolver delirium aumenta com a idade e é uma grande preocupação para adultos mais velhos que se apresentam ao DE, com estimativas de que aproximadamente 10% dos idosos tenham delirium na apresentação (BARRON; HOLMES, 2013; LAMANTIA et al., 2014; MARIZ et al., 2016; PÉREZ-ROS; MARTÍNEZ-ARNAU, 2019). Essa síndrome está associada a um aumento da mortalidade, prolongamento do tempo de hospitalização e diminuição da funcionalidade no médio-longo prazo (HAN et al., 2010, 2011; NAUGHTON et al., 1995; VIDA et al., 2006).

A apresentação clínica pode ser sutil e até 90% dos adultos mais velhos apresentam o subtipo hipoativo, parecendo calmos e retraídos em vez de agitados (HAN et al., 2009). O diagnóstico é ainda mais desafiador no DE, onde o paciente muitas vezes não é conhecido pela equipe de atendimento e membros da família ou cuidadores podem não estar presentes para fornecer a história. Além disso, delirium muitas vezes não é reconhecido pelos profissionais de saúde do DE se não houver o uso de ferramentas de triagem padronizadas.

Apesar das Diretrizes Americanas de Emergências Geriátricas recomendarem a triagem ativa para delirium em todos os pacientes geriátricos que se apresentam no DE, realizar tal triagem em todos os idosos pode não ser uma estratégia viável ou eficaz em todos os serviços (AMERICAN COLLEGE OF EMERGENCY PHYSICIANS et al., 2014). No entanto, avaliar delirium em um subgrupo de idosos de alto risco pode ser prático e benéfico. A maioria dos estudos que avaliam os fatores de risco para delirium foi realizada em outros ambientes, como UTIs ou enfermarias hospitalares.

Uma revisão sistemática avaliou os fatores de risco para delirium incidente entre

idosos hospitalizados (AHMED; LEURENT; SAMPSON, 2014). Em suas análises combinadas, eles descobriram que demência, gravidade da doença, deficiência visual, cateterização urinária, baixo nível de albumina e tempo de internação hospitalar estavam significativamente associados à incidência de delirium no ambiente hospitalar. Em relação aos pacientes gravemente enfermos internados na UTI, duas revisões se concentraram em identificar os fatores de risco. Mattar et al (2012) encontraram 22 estudos em três ambientes diferentes de UTI: UTI médica, UTI cirúrgica e UTI cardíaca (MATTAR et al., 2013). Eles não realizaram uma meta-análise, mas descobriram que o uso de benzodiazepínicos e opióides eram importantes fatores de risco para delirium em todos esses ambientes. Zaal et al (2015) avaliaram os fatores de risco para delirium no ambiente de UTI como um todo. Eles incluíram um total de 33 estudos e encontraram forte evidência de que idade, demência, hipertensão, cirurgia de emergência ou trauma pré-UTI, gravidade da doença, ventilação mecânica, acidose metabólica, delirium no dia anterior e coma são fatores de risco para delirium na UTI. Os autores não realizaram uma meta-análise devido à alta heterogeneidade entre os estudos (ZAAL et al., 2015). Krewulak et al (2020) avaliaram abrangentemente os fatores de risco e desfechos entre os subtipos de delirium em UTIs de adultos. Eles incluíram um total de 20 estudos e encontraram resultados inconsistentes e heterogêneos, destacando a necessidade de padronizar a notificação e a metodologia em estudos que examinam diferentes subtipos de delirium (KREWULAK et al., 2020). Os fatores de risco para delirium também foram avaliados em populações cirúrgicas específicas, como cirurgia vascular (OLDROYD et al., 2017).

Nenhuma das revisões sistemáticas anteriores se concentrou ou incluiu estudos que avaliam pacientes geriátricos no ambiente de emergência. Apenas revisões narrativas avaliaram os fatores de risco para delirium na emergência, mas falharam em incluir todo o corpo de evidências (ROSEN et al., 2015; VASILEVSKIS et al., 2012). Ademais, tais

revisões não consideraram as diferenças nos fatores de risco para os subtipos de delirium: prevalente e incidente. Delirium prevalente é definido como delirium na apresentação do paciente à emergência (ou seja, na chegada). Delirium incidente é definido como aquele em que pacientes que inicialmente não apresentavam delirium o desenvolveram durante a estada na emergência ou durante a hospitalização como um todo. Embora os fatores de risco para delirium prevalente e incidente possam se sobrepor, o delirium incidente também incluirá fatores de risco iatrogênicos relacionados ao ambiente de emergência. Com o objetivo de identificar os fatores de risco para delirium prevalente e incidente na emergência e garantir que todas as variáveis importantes potencialmente associadas ao delirium fossem consideradas para o estudo de coorte subsequente, um protocolo (OLIVEIRA J E SILVA et al., 2020) e uma revisão sistemática com meta-análise (OLIVEIRA J E SILVA et al., 2021) (apresentada no *Artigo 1* e produto desta tese) foram publicados.

Além de identificar fatores que nos ajudem na identificação e prevenção do delirium, entender seu prognóstico é fundamental. Nesse sentido, estudos em DEs indicam que o delirium está associado a um aumento no risco de morte em 30 dias e em períodos de acompanhamento mais longos (HAN et al., 2010; ISRANI et al., 2018; KENNEDY et al., 2014). Entretanto, pouco se sabe sobre a mortalidade a curto prazo (<30 dias) relacionada ao problema. Como o DE é a linha de frente para atendimento médico emergencial e muitas vezes a primeira oportunidade de diagnosticar o delirium, uma melhor compreensão da mortalidade a curto prazo dessa condição pode aumentar a urgência da triagem consistente para o delirium, melhorar a capacidade de comunicar o prognóstico aos pacientes e suas famílias e permitir intervenções médicas oportunas para potencialmente reduzir as taxas de morbidade e mortalidade. Ademais, algumas evidências sugerem que o delirium que não é diagnosticado na emergência provavelmente não será reconhecido posteriormente durante a internação na enfermaria (HAN et al., 2009).

## 3. MARCO CONCEITUAL

Esta tese abrange três marcos conceituais relevantes. O primeiro marco, representado na **Figura 1**, apresenta o modelo conceitual dos fatores de risco para delirium prevalente e incidente na perspectiva da unidade de emergência. Esse modelo fornece um contexto para compreender os fatores associados a uma proporção significativa de idosos que buscam atendimento nesse serviço, bem como os fatores relacionados às intervenções comumente realizadas no cuidado desses pacientes.

**Figura 1**. Modelo conceitual de fatores de risco para delirium na emergência. (OLIVEIRA J E SILVA et al., 2020)

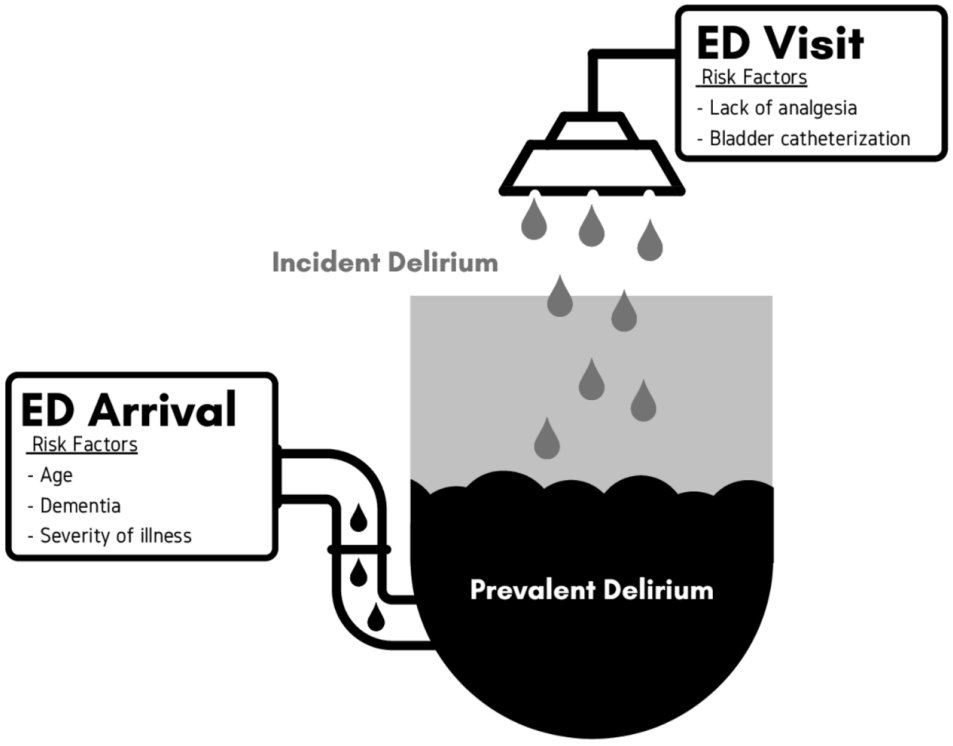
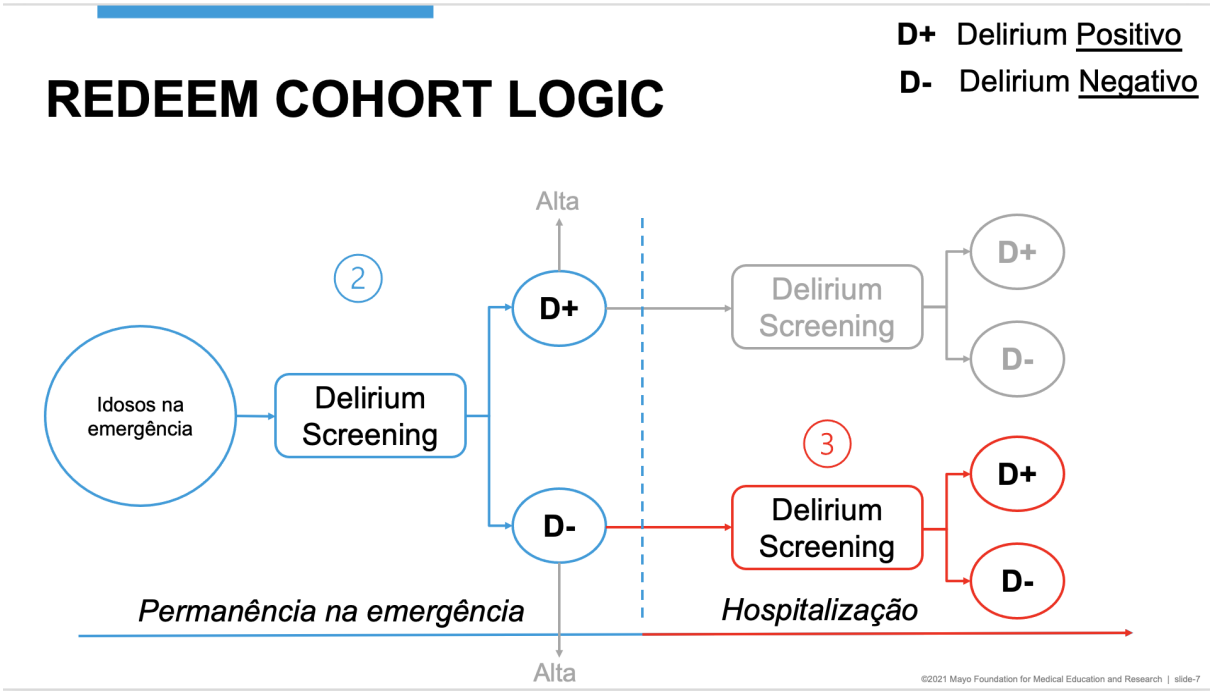



**Figure 1** Conceptual model of risk factors and prevalent and incident delirium from the ED perspective. ED, emergency department.

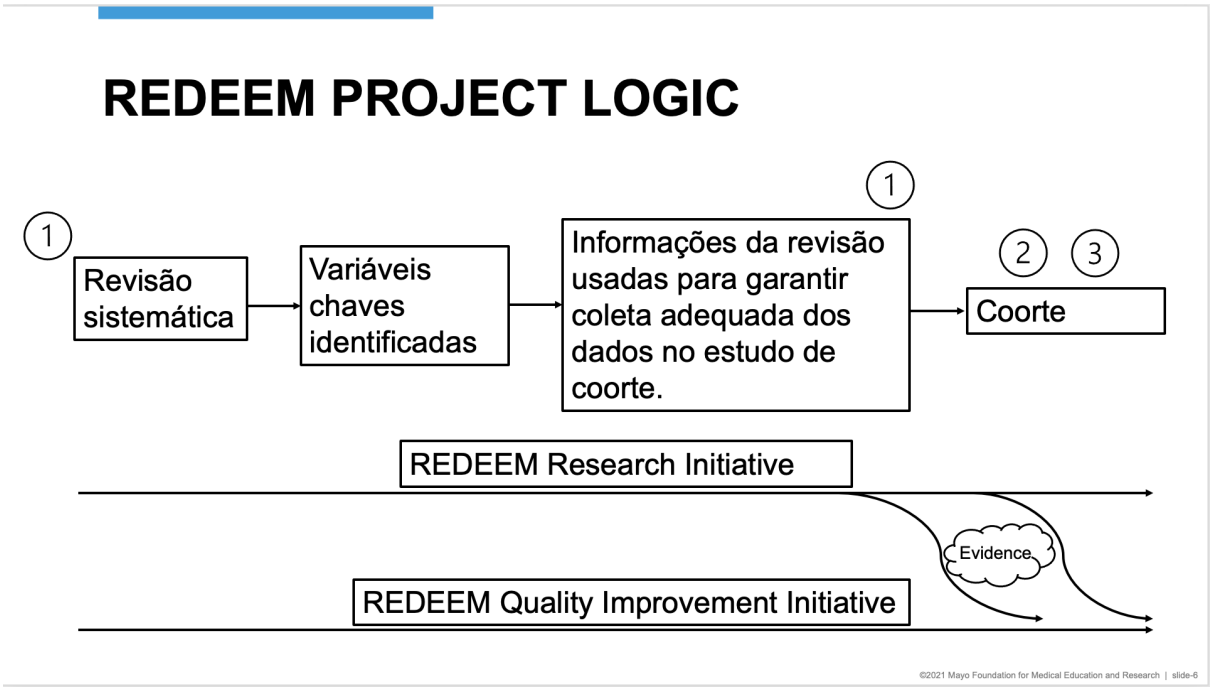
O segundo, ilustrado na **Figura 2**, refere-se ao desenho do estudo de coorte que fora desenvolvido para a realização dos estudos descritos nos *Artigos 2* e *3* desta tese.

**Figura 2.** Desenho da coorte REDEEM.




Por último, o marco conceitual ilustrado na **Figura 3** representa a lógica por trás da tese como um todo. Começamos nosso projeto abordando o objetivo 1, que consistia em uma revisão sistemática dos fatores de risco para delirium. Com essa etapa concluída, identificamos as principais variáveis que precisariam ser avaliadas em nossos estudos nos objetivos subsequentes. Utilizamos essas informações para garantir formulários adequados de coleta de dados para nosso estudo de coorte. Durante o projeto REDEEM, participamos ativamente de uma iniciativa de melhoria da qualidade na emergência. Todas as evidências produzidas foram diretamente aplicadas a essa iniciativa de melhoria da qualidade para aprimorar o atendimento aos nossos pacientes na emergência.

**Figura 3.** Lógica do projeto REDEEM.



## 4. JUSTIFICATIVA

A implementação da triagem ativa para delirium na população de idosos na emergência é desafiadora no fluxo do departamento, onde o foco é principalmente em condições que requerem tratamento imediato, e as avaliações abrangentes geralmente são adiadas para os cenários de enfermaria ou ambulatório. Embora as ferramentas de triagem diagnóstica, como o *Delirium Triage Scale* (DTS) e o *brief Confusion Assessment Method* (bCAM), tenham bom desempenho diagnóstico no cenário da emergência, (HAN et al., 2013) a adoção dessa abordagem ainda não é amplamente implementada. Desafios comuns na emergência incluem restrições de tempo e incorporação da triagem no fluxo de trabalho existente. Estratégias eficazes e viáveis de implementação que incorporem triagem ativa para delirium com ferramentas padronizadas validadas no DE são necessárias. Realizar a avaliação para delirium em um subgrupo de pacientes idosos de maior risco pode ser uma estratégia mais prática e benéfica do que triar todos os pacientes idosos. No entanto, há poucas evidências disponíveis para identificar quem são esses pacientes de alto risco no DE.

Estudos anteriores que avaliaram os fatores de risco para delirium na emergência tiveram um número limitado de pacientes com delirium. (HAN et al., 2009; KENNEDY et al., 2014; SRI-ON et al., 2016) Desde a publicação das Diretrizes Americanas de Emergências Geriátricas em 2014 e a validação da abordagem de triagem usando o DTS seguido pelo bCAM, nenhum estudo avaliou os fatores de risco para apresentação de delirium na emergência, e os modelos de predição propostos anteriormente apresentaram desempenho limitado ou incluíram variáveis que não estão rotineiramente disponíveis na prática clínica. O desenvolvimento de um modelo de predição que inclua variáveis disponíveis durante a estadia na emergência e, idealmente, na chegada ao pronto-socorro, pode ajudar a identificar pacientes com maior risco de delirium e a triagem pode ser direcionada. Tal modelo poderia levar a um sistema de alerta eletrônico que identifica pacientes com maior risco

automaticamente. A identificação precoce desses pacientes permite detecção mais rápida, intervenção precoce e potencialmente melhores resultados.

Embora os fatores de risco para delirium incidente (isto é, delirium iniciado durante a estadia na emergência ou hospitalização) possam se sobrepor aos fatores de risco para delirium prevalente (isto é, delirium na apresentação no pronto-socorro), o delirium incidente pode ser afetado por fatores modificáveis, como analgesia inadequada, uso de medicamentos ou fatores ambientais. Estudos anteriores mostraram resultados conflitantes em relação aos fatores modificáveis no pronto-socorro que podem aumentar o risco de delirium em idosos durante a hospitalização, como cateterismo vesical, uso de opióides e uso de benzodiazepínicos. (NOEL; CIRBUS; HAN, 2019) As ferramentas clínicas utilizadas para a triagem de delirium são as mesmas na emergência e nas unidades de enfermaria do Hospital Saint Marys da Mayo Clinic (Rochester, Estados Unidos), como parte do protocolo institucional. Usar o mesmo instrumento com duas ou mais medidas individuais permite identificar pacientes que inicialmente não apresentavam delirium na emergência, mas posteriormente desenvolveram delirium. A identificação de fatores de risco modificáveis para delirium incidente em pacientes geriátricos admitidos através do pronto-socorro pode ajudar a mitigar os riscos e desenvolver estratégias de prevenção.

## 5. OBJETIVOS

### Objetivos gerais

1. Identificar os principais fatores de risco para delirium (tanto prevalente quanto incidente) em pacientes idosos na emergência e explorar a possibilidade de uma triagem direcionada em indivíduos de maior risco.

2. Avaliar o impacto prognóstico da presença de delirium em pacientes idosos na emergência.

### Objetivos específicos

1. Realizar uma revisão sistemática com meta-análise para identificar fatores de risco para delirium prevalente e incidente na emergência, garantindo que todas as variáveis importantes potencialmente associadas ao delirium fossem consideradas para os estudos subsequentes desta tese. (*Artigo 1)*

2. Criar uma coorte de pacientes idosos que foram rastreados para delirium na emergência usando ferramentas padronizadas para desenvolver um escore de estratificação de risco que identifique idosos com alto risco de delirium na chegada à emergência. A partir desse escore, explorar a possibilidade de usar tal escore para triagem "direcionada" na emergência. (*Artigo 2*)

3. Utilizando a mesma coorte do artigo 2, porém com foco nos idosos que chegam sem delirium e o desenvolvem no decorrer da hospitalização, identificar fatores modificáveis na emergência que impactam a incidência de delirium. (*Artigo 3*)

4. Identificar se a presença de delirium na emergência está ou não associado a maior mortalidade no curto (7 dias) e médio prazo (30 dias). (*Artigo 4*)

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## 7. ARTIGOS

Artigo 1

(OLIVEIRA J E SILVA et al., 2021)

**Oliveira J E Silva L**, Berning MJ, Stanich JA, Gerberi DJ, Murad MH, Han JH, Bellolio F. Risk Factors for Delirium in Older Adults in the Emergency Department: A Systematic Review and Meta-Analysis. **Ann Emerg Med**. 2021 Oct;78(4):549-565. doi: 10.1016/j.annemergmed.2021.03.005. Epub 2021 Jun 12. PMID: 34127307.

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**ABSTRACT**

Objective: We conducted a systematic review and meta-analysis to identify risk factors for delirium in ED geriatric patients, and to identify ED-based modifiable risk factors for developing delirium during hospitalization.

Methods: We searched EBM Reviews, EMBASE, MEDLINE, Scopus, and Web of Science for observational studies from inception until July 2020. We included studies that evaluated potential risk factors for either prevalent or incident delirium among older adults (age ≥ 60 years) presenting to the ED. When appropriate, we meta-analyzed estimates for risk factors using random-effects model. The certainty in the evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. A protocol was registered in PROSPERO (CDR42020175261).

Results: A total of 4,513 citations were reviewed and 34 studies met criteria for inclusion: 27 evaluating risk factors for ED delirium (13,412 patients) and 7 evaluating ED-based risk factors for developing delirium during hospitalization (2,238 patients). The prevalence of ED delirium ranged from 7% to 35%. Four factors had strong associations with ED delirium and graded as high certainty evidence, including nursing home residence (4 studies, OR 3.45, 95% CI 2.17 to 5.48), cognitive impairment (7 studies, OR 4.46, 95% CI 3.38 to 5.89), hearing impairment (3 studies, OR 2.57, 95% CI 1.03 to 6.41), and a history of stroke (3 studies, OR 3.20, 95% CI 1.17 to 8.75). The rate of developing delirium during hospitalization ranged from 11% to 27%. A length of stay in the ED greater than 10 hours was associated with higher risk of delirium (1 study, OR 2.23, 95% CI 1.13 to 4.41). One study reported that severe pain rather than the use of opioids was associated with the development of delirium.

Conclusion: These findings can be used to target delirium screening in the ED, and to inform the development of novel ED delirium risk scores or prevention interventions.

## INTRODUCTION

### Background

Delirium is a neuropsychiatric emergency characterized by a disturbance in attention and awareness that is accompanied by an acute loss in cognition over a short period of time, which cannot be explained by a preexisting or evolving neurocognitive disorder such as dementia.[1] Approximately 10% of undifferentiated older adults will have delirium during the emergency department (ED) stay.[2] This syndrome is a major concern for geriatric patients presenting to EDs because its diagnosis is associated with prolonged hospitalization,[3] functional decline,[4] cognitive decline,[5,6] and higher health care costs.[7] More importantly, delirium is independently associated with increased mortality.[8] Despite these negative consequences, delirium can be missed by ED providers in 57% to 83% of cases when active screening is not performed. [9,10] When using an active approach with structured instruments, the diagnostic performance is improved. The Delirium Triage Screen (DTS) tool, for example, has a sensitivity of 98%, while the brief Confusion Assessment Method (bCAM) has a sensitivity of 84% and specificity of 96%, even when used by non-clinicians.[11]

### Importance

While hyperactive (agitated) delirium is easily diagnosed due to the obvious and flourished symptomatology, most cases of ED delirium in the geriatric population will be hypoactive.[12] Hypoactive delirious older adults are quiet and withdrawn, and unless actively searched for, the diagnosis will be missed. Overlooked delirium may have downstream consequences as patients whose delirium was not detected in the ED had the highest 6-month

mortality when compared to detected delirium and non-delirious patients.[13] Active screening by using standardized diagnostic delirium tools has been advocated and missing ED delirium has been described as a quality-of-care problem.[14] In this context, the Geriatric ED Guidelines[15] recommend that screening for delirium should be standard of care. Nevertheless, the impact of ED screening on improved detection rates and patient-important outcomes is questionable.[16] Also, screening every single older adult who presents to the ED may not be feasible due to the challenges of implementing such strategy in the often-chaotic acute care setting. Most recently, the Geriatric Emergency Applied Research (GEAR) network emphasized this challenge and set as a key priority the development of a screening instrument or risk score that does not entail additional clinician workload.[17] The identification of a subset of high-risk patients is, therefore, paramount for optimizing the delirium screening process in the ED. Besides that, the risk factors that make a patient susceptible to delirium may be similar across the spectrum of geriatric needs.

Only narrative reviews have evaluated risk factors for delirium in the ED, but they failed to include the whole body of evidence or to provide quantitative estimates.[18,19] Also, they have not taken into consideration the differences in risk factors for delirium at ED presentation (i.e. prevalent delirium or delirium diagnosed during the early ED evaluation) and delirium that develops during hospitalization (i.e. incident delirium) in those patients who are initially non-delirious. A sizeable share of delirium is preventable, and evidence exists to support non-pharmacologic multicomponent interventions in decreasing the risk of incident delirium among hospitalized patients.[20] While risk factors for prevalent and incident delirium may overlap, delirium that develops during hospitalization will be impacted by ED-related "iatrogenic" risk factors. Identifying these factors can cultivate change if they are modifiable and allow the ED to funnel recourses to patients who absolutely require them.

**Goal of this investigation**

We aimed to systematically evaluate the body of evidence available to answer two main questions: 1) What are the most important risk factors for having delirium in the ED? 2) What are the ED-based modifiable risk factors for developing delirium during hospitalization? For the first question, we evaluated observational studies that reported the prevalence of ED delirium in geriatric patients with and without the potential risk factors. For the second question, we evaluated observational studies that evaluated at least one ED-based modifiable risk factor for developing delirium later in the hospitalization in geriatric patients who were free of delirium in the ED.

## METHODS

### Study design

This was a systematic review and meta-analysis to evaluate risk factors for prevalent and incident delirium among older adults presenting to the ED. Prevalent delirium was defined as delirium in the ED, and incident delirium was defined as the development of delirium during hospitalization in patients who were initially non-delirious at ED presentation. A protocol was published[21] and registered in PROSPERO (CDR42020175261) before beginning the investigation. This manuscript follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[22]

### Eligibility criteria

We included original observational studies (cross sectional, case-control, and cohort studies) that evaluated potential risk factors for either prevalent or incident delirium among older adults (age ≥ 60 years) presenting to the ED. Conference abstracts were considered for

inclusion, and there was no restriction for language or year of publication. Case-reports, narrative reviews, and opinion articles were excluded.

In order to identify potential risk factors for prevalent ED delirium, we included studies that reported a quantitative relationship between at least one potential risk factor and ED delirium. For this purpose, only studies in which delirium was assessed during the ED clinical course were considered. Studies in the primary care, inpatient, or ICU settings were excluded. For example, studies that measured delirium at admission on a hospital floor or after the admitted patient has arrived to the floor (i.e. bypassing the ED) were not considered because we were specifically interested in delirium measured during the ED clinical course. As our goal was to identify clinically relevant characteristics that could be used by ED providers, we excluded studies that reported only information regarding blood biomarkers not commonly used in Emergency Medicine practice (e.g. TNF-a or IL-6 levels). Also, we considered only variables that could be available in the early ED stay as we aimed to identify potential risk factors to optimize delirium screening. ED diagnoses, laboratory or imaging results, and etiologies of delirium, therefore, were not considered because this information is often available after extensive workup and at the end of the ED stay (i.e. close to disposition). In other words, these variables are not useful when the goal is to identify risk factors for target delirium screening in the early ED stay.

As for incident delirium, we included studies that evaluated at least one ED-based modifiable risk factor for developing delirium later in the hospitalization. For these studies to be eligible, older adults had to be free of delirium upon ED arrival and incident delirium had to be measured during hospitalization.

For both prevalent and incident delirium, we only considered studies with more than 10 patients with delirium and those that measured delirium either through the chart review method validated by *Inouye et al*[23] or through a standardized previously validated diagnostic

tool such as the Confusion Assessment Method (CAM),[24] Confusion Assessment Method for the ICU (CAM-ICU),[25] brief Confusion Assessment Method (bCAM),[11] 3-minute Diagnostic Interview for Confusion Assessment Method (3D-CAM),[26] and the 4AT.[27] Studies in which delirium was measured through any version of the Diagnostic and Statistical Manual of Mental Disorder (DSM) criteria were also considered. Studies that measured delirium using only ICD codes were excluded due to the very low sensitivity of this method.[23] Studies of either delirium tremens or drug-induced excited delirium were excluded due to the significant difference in pathophysiology.

Studies were considered for inclusion even if the main purpose of investigators was not to specifically address risk factors. If the report had data available regarding the presence of delirium in those with and without a potential risk factor (e.g. certain demographic variable), we considered potentially eligible if delirium was measured appropriately using a standardized diagnostic tool.

Search strategy

A literature search was developed and executed by an academic medical librarian with input from the study investigators. The search strategies were created using a combination of keywords and standardized index terms related to risk factors and delirium. The initial search was run in March 2020 in Ovid EBM Reviews, Ovid EMBASE (1974+), Ovid MEDLINE (1946+ including e-pub ahead of print, in-process and other non-indexed citations), Scopus (1970+), and Web of Science (1975+). An updated search was run in July 2020 using the same strategy. Abstracts from main emergency medicine (e.g. ACEP, SAEM) and geriatrics (e.g. AGS, BGS, EUGMS) conferences were included in the search. Reference lists of relevant papers and previous narrative reviews were hand-searched in order to identify

citations that did not appear in the main searches. Detailed search strategy is provided in the *Appendix S1*.

Study selection, and data extraction

In phase 1, two investigators independently screened all titles and abstracts for eligibility. In phase 2, studies considered potentially relevant were retrieved in full-text and assessed for eligibility independently. The investigators were not blinded to the authors, journals, or results of studies. We calculated Cohen's unweighted kappa (k) to measure chance corrected agreement between reviewers for phase 2 of the study selection. Any disagreements were harmonized by consensus and discussion.

Pertinent data were extracted independently and in duplicate for all studies using a standardized predefined extraction form. Extracted data included country, study design, inclusion/exclusion criteria, potential risk factors, raw numbers regarding the presence or absence of delirium among patients with and without the potential risk factor in order to reconstruct 2x2 contingency tables, and delirium measurement details. Unadjusted and adjusted effect estimates reported by the studies were extracted. For adjusted effect estimates, we extracted the estimate from the model that adjusted for the maximum number of covariates as reported in the original report. This often represented the primary adjusted model identified by the authors. Only data available in published manuscripts and abstracts were used.

Risk of bias and certainty in the evidence

Risk of bias was assessed at the study level using a modified Newcastle-Ottawa Scale tool[28] for observational studies. The quality was assessed in duplicate for all studies. The details are available in *Appendix S2*. The certainty in the evidence available for each risk

factor was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods.[29,30] The GRADE approach involves consideration of five domains that may decrease the certainty in the evidence (risk of bias, inconsistency, indirectness, imprecision, and publication bias) and three domains that may increase the certainty (large effect, dose response, and plausible confounding).[29] **Table 1** illustrates details about the interpretation of levels of certainty in the evidence using a modified GRADE approach for the evaluation of risk factors.

**Table 1.** Different levels of certainty in the evidence using a modified GRADE approach for risk factors.[30]

| **Certainty level** | **Definition** |
|---|---|
| "High" | We are very confident that the variation in risk of delirium associated with the risk factor lies close to that of the estimate. |
| "Moderate" | We are moderately confident that the variation in risk of delirium associated with the risk factor lies close to the estimate, but there is a possibility that it is substantially different from the estimate. |
| "Low" | Our certainty in the estimate is limited: the variation in risk of delirium associated with the risk factor may be substantially different from the estimate. |
| "Very low" | We have very little certainty in the estimate: the variation in risk of delirium associated with the risk factor is likely to be substantially different from the estimate. |

Data synthesis

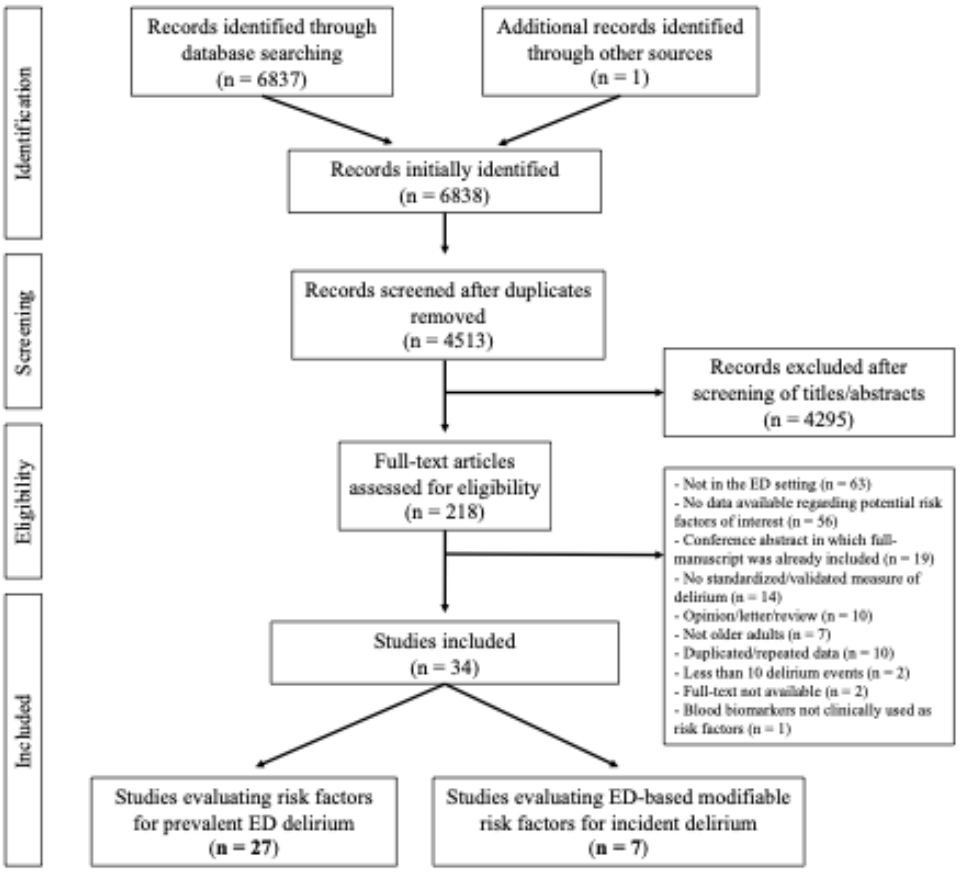
If only one study had data available regarding the association between a potential risk factor and delirium, we reported in our Tables the estimate as extracted from the original manuscript (i.e. no meta-analysis was performed). When two or more studies had data available regarding the association between a potential risk factor and delirium, we calculated meta-analytic estimates for that potential association. Whenever both unadjusted and adjusted estimates were available, adjusted effect estimates were preferred over unadjusted ones because they represent an effect estimate closer to the truth (i.e. less biased). If estimates were available from different overlapping cohorts, we used data from the report with the largest sample size, avoiding repeated data in the meta-analysis. When appropriate, we used Review Manager (version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) for meta-analyses, using a random-effects model as described by DerSimonian-Laird.[31] The random-effects model was a conservative choice given expected heterogeneity within and across studies. For the pooling of adjusted effect estimates, we used the method of inverse variance. For each risk factor, we calculated pooled odds ratios (ORs) with 95% confidence intervals (CIs). For potential risk factors measured as continuous variables in which studies used different scales, we transformed standardized mean differences into ORs.[32] We assessed statistical heterogeneity by the $I^2$ statistic proposed by Higgins and Thompson.[33]

**RESULTS**

Study selection

The search strategy identified 4,513 citations. (**Figure 1**) After screening the titles and abstracts, we identified 218 potentially relevant studies. After full-text review, a total of 34 reports met criteria for inclusion; all observational studies. Twenty-seven[4,9,12,34–57] reports met the eligibility criteria with data available regarding potential risk factors for ED delirium, while 7 reports[58–64] met eligibility with data available regarding ED-based modifiable risk factors for developing delirium during hospitalization (incident delirium). Seven conference abstracts were included. Interobserver agreement beyond chance (k) for phase 2 was 0.6 (95% CI 0.5 to 0.7), with an overall agreement of 84%. For incident delirium studies, only one[58] did not have the main purpose of addressing risk factors. For prevalent ED delirium studies, 13 studies[4,9,35,37,38,40,41,47,50,52,54–56] did not specifically aim to evaluate risk factors but had data of interest.

**Figure 1.** Systematic review study selection flow.




Study characteristics

The main characteristics of the included studies are summarized in **Table 2**. Most studies included undifferentiated older adults presenting to the ED, except for 3 studies that included specific ED populations (heart failure,[46] frail,[47] and hip fracture[64]). Study designs included cohort and cross-sectional studies.

**Table 2.** Baseline characteristics of included studies.

| **Study/ Country** | **Study design** | **Study population** | **Main exclusion criteria** | **Delirium events, total sample size** | **Prevalent or incident delirium, diagnostic delirium tool** |
|---|---|---|---|---|---|
| **Prevalent ED delirium studies** | | | | | |
| DELINEATE cohort‡,[4,51,52] United States | Prospective cohort | Undifferentiated older adults age ≥ 65 years, in the ED for less than 4 hours at the time of enrollment, and unlikely to be discharged home according to the ED physician. | Barriers to communication (Non-English speaking, deaf, comatose, nonverbal, or unable to follow simple commands). | Delirium n = 105 Total n = 228[$] Rate 46.1% | Prevalent ED delirium ascertained with the bCAM. |
| Duman Atilla[53] 2014, Turkey | Prospective cohort | Undifferentiated older adults age ≥ 65 years who were not | Critically ill patients, severe mental retardation, | Delirium n = 49 Total n = 693 | Prevalent ED delirium ascertained |

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| | | discharged directly from the ED. | severe dementia, barriers to communication (aphasia, deafness, blindness). | Rate 7.1% | with the CAM. |
| Élie[54] 2000, Canada | Prospective cohort | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Non-English or French speaking. | Delirium n = 43 Total n = 447 Rate 9.6% | Prevalent ED delirium ascertained with the CAM. |
| Ellis[55] (conference abstract) 2017, United States | Prospective cohort | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Non-English or Spanish speaking. | Delirium n = 146 Total n = 1138 Rate 12.8% | Prevalent ED delirium ascertained with the 3D-CAM. |
| Fallon[56] 2018, Ireland | Prospective cohort | Undifferentiated older adults age ≥ 70 years presenting to the ED. | Not specified. | Delirium n = 17 Total n = 198 Rate 8.6% | Prevalent ED delirium ascertained with the CAM-ICU. |

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| Gil[57] (conference abstract) 2019, Brazil | Cross-sectional | Undifferentiated clinically stable older adults age ≥ 70 years presenting to the ED. | Clinically unstable patients. | Delirium n = 243 Total n = 2732 Rate 8.9% | Prevalent ED delirium ascertained with the CAM. |
| Han's[12,34,35] cohorts[†], United States | Prospective cohort | Undifferentiated older adults age ≥ 65 years, in the ED for less than 12 hours at the time of enrollment. | Barriers to communication (Non–English-speaking, deaf, blind, comatose, nonverbal, or unable to follow simple commands). | Delirium n = 155 Total n = 1084[&] Rate 14.3% | Prevalent ED delirium ascertained with the CAM-ICU. |
| Hare[36] 2014, Australia | Prospective cohort | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Barriers to communication (Non-English speaking, aphasic, unable to provide consent or no relative or | Delirium n = 23 Total n = 320 Rate 7.2% | Prevalent ED delirium ascertained with the CAM. |

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| | | | caregiver to consent), too "drowsy", deemed to critically ill by ED provider. | | |
| Hustey[37] 2002, United States | Prospective cohort | Undifferentiated older adults age ≥ 70 years presenting to the ED. | Critically ill patients, barriers to communication (unable to communicate, non-English speaking in the absence of translator). | Delirium n = 30 Total n = 297 Rate 10.1% | Prevalent ED delirium ascertained with the CAM. |
| Hustey[9] 2003, United States | Prospective cohort | Undifferentiated older adults age ≥ 70 years presenting to the ED. | Critically ill patients, barriers to communication (unable to communicate, non-English speaking in the | Delirium n = 19 Total n = 271 Rate 7.0% | Prevalent ED delirium ascertained with the CAM. |

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| | | | absence of translator). | | |
| Kelly[38] (conference abstract) 2019, Ireland | Prospective cohort | Undifferentiated older adults age ≥ 75 years presenting to the ED. | Not specified. | Delirium n = 34 Total n = 148 Rate 23.0% | Prevalent ED delirium ascertained with the 4AT. |
| Kennedy[39] 2014, United States | Prospective cohort | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Unable to provide consent (or no surrogate to provide consent), longer than 4 hours in the ED, non-English speaking, ED provider deemed that study participation would interfere with timely medical care. | Delirium n = 63 Total n = 676 Rate 9.3% | Prevalent ED delirium ascertained with the CAM. |

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| Mailhot[40] 2020, United States | Prospective cohort | Undifferentiated older adults age ≥ 70 years with a family caregiver available at presentation to the ED. | Non-English speaking, head trauma. | Delirium n = 30 Total n = 108 Rate 27.8% | Prevalent ED delirium ascertained with the CAM. |
| Naughton[41] 1995, United States | Prospective cohort | Undifferentiated older adults age ≥ 70 years presenting to the ED. | Critically ill patients, non-English speaking. | Delirium n = 18 Total n = 188 Rate 9.6% | Prevalent ED delirium ascertained with the CAM. |
| Nguyen[42] 2017, Canada | Historical (retrospective) cohort | Undifferentiated older adults age ≥ 75 years with medication list available. | Transfers to intensive or palliative care, transfers to other hospitals, discharged in less than 48 hours. | Delirium n = 230 Total n = 1205 Rate 19.1% | Prevalent ED delirium ascertained with chart-based method developed by Inouye. |

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| Ohl[43] 2019, Brazil | Cross-sectional | Undifferentiated older adults age ≥ 60 years presenting to the ED with less than 24 hours in the ED at enrollment. | Barriers to communication (language barriers), history of dementia. | Delirium n = 56 Total n = 200 Rate 28.0% | Prevalent ED delirium ascertained with the CAM. |
| Rangel Selvera[44] (conference abstract) 2011, Spain | Cross-sectional | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Not specified. | Delirium n = 52 Total n = 150 Rate 34.7% | Prevalent ED delirium ascertained with the CAM. |
| Ritter[45] 2018, Brazil | Prospective cohort | Undifferentiated older adults age ≥ 60 years presenting to the ED and able to undergo study evaluations. | Critically ill patients and patients who were "immediately discharged from the ED". | Delirium n = 31 Total n = 110 Rate 28.2% | Prevalent ED delirium ascertained with the CAM. |
| Rizzi[46] 2015, Spain | Prospective cohort | Adult patients (94.1% over 65 years) | Critically ill patients, patients with | Delirium n =35 Total | Prevalent ED delirium |

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| | | presenting to the ED with decompensated heart failure. | ST-segment elevations. | n = 239<br>Rate<br>14.6% | ascertained with the bCAM. |
| Ryan[47] (conference abstract) 2019, Ireland | Cohort | Community dwelling older adults identified as frail during the ED triage. | Not specified | Delirium<br>n = 16<br>Total<br>n = 121<br>Rate<br>13.2% | Prevalent ED delirium ascertained with the 4AT. |
| Singler[48] 2014, Germany | Prospective cohort | Undifferentiated older adults age ≥ 75 years presenting to the ED. | Barriers to communication (unable to communicate, non-German speaking), clinically unstable (cardiorespiratory instability). | Delirium<br>n = 19<br>Total<br>n = 133<br>Rate<br>14.3% | Prevalent ED delirium ascertained with the CAM. |

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| Sri-on[49] 2016, Thailand | Prospective cohort | Undifferentiated older adults age ≥ 65 years presenting to the ED. | Barriers to communication (blind, deaf, aphasic, or non-Thai speaking). Patients with severe dementia, not responsive to verbal stimuli, critically ill patients. | Delirium n = 27 Total n = 232 Rate 11.6% | Prevalent ED delirium ascertained with the CAM-ICU. |
| Tonarelli[50] (conference abstract) 2018, Italy | Cohort | Undifferentiated older adults age ≥ 75 years presenting to the ED. | Not specified. | Delirium n = 522 Total n = 2494 Rate 20.9% | Prevalent ED delirium ascertained with the 4AT. |
| **Studies evaluating the development of delirium during hospitalization (incident delirium)** | | | | | |

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| Bo[58] 2009, Italy | Prospective cohort | Undifferentiated older adults age ≥ 70 years, free of delirium upon arrival, and who were admitted to the hospital. | Coma, barriers to communication (aphasia, stroke, language barrier), history of psychiatric disorder or alcohol abuse, intubated patients, absence of caregiver. | Incident delirium n = 28 Total n = 252 Rate 11.1% | Incident delirium ascertained with the CAM. |
| Bo[59] 2016, Italy | Prospective cohort | Undifferentiated older adults age ≥ 75 years presenting to the ED, free of delirium upon arrival, and who were admitted to the hospital. | Coma, barriers to communication (aphasia, stroke, language barrier), history of primary psychiatric disorder or alcohol abuse. | Incident delirium n = 52 Total n = 330 Rate 15.8% | Incident delirium ascertained with the 4AT and DSM-V criteria. |

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| Émond[84] 2017, Canada | Historical (retrospective) cohort | Undifferentiated older adults age ≥ 65 years, free of delirium upon arrival, exposed to the ED for at least 12 hours and admitted to the any hospital ward. | Critically ill patients requiring ICU care, history of severe dementia or psychiatric conditions such as schizophrenia and bipolar disorder, residents or in transition to long-term care facilities. | Incident delirium n = 36 Total n = 200 Rate 18.0% | Incident delirium ascertained with the chart-based method developed by Inouye. |
| Evensen[61] 2018, Norway | Prospective cohort | Undifferentiated older adults age ≥ 75 years, free of delirium upon arrival, and admitted to the hospital. | No further details specified. | Incident delirium n = 49 Total n = 254 Rate 19.3% | Incident delirium ascertained using DSM IV/V criteria together with the chart-based method |

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| | | | | | developed by Inouye. |
| Daoust[62] 2020, INDEED* cohort, Canada | Prospective cohort | Undifferentiated older adults age ≥ 65 years, free of delirium upon arrival, with an ED stay ≥ 8 hours, admitted to the hospital, and considered independent or semi-independent. | Critically ill patients requiring ICU or palliative care unit care, unable to consent, living in a long-term care facility, non-English or French speaking, history of psychiatric disorders (schizophrenia, psychosis, bipolar disorder). | Incident delirium n = 41 Total n = 338 Rate 12.1% | Incident delirium ascertained with the CAM. |

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| Inouye[63] 1996, United States | Prospective cohort | Undifferentiated older adults age ≥ 70 years, free of delirium upon arrival, and admitted to general medical floors. | Patients discharged in less than 48 hours, physicians declined patient participant, not able to be interviewed (critically ill, intubation, coma, severe aphasia, or terminal condition). | Incident delirium n = 35 Total n = 196 Rate 17.9% | Incident delirium ascertained with the CAM. |
| Thompson[64] 2018, Canada | Historical (retrospective) cohort | Older adults age ≥ 65 years with an ED diagnosis of hip fracture admitted to the hospital for hip fracture repair/surgery. | Patients who did not undergo surgery for hip fracture, had a missing ED record, were considered palliative care patients, or left | Incident delirium n = 181 Total n = 668 Rate 27.1% | Incident delirium ascertained by CAM together with the chart-based method developed by Inouye. |

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|---|---|---|---|---|---|
| | | | against medical advice. | | |

‡DELINEATE, Delirium in the Emergency Department and Its Extension into Hospitalization. This study involved several different reports (Yuan 2016[51], Han 2017b[4], Cirbus 2018[52]). This study used a control group that was a random sample of non-delirious patients and for this reason had a similar number of delirious and non-delirious patients.

†These overlapping cohorts included three different reports that had data available from different variables (Han 2009a[34], Han 2009b[12], Han 2017a[35]). One cohort was developed from May 2007 to August 2008, while the other was developed from July 2009 and February 2012. One report[35] included both cohorts with the total of 1084 patients.

*INDEED, Incidence and Impact Measurement of Delirium Induced ED Stay.

Risk factors and ED delirium

For ED delirium studies, there were a total of 13,412 geriatric patients in whom delirium was assessed during the ED clinical course. The prevalence of ED delirium in the overall population of undifferentiated older adults ranged from 7%[9,36,53] to 34.7%[44] in studies in which the design allowed to estimate prevalence. The methodological quality of the 27 ED delirium studies was heterogeneous, including 6 studies deemed to be at high risk of bias, 8 at unclear risk of bias, and 13 at low risk of bias. The detailed risk of bias assessment for each study is available in the *Appendix S2*. The full GRADE assessment for each potential risk factor evaluated, taking into consideration other domains beyond risk of bias, is detailed in the *Appendix S3*.

We evaluated 57 potential risk factors for prevalent ED delirium. (**Table 3 and 4**). When demographics, medications, vulnerabilities, comorbidities, and previous history were

evaluated as potential risk factors, the majority of patient characteristics were not significantly associated with an increased risk of ED delirium. (**Table 3**) Most variables had estimates representing weak associations with moderate to low certainty in the evidence. We found only 4 variables with strong associations (relative effect estimate ≥ 2) graded as high certainty evidence, including nursing home residence (4 studies,[4,34,46,54] OR 3.45, 95% CI 2.17 to 5.48), cognitive impairment (7 studies,[12,39,42,45,46,48,49] OR 4.46, 95% CI 3.38 to 5.89), hearing impairment (3 studies,[12,42,49] OR 2.57, 95% CI 1.03 to 6.41), and history of stroke (3 studies,[39,45,53] OR 3.20, 95% CI 1.17 to 8.75). By considering together all unadjusted data from studies that reported these 4 risk factors, the prevalence of ED delirium in patients with and without the risk factors was as following: nursing home residence (4 studies, 51/152 [33.6%] vs. 287/1846 [15.5%]), cognitive impairment (11 studies, 502/1231 [41.4%] vs. 534/4659 [11.5%]), hearing impairment (5 studies, 103/399 [25.8%] vs. 98/825 [11.9%]), and history of stroke (6 studies, 70/259 [27.0%] vs. 194/1767 [11.0%]). Despite very low certainty in the estimates, malnutrition and frailty were also found to have strong associations with ED delirium. (**Table 3**).

**Table 3.** Potential risk factors (demographics, medications, vulnerabilities, comorbidities and previous history) for ED delirium and its effect estimates.

| **Potential risk factor for ED delirium** | **Number of studies (number of patients)** | **Effect estimates¶ (95% confidence interval), random effects meta-analysis** | **$I^2$** | **Certainty in the evidence using the GRADE approach¥** |
|---|---|---|---|---|
| **Demographics** | | | | |

| | | | | |
|---|---|---|---|---|
| Age | 4[39,45,46,48] (1158) | OR 1.20 (0.94 to 1.53)[†] | 34% | High |
| Race, non-white | 4[4,35,39,40] (2096) | OR 1.45 (0.93 to 2.28) | 24% | Very low |
| Sex, male | 3[45,46,48] (482) | OR 1.77 (0.70 to 4.47) | 48% | Low |
| Marital status, not married | 1[45] (110) | OR 5.33 (1.38 to 20.60) | NA | Low |
| Nursing home residence | 4[4,34,46,54] (1255) | OR 3.45 (2.17 to 5.48) | 0% | High |
| Any dependent living[*] | 7[4,35,39,46,48,49,54] (3035) | OR 3.07 (2.32 to 4.06) | 0% | Moderate |
| Recent hospitalization | 2[12,48] (436) | OR 1.71 (0.62 to 4.74) | 37% | Very low |
| **Medications** | | | | |
| Polypharmacy[‡] | 1[42] (1205) | OR 1.00 (0.66 to 1.51) | NA | Moderate |
| Outpatient opioids | 1[57] (2732) | RR 1.73[§] (0.63 to 4.76) | NA | Moderate |
| Outpatient benzodiazepines | 1[57] (2732) | RR 1.04[§§] (0.69 to 1.56) | NA | High |
| Outpatient anticholinergics[‡‡] | 1[57] (2732) | RR 1.64[§] (1.07 to 2.54) | NA | High |

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|---|---|---|---|---|
| Outpatient antipsychotics | 1[39] (676) | OR 3.29 (1.26 to 8.57) | NA | Moderate |
| Outpatient psychostimulants | 1[57] (2732) | RR 2.49[§] (0.60 to 10.30) | NA | Moderate |
| Outpatient antidepressants | 1[39] (676) | OR 1.46 (0.82 to 2.58) | NA | Low |
| Outpatient proton-pump inhibitors | 1[57] (2732) | RR 1.61[§] (1.10 to 2.34) | NA | High |
| Outpatient antiemetics | 1[57] (2732) | RR 1.04[§] (0.61 to 1.79) | NA | High |
| Outpatient antihistamines | 1[57] (2732) | RR 1.27[§] (0.54 to 3.02) | NA | Moderate |
| Outpatient antihypertensives | 1[43] (200) | OR 0.37 (0.20 to 0.70) | NA | Very low |
| **Vulnerabilities, comorbidities, and previous history** | | | | |
| Functional dependence | 2[12,46] (542) | OR 2.04 (0.50 to 8.32) | 93% | Low |
| Mobility impairment | 2[42,48] (1338) | OR 1.34 (0.80 to 2.26) | 0% | Moderate |
| Malnutrition | 1[38] (148) | OR 7.94 (2.86 to 22.08) | NA | Very low |
| Frailty | 2[38,56] (346) | OR 8.92 (1.34 to 59.40) | 56% | Very low |

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|---|---|---|---|---|
| Cognitive impairment | 7[12,39,42,45,46,48,49] (2818) | OR 4.46 (3.38 to 5.89) | 0% | High |
| Visual impairment | 1[42] (1205) | OR 1.10 (0.78 to 1.56) | NA | Moderate |
| Hearing impairment | 3[12,42,49] (1740) | OR 2.57 (1.03 to 6.41) | 74% | High |
| History of stroke | 3[39,45,53] (1479) | OR 3.20 (1.17 to 8.75) | 69% | High |
| History of seizures | 3[39,42,53] (2574) | OR 2.47 (1.24 to 4.92) | 0% | Low |
| History of previous delirium | 3[42,45,46] (1554) | OR 2.67 (1.73 to 4.11) | 0% | Moderate |
| History of Parkinson disease | 1[42] (1205) | OR 1.10 (0.51 to 2.36) | NA | Low |
| History of anxiety | 1[42] (1205) | OR 1.70 (1.09 to 2.66) | NA | Moderate |
| History of depression | 2[36,42] (1525) | OR 1.59 (0.39 to 6.55) | 89% | Very low |
| History of chronic pain | 1[42] (1205) | OR 1.00 (0.70 to 1.50) | NA | Moderate |
| History of constipation | 1[42] (1205) | OR 1.30 (0.90 to 1.90) | NA | Moderate |
| History of arrhythmias | 2[39,46] (915) | OR 1.09 (0.49 to 2.42) | 68% | Low |

| | | | | |
|---|---|---|---|---|
| History of coronary artery disease | 4[39,40,46,53] (1716) | OR 0.90 (0.64 to 1.25) | 0% | Moderate |
| History of hypertension | 5[40,43,45,46,53] (1322) | OR 0.79 (0.55 to 1.14) | 0% | Low |
| History of dyslipidemia | 4[40,43,45,46] (657) | OR 0.63 (0.40 to 0.99) | 19% | Low |
| History of chronic heart failure | 2[45,53] (803) | OR 1.11 (0.64 to 1.92) | 0% | Low |
| History of COPD | 5[39,40,45,46,53] (1826) | OR 1.06 (0.74 to 1.52) | 0% | Moderate |
| History of diabetes | 6[39,40,43,45,46,53] (2026) | OR 0.98 (0.73 to 1.31) | 0% | Moderate |
| History of renal disease | 4[40,45,46,53] (1150) | OR 0.85 (0.53 to 1.36) | 0% | Moderate |
| History of malignancy | 2[45,53] (803) | OR 1.08 (0.41 to 2.86) | 44% | Very low |
| Charlson comorbidity index | 6[4,35,39,40,46,49] (2567) | OR 1.63 (1.22 to 2.18)[††] | 46% | Moderate |

NA, not applicable; OR, odds ratio; RR, risk ratio; COPD, Chronic Obstructive Pulmonary Disease.

¥The complete assessment with the GRADE evidence table can be found in the *Appendix S3.1*.

¶Whenever both unadjusted and adjusted estimates were available, adjusted effect estimates were preferred over unadjusted ones because they represent an effect estimate closer to the truth (i.e. less biased). Meta-analysis was only performed when 2 or more studies had data available for the variable.

*Any dependent living including rehabilitation centers, assisted living, and other types of dependent living besides nursing homes.

†The interpretation of this pooled odds ratio for age is as following: "the odds of being older in those with ED delirium is approximately 1.20 times higher compared to those without ED delirium."

††The interpretation of this pooled odds ratio for Charlson index is as following: "the odds of having more comorbidities (i.e. greater Charlson index) in those with ED delirium is approximately 1.63 times higher compared to those without ED delirium."

‡Polypharmacy was defined as > 9 medications in the study by Nguyen et al. Unadjusted data from 8 other studies are reported in the Appendix S4.

‡‡Yuan 2016[51] reported an adjusted odds ratio for the association between anticholinergic cognitive burden and ED delirium (odds ratio 1.1, 95% CI 0.92 to 1.34, p = 0.265).

§This represents the adjusted risk ratio from *Gil et al*[57] (the odds ratio was not reported).

§§This represents the adjusted risk ratio from *Gil et al*[57](the odds ratio was not reported). Another study (*Yuan 2016)*[51] reported an adjusted odds ratio of 3.10 (95% CI 1.10 to 8.72) for the association between home use of benzodiazepines and ED delirium.

When ED triage vital signs and primary complaints were evaluated as potential risk factors for ED delirium, the most prominent risk factor was an ED chief complaint of altered mental status (3 studies,[35,40,52] OR 13.33, 95% CI 6.29 to 28.23, moderate certainty). Severity of illness was strongly associated with ED delirium but the certainty in the estimate was low. (**Table 4**) Forest plots of the meta-analyses from **Table 3** and **Table 4** are available in the *Appendix S4*.

**Table 4.** ED triage vital signs and primary (chief) complaints as potential risk factors for ED delirium and its effect estimates.

| **Potential risk factor for ED delirium** | **Number of studies** | **Effect estimates¶ (95% confidence interval),** | **$I^2$** | **Certainty in the evidence using** |
|---|---|---|---|---|

| | **(number of patients)** | **random effects meta-analysis** | | **the GRADE approach¥** |
|---|---|---|---|---|
| **ED triage vital signs** | | | | |
| Triage temperature†, ºF | 1[39] (676) | MD 0.10 (-0.35 to 0.55) | NA | Moderate |
| Triage heart rate††, bpm | 1[39] (676) | MD 0.00 (-4.17 to 4.17) | NA | Moderate |
| Triage systolic blood pressure, mmHg | 1[39] (676) | MD -4.00 (-10.25 to 2.25) | NA | Moderate |
| Triage respiratory rate*, bpm | 1[39] (676) | MD 0.80 (0.15 to 1.45) | NA | Moderate |
| Triage oxygen saturation | 1[39] (676) | MD 0.00 (-0.58 to 0.58) | NA | Moderate |
| **ED chief complaint/concern** | | | | |
| Altered mental status | 3[35,40,52] (1420) | OR 13.33 (6.29 to 28.23) | 51% | Moderate |
| Chest pain | 4[35,39,40,52] (2096) | OR 0.43 (0.19 to 0.98) | 52% | Moderate |
| Shortness of breath | 3[35,40,52] (1420) | OR 0.40 (0.19 to 0.84) | 27% | Moderate |
| Syncope | 3[35,40,52] (1420) | OR 0.63 (0.12 to 3.31) | 66% | Low |

| | | | | |
|---|---|---|---|---|
| Abdominal pain | 3[35,40,52] (1420) | OR 1.17 (0.63 to 2.14) | 0% | Low |
| Generalized weakness | 3[35,40,52] (1420) | OR 1.56 (0.99 to 2.45) | 0% | Low |
| Gastrointestinal including nausea and vomiting | 2[45,52] (338) | OR 0.39 (0.08 to 1.80) | 43% | Very low |
| **Illness severity** | | | | |
| SIRS positive | 2[12,49] (535) | OR 1.80 (0.48 to 6.75) | 70% | Low |
| Severity of illness‡ | 4[4,35,39,54] (2148) | OR 2.22 (1.30 to 3.77) | 81% | Low |

NA, not applicable; ºF, Fahrenheit degrees; bpm, beats per minute; MD mean difference; OR, odds ratio.

¥The complete assessment with the GRADE evidence table can be found in the *Appendix S3.1*.

¶Whenever both unadjusted and adjusted estimates were available, adjusted effect estimates were preferred over unadjusted ones because they represent an effect estimate closer to the truth (i.e. less biased). Meta-analysis was only performed when 2 or more studies had data available for the variable.

†Sri-on et al[49] also reported triage temperature, but in Celsius and as a categorical variable (no difference between those with ED delirium and those without, $p > 0.99$).

††Sri-on et al[49] also reported triage heart rate, but as a categorical variable (no difference in triage tachycardia between those with ED delirium and those without, $p = 0.261$).

*Kennedy et al[39] also reported respiratory rate as a categorical variable (> 20) and reported an adjusted effect estimate of 2.80 (95% CI 1.2 to 6.10). Sri-on et al[49] reported respiratory rate but as a categorical variable (no difference in abnormal respiratory rate between those with ED delirium and those without, $p = 0.685$).

‡The interpretation of this odds ratio for severity of illness is as following: “the odds of having greater severity of illness in those with ED delirium is approximately 2.22 times higher compared to those without ED delirium.”

ED-based risk factors and delirium during hospitalization

For incident delirium studies, there were a total of 2,238 geriatric patients free of delirium in the ED who were assessed for the development of delirium during hospitalization. The overall incidence of delirium during hospitalization in these studies ranged from 11%[58] to 27%.[64] The quality of the 7 studies was also heterogeneous but of overall better quality, including 4 studies deemed to be at low risk of bias, and 3 at unclear risk of bias.

We evaluated 9 potential ED-based modifiable risk factors for the development of new hospital delirium. Only one variable was suitable for meta-analysis, which showed a significant association between urinary catheterization in the ED and an increased risk of developing delirium during hospitalization (2 studies,[59,62] OR 2.53, 95% CI 1.31 to 4.88, moderate certainty). (**Table 5**)

ED length of stay as a risk factor for developing delirium during hospitalization was reported heterogeneously in the literature. A length of stay in the ED greater than 10[59] or greater than 12[63] hours were significantly associated with a higher risk of developing delirium (ED LOS > 10 hours:[59] OR 2.23, 95% CI 1.13 to 4.41, high certainty; ED LOS > 12 hours:[63] 2.46, 95% CI 1.16 to 5.24, moderate certainty). (**Table 5**)

Lastly, the presence of severe pain rather than the use of opioids was found to be significantly associated with the development of delirium in one study.[62] The effect estimate for the association between severe pain in the ED and development of subsequent delirium was graded at high certainty (1 study,[62] OR 3.29, 95% CI 1.38 to 7.88). The evidence regarding use of medications from the Beers list including benzodiazepines as contributors to a potential increase in delirium risk was very limited. (**Table 5**).

**Table 5.** Potential ED-based modifiable risk factors for developing delirium during hospitalization (incident delirium).

| **Potential ED-based modifiable risk factor for developing delirium during hospitalization** | **Number of studies (number of patients)** | **Effect estimates[¶] (95% confidence interval), random effects meta-analysis** | **$I^2$** | **Certainty in the evidence using the GRADE approach[¥]** |
|---|---|---|---|---|
| ED length of stay (LOS) | 1[61] (254) | OR 0.85 (0.69 to 1.04)[†] | NA | Low |
| ED LOS[*] > 4 hours | 1[61] (254) | OR 0.78 (0.41 to 1.47) | NA | Very low |
| ED LOS[*] > 5 hours | 1[59] (330) | OR 0.94 (0.52 to 1.71) | NA | Low |
| ED LOS[*] > 10 hours | 1[59] (330) | OR 2.23 (1.13 to 4.41) | NA | High |
| ED LOS[*] > 12 hours | 1[63] (196) | OR 2.46 (1.16 to 5.24) | NA | Moderate |
| Inadequate lighting | 1[62] (338) | OR 1.51 (0.78 to 2.90) | NA | Very low |
| ED physical restraint | 1[62] (338) | OR 0.71 (0.37 to 1.37) | NA | Low |
| Lack of orientation aids (clock, watch, etc.) | 1[62] (338) | OR 1.66 (0.86 to 3.20) | NA | Very low |
| Urinary catheterization | 2[59,62] (666) | OR 2.53 (1.31 to 4.88) | 0% | Moderate |
| Severe pain in the ED | 1[62] (338) | OR 3.29 (1.38 to 7.88) | NA | High |

| | | | | |
|---|---|---|---|---|
| Opioids during ED stay | 1[62] (338) | OR 1.25 (0.55 to 2.83) | NA | Low |
| No opioids or nerve block in the ED | 1[64] (668)‡ | OR 2.10 (1.30 to 3.20) | NA | Moderate |
| Use of medications from the Beers list in the ED‡‡ | 1[60] (200) | OR 0.91 (0.10 to 8.02) | NA | Very low |

¶Whenever both unadjusted and adjusted estimates were available, adjusted effect estimates were preferred over unadjusted ones because they represent an effect estimate closer to the truth (i.e. less biased). Meta-analysis was only performed when 2 or more studies had data available for the variable.

†This odds ratio is the adjusted effect estimate reported by Evensen et al.[61] This odds ratio was derived from using ED LOS as a continuous variable in a multivariable logistic regression model rather than dichotomizing ED LOS using a cutoff of hours.

*These cutoffs were originally reported by the manuscripts.

‡This study included only hip fracture ED geriatric patients.

‡‡Defined as new medications administered in the ED that were present in the 2003 Beers criteria.

## LIMITATIONS

There are several limitations that need to be acknowledged. First, data availability was heterogeneous with certain risk factors being available in several reports (e.g. cognitive impairment) as opposed to other variables being available in only one. Second, not all studies reported adjusted effect estimates for the associations. Nevertheless, whenever both unadjusted and adjusted data were available, we used the adjusted estimate as they are theoretically closer to the truth and less biased (i.e. they account for potential confounders identified by the authors in the original manuscript). Several variables, however, had only

unadjusted data and confounding may significantly change some of the effect estimates calculated by our meta-analyses. In order to account for such uncertainty, we downgraded one level for risk of bias whenever the estimate came mostly from unadjusted data. The evidence levels provided by the GRADE assessment allows the users of this systematic review to grasp the uncertainty of estimates. Third, this review did not evaluate the different etiologies behind ED delirium. The identification of etiologies is paramount once the diagnosis is made but it helps little when trying to decide who benefit from active screening. Lastly, although we included only studies that have ascertained delirium using previously validated and structured diagnostic tools, the diagnostic accuracy of these instruments are not perfect[65] and misclassification both in the ED and during hospitalization may have occurred.

## DISCUSSION

In this systematic review, we found several characteristics associated with increased risk of ED delirium. The strongest risk factors for prevalent ED delirium with high certainty behind the evidence were nursing home residence, cognitive impairment, hearing impairment, and history of previous stroke. These characteristics can be used to identify groups at higher risk of having delirium which can otherwise be missed. These variables could be obtained early in the course of the ED evaluation and may be potentially used to target active delirium screening.

Targeting patients at high risk for presenting to the ED with delirium can heighten awareness early in the clinical evaluation and allow for other interventions to be deployed downstream. The issue, however, is that the number of clinical factors that could potentially flag an increased risk of ED delirium for an undifferentiated geriatric patient presenting to the ED is overwhelming. In this context, it may be challenging to identify variables that could be used to prioritize care processes such as active delirium screening during the early ED

evaluation. The selection of clinical characteristics with strong associations with ED delirium supported by high GRADE evidence could help in this endeavor. Our review quantified the effect estimate for each potential risk factor ever evaluated in the ED specific literature and graded the certainty in the evidence to aid clinicians and stakeholders when trying to identify a subset of patients at high risk of ED delirium.

Nursing home residence, or any type of dependent living (e.g. rehabilitation or assisted living) may all suggest that the patient is frail. Frailty by definition is the accumulation of deficits or decreased reserve from cumulative decline which impairs one's ability to compensate for stressors.[66] Living in a nursing home suggests a patient needs help conducting activities of daily living which is essential to frailty assessment. In fact, the prevalence of frailty among nursing home patients may be as high as 75.6%.[67] The relationship between frailty and delirium has been specifically evaluated in another meta-analysis, which showed a significant and strong association between these two variables.[68] We also found a strong association between frailty and ED delirium, but with limited quality evidence (very low certainty based on GRADE). Identification of frailty patients could be instrumental in finding the group that most likely will benefit from downstream resources. Finding a simple yet accurate frailty tool is important for the ED setting. Most recently, the Clinical Frailty Scale (CFS), has been validated in the ED to predict 30-day mortality,[69] with appropriate inter-rater reliability.[70,71] The idea of first identifying frailty to then prioritize other types of geriatric assessments seems like a reasonable approach because frailty also predicts other important outcomes such as recurrent falls.[72] Nevertheless, ED stakeholders may want to use simpler and more readily available clinical characteristics to prioritize delirium screening in the ED. Besides its correlation with frailty,[67,73] nursing home residence and other types of dependent living, as well as hearing impairment, are strongly associated with increased risk of ED delirium. These variables are

thus suitable for the purpose of prioritizing delirium screening. History of stroke was also strongly associated with ED delirium, which provides indirect evidence that those with impaired brain function have significant higher risk of delirium and can also be targeted for active delirium screening.

Cognitive impairment and a chief complaint of altered mental status were amongst the strongest risk factors for ED delirium. A geriatric patient presenting to the ED with a chief complaint identified as altered mental status should probably be interpreted as equivalent to delirium. Han et al, using a diagnostic test accuracy analysis approach, calculated the specificity of this "complaint" for the diagnosis of ED delirium and found it to be 98.9% specific with a positive likelihood ratio of 33.82.[74]

Dementia and other types of cognitive impairments, are a well-known strong risk factor for delirium across all healthcare settings.[75] Delirium among patients with dementia has been linked to long-term cognitive and functional decline, readmission, institutionalization, and increased mortality.[76–78] In the context of robust available evidence, flagging patients with dementia as high risk for delirium, and therefore targeting them for active delirium screening, is imperative to their ED care, as their outcomes are significantly impacted should delirium be present or develop.

Besides aiding in the identification of potential targets for active delirium screening in the ED, our review also attempted to identify ED-based modifiable risk factors that may impact the development of delirium during hospitalization. We found that an increased ED length of stay (LOS), urinary catheterization, and severe pain were importantly associated with a higher risk of having new delirium once the patient is admitted. Minimizing the amount of time that older adults spend in the ED, avoiding unnecessary urinary catheterization, and optimizing pain management as much as possible are key actionable

targets to potentially prevent delirium.

Increasing boarding times with its associated delirium risk has been consistently shown since the study by Inouye et al in 1999 demonstrated that an ED LOS > 12 hours was associated with an increased risk of developing delirium during hospitalization.[63] This is incredibly important for geriatric patients who are forced to board in the ED when hospital bed availability is problematic. The development of geriatric EDs, tailored for the care of older adults, may minimize the "iatrogenic" effect of maintaining these patients boarded. However, most EDs will not have specialized geriatric assessments available and the expedition of these patients' disposition to a less deliriogenic setting is paramount to minimize their risk. Although an increased ED LOS seems clearly associated with an increased risk of developing delirium during hospitalization, the evidence behind the specific reasons is very limited. This may hinder the implementation of traditional delirium prevention measures. We did find one study[62] looking at variables such as inadequate lighting, physical restraint, and lack of orientation aids, but results were imprecise, with low to very low certainty in the effect estimates.

Urinary catheters have been linked to delirium in hospitalized patients and the number of catheters and drainages before the diagnosis of blood stream infection was an independent predictor of delirium in patients admitted to the ICU.[79] Noel et al reported an increased duration of delirium in those with an urinary catheter despite adjustment for known confounders.[80] Although largely motivated by lowering risk of infection, quality improvement initiatives have successfully reduced the use of urinary catheters in the ED.[81]

Finally, the association of pain and delirium has been largely studied in post-operative patients and many studies have linked the two even after controlling for confounders.[82,83] Optimization of pain management is paramount to reduce the risk of incident delirium in

geriatric hospitalized patients. In fact, one study investigated the relationship between pain, opioid treatment, and incident delirium in older adults, finding that severe pain, not opioids, was associated with the development of delirium.[62] Besides that, in a population of ED hip fracture patients, the lack of opioid analgesia or nerve block was significantly associated with an increased risk of developing delirium.[64]

## CONCLUSIONS

Nursing home residence, cognitive impairment, hearing impairment, and history of stroke were significantly associated with ED delirium. ED length of stay and severe pain increase the risk of developing delirium during hospitalization after being delirium free in the ED. Based on the current best available evidence, we identified key risk factors for ED delirium as well as ED-based modifiable risk factors for delirium that develops during hospitalization. These findings can be used to supplement clinical judgment, facilitate shared decision making, to target delirium screening in the ED, and to inform the development of novel ED delirium risk scores and prevention interventions.

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Artigo 2

(OLIVEIRA J E SILVA et al., 2022b)

**Oliveira J E Silva L**, Stanich JA, Jeffery MM, Mullan AF, Bower SM, Campbell RL, Rabinstein AA, Pignolo RJ, Bellolio F. REcognizing DElirium in geriatric Emergency Medicine: The REDEEM risk stratification score. **Acad Emerg Med**. 2022 Apr;29(4):476-485. doi: 10.1111/acem.14423. Epub 2021 Dec 17. PMID: 34870884; PMCID: PMC9050857.

Academic Emergency Medicine - CAPES A1

**ABSTRACT**

Study objective: To derive a risk score that uses variables available early during the ED encounter to identify high-risk geriatric patients who may benefit from delirium screening.

Methods: This was an observational study of older adults age ≥ 75 years who presented to an academic ED and who were screened for delirium during their ED visit. Variable selection from candidate predictors was performed through a LASSO-penalized logistic regression. A risk score was derived from the final prediction model, and predictive accuracy characteristics were calculated with 95% confidence intervals (CIs).

Results: From the 967 eligible ED visits, delirium was detected in 107 (11.1%). The area under the curve for the REcognizing DElirium in Emergency Medicine (REDEEM) score was 0.901 (95% CI 0.864 to 0.938). The REEDEM risk score included 10 different variables (7 based on triage information and 3 obtained during early history taking) with a score ranging from -3 to 66. Using an optimal cutoff of ≥ 11, we found a sensitivity of 84.1% (90 of 107 ED delirium patients, 95% CI 75.5% to 90.2%) and a specificity of 86.6% (745 of 860 non-ED delirium patients, 95% CI 84.1% to 88.8%). A lower cutoff of ≥ 5 was found to minimize false negatives with an improved sensitivity at 91.6% (98 of 107 ED delirium patients, 95% CI 84.2% to 95.8%).

Conclusion: A risk stratification score was derived with the potential to augment delirium recognition in geriatric ED patients. This has the potential to assist on delirium targeted screening of high-risk patients in the ED. Validation of REDEEM, however, is needed prior to implementation.

**INTRODUCTION**

Delirium is an acute brain failure that commonly occurs in older adults presenting to the emergency department (ED).[1] Its diagnosis has been associated with decreased long-term functionality[2] and increased mortality[3]. As ED delirium is often hypoactive[4] and frequently missed[5], active screening for delirium has been recommended for all older adults by geriatric ED guidelines.[6] Despite the frequent occurrence of delirium in geriatric patients and its negative consequences, there are several practical challenges precluding the implementation of universal screening of all geriatric patients for delirium in the ED. The increasing number of older adults presenting to the ED and the large amount of competing standardized care processes in the ED (e.g., several mandatory screenings) add a significant burden to providers and to the entire ED workflow. The identification of a subset of high-risk patients would allow for a targeted screening strategy, decreasing low yield or unnecessary screenings. In this context, the development of a delirium risk score that does not significantly increase nurse or physician workload is a priority of the Geriatric Emergency Care Applied Research (GEAR) network.[7]

Prediction models and risk stratification scores are most useful when clinicians fail to efficiently identify a condition through routine care, and when there are serious consequences associated with missing the diagnosis.[8] Delirium is missed in up to 83% of cases in the ED; and because delirium has numerous prognostic implications,[9,10] there could be substantial benefits from improving detection. A stratification tool that flags patients who are high risk for delirium could augment providers' ability to recognize delirium while increasing the feasibility of implementation of screening. The development of such system, however, is challenging because delirium is fluctuant and has multiple risk factors.[11,12] In the ED setting recognizing delirium is even more difficult as providers may have limited information about the patient (e.g., unreliable history and/or no caregivers present). While a systematic review identified 28 delirium prediction models in the inpatient setting, none of these models were

built for the ED.[13] Moreover, existing ED-specific risk stratification models had limited diagnostic accuracy and used variables not readily available to clinicians early in the ED course.[4,14,15]

In this study, our objective was to develop a risk stratification system that uses variables available early during the ED encounter to identify high-risk patients who should be screened for delirium.

## METHODS

This manuscript adheres to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines.[16] This study was approved by our Institutional Review Board and only patients who provided research authorization for medical records review were included.

### Study design, setting, and participants

This was an observational study of adults aged 75 years or older who presented to an academic quaternary ED in Minnesota with approximately 80,000 patient visits per year. We included all patients who presented over a 14-month period (December 2nd, 2019, through February 1st, 2021) and who were screened for delirium during their ED visit. Delirium screening was recommended for all older adults age ≥ 75 years except those deemed not assessable for delirium (e.g., stuporous, or comatose patients). The decision to screen an individual patient, however, took place at the discretion of the bedside nurse.

### Delirium measurement (outcome)

The presence of ED delirium was ascertained by ED nurses with the validated sequential 2-step approach: the Delirium Triage Screen (DTS) and the brief Confusion

Assessment Method (bCAM).[17,18] The DTS tool has a sensitivity of 98% and can be used as a rule-out screening tool.[17] The bCAM has a sensitivity of 84% and specificity of 96%.[17] Patients had DTS performed first, and if negative, patients were ruled out of having delirium based on the high sensitivity of DTS. If DTS was positive, then bCAM was applied. A patient was considered positive for delirium if they had a positive bCAM because of the high specificity of bCAM. A positive DTS followed by a negative bCAM was considered negative for delirium. Patients without a DTS recorded but with a negative bCAM were considered negative for delirium. Delirium screening was available in the electronic health record (EHR). For patients who had more than one screening during the ED evaluation, if one of the screenings was positive, we classified them in the group of ED delirium.

For patients in which the delirium screening was unclear (e.g., positive DTS followed by an incomplete bCAM, or both DTS and bCAM incomplete), two physicians (one board-certified emergency physician [J.S.] and one physician-scientist [L.O.J.S.]) performed independent individual chart review and assessed for the presence of ED delirium through the chart-based method developed by Inouye and colleagues.[19] This method has had reported sensitivity of 74%, specificity of 83%, and a likelihood ratio for a positive result of 4.4.[19] Disagreements were resolved by a third reviewer (board certified emergency physician [F.B.]).

Risk factors (candidate predictors)

Our main goal was to create a risk stratification score that assists in the prioritization of delirium screening prior to the completion of the ED evaluation; therefore, to identify candidate predictors, we used findings from our previously published systematic review [11,12] and other variables that that could be rapidly accessed early in the ED course. The following variables were extracted automatically from the EHR: age, sex, marital status, ethnic group,

race, residence status (private residence, assisted living, skilled nursing facility, or unknown), means of arrival (ambulance or not), Emergency Severity Index (ESI) triage level,[20] initial vital signs (first-listed vitals in the EHR), chief complaint,[21] nurse-based fall risk assessment,[22] and presence of comorbidities such as visual or hearing impairment, history of dementia, history of stroke/TIA, history of previous delirium, history of depressive disorders, history of anxiety disorders, and history of seizure disorders. Comorbidities (prior history) were measured with previously validated lists of International Classification of Disease (ICD) codes (*Appendix 1*).[23,24] The inclusion of fall risk assessment and their components as potential candidate predictors was based on a recent study for prediction of inpatient delirium.[25] The Memorial ED Fall Risk Assessment Tool (MEDFRAT)[22] was routinely applied by nurses early in the course of patients' ED stay, transforming its results to information that could be used as potential predictors of delirium in the ED. Full details on the measurement of each of these variables are available in the *Appendix 1*. Initial vital signs were categorized based on extreme values. Patients in the lower 10% for oxygen saturation were flagged as having low levels, whereas patients in either the lower 10% or upper 10% for heart rate, respiratory rate, blood pressure, and temperature were flagged as extreme and abnormal.[26] *Appendix 2* provides the cut-offs used to divide extreme vital signs from the normal range. All these extracted variables were deemed candidate predictors for the final model.

Missing data

Data was complete for all variables except for fall risk score (2.7% missing), temperature (3.4% missing), heart rate (0.7% missing), and respiratory rate (2.8% missing). Missing data for fall risk assessment elements were coded/scored as 0 when an item was not

present, while missing data for temperature, heart rate, and respiratory rate were imputed to be the median vitals from the non-missing data.

Variable selection and risk score development

To prevent over-fitting, variable selection from candidate predictors was performed through a least absolute shrinkage and selection operator (LASSO) penalized logistic regression.[27,28] The penalization parameter lambda (λ) was chosen through 10-fold cross-validation on the data and any variable with model estimates not shrunk to 0 were chosen for the final model. Selected variables were weighted by their respective LASSO-penalized regression estimates. These weighted variables were then rounded to a decimal and multiplied by 10 to create a variable risk score, then summed to return the REcognizing DElirium in Emergency Medicine (REDEEM) risk score. The rounding to a decimal instead of an integer was done to allow for more granularity in the range of possible REDEEM scores.

Discrimination (how well the features in the model separated those with from those without ED delirium) was assessed by the area under the receiver operating characteristic curve (AUC), and calibration of our final model was assessed by the Hosmer-Lemeshow goodness-of-fit test.

To divide groups into low and high-risk patients, a risk score cutoff was determined using Youden's index[29] to maximize the sensitivity and specificity of the risk score predictions. Also, we alternatively determined the risk score cut-off that would maximize sensitivity (i.e., favoring the detection of a higher proportion of delirium cases at the cost of more false positives) with the requirement that specificity could not drop below 70%. Accuracy, sensitivity, specificity, as well as positive and negative predictive values were calculated along with their 95% confidence intervals (CIs) using an asymptotic binomial

approximation. Positive and negative likelihood ratios were calculated along with 95% CIs using a logarithmic transformation on binomial proportions.

All statistical analyses were performed with R software version 3.6.2 by a statistician. For descriptive statistics, continuous features were summarized as median and interquartile ranges (IQRs) or means and standard deviations (SD) as appropriate based on data distribution. Categorical features were summarized as counts and percentages.

## RESULTS

There were 1,060 ED visits in which delirium screening was performed; 93 of these were excluded due to lack of research authorization, leaving a final sample size of 967 by 897 distinct patients. Median age of our cohort was 83 years (IQR 79-88), 54.4% were female, and 97.7% were White. Individual chart review to assess for the presence of delirium was required in 49 visits (5.1%). The inter-rater agreement for delirium assessment in these visits requiring chart review was substantial (kappa 0.80, 95% CI 0.63 to 0.96: overall agreement 89.8%). Overall, ED delirium was detected in 107 (11.1%). (Flowchart available in *Appendix 3*) Most delirium-positive episodes were hypoactive delirium (N=80, 74.8%). Description of the cohort stratified by delirium screening is detailed in *Table 1*.

**Table 1.** Baseline characteristics of the REDEEM cohort.

| | n (%) or median (IQR) | | | |
|---|---|---|---|---|
| | **Screened Negative for ED Delirium (N=860)** | **Screened Positive for ED Delirium (N=107)** | **Total (N=967)** | **Missing Data, N (%)** |
| ***Age and sex*** | | | | |
| Age (years) | 83 (79, 88) | 85 (79, 90) | 83 (79, 88) | - |

| | | | | |
|---|---|---|---|---|
| Female | 466 (54.2%) | 60 (56.1%) | 526 (54.4%) | - |
| ***Ethnicity*** | | | | |
| Hispanic, or Latino | 6 (0.7%) | 2 (1.9%) | 8 (0.8%) | - |
| Not Hispanic or Latino | 841 (97.8%) | 104 (97.2%) | 945 (97.7%) | - |
| Unknown Ethnicity | 13 (1.5%) | 1 (0.9%) | 14 (1.4%) | - |
| ***Race*** | | | | |
| White | 831 (96.6%) | 104 (97.2%) | 935 (96.7%) | - |
| African American | 8 (0.9%) | 1 (0.9%) | 9 (0.9%) | - |
| Asian | 8 (0.9%) | 0 (0.0%) | 8 (0.8%) | - |
| Other Race | 11 (1.3%) | 2 (1.9%) | 13 (1.3%) | - |
| Unknown Race | 2 (0.2%) | 0 (0.0%) | 2 (0.2%) | - |
| ***Residence status*** | | | | |
| Private residence | 568 (66.0%) | 51 (47.7%%) | 619 (64.0%) | - |
| Assisted living | 89 (10.3%) | 20 (18.7%) | 109 (11.3%) | - |
| Skilled nursing facility | 64 (7.4%) | 30 (28.0%) | 94 (9.7%) | - |
| Unknown | 139 (16.2%) | 6 (5.6%) | 145 (15.0%) | - |
| ***Prior history and comorbidities*** | | | | |
| History of dementia | 226 (26.3%) | 59 (55.1%) | 285 (29.5%) | - |
| History of stroke or TIA | 206 (23.9%) | 37 (34.6%) | 243 (25.1%) | - |
| History of delirium | 119 (13.8%) | 17 (15.9%) | 136 (14.1%) | - |
| History of depression | 233 (27.1%) | 41 (38.3%) | 274 (28.3%) | - |
| History of anxiety | 247 (28.7%) | 38 (35.5%) | 285 (29.5%) | - |
| History of seizures | 27 (3.1%) | 11 (10.3%) | 38 (3.9%) | - |
| Visual impairment | 61 (7.1%) | 11 (10.3%) | 72 (7.4%) | - |
| Hearing impairment | 112 (13.0%) | 18 (16.8%) | 130 (13.4%) | - |
| ***Fall risk assessment*** | | | | |
| ED Fall Risk Score | 2 (0, 3) | 8 (5, 9) | 2 (0, 4) | 26 (2.7%) |
| History of falling prior 3 months | 313 (36.4%) | 50 (46.7%) | 363 (37.5%) | 21 (2.2%) |

| | | | | |
|---|---|---|---|---|
| Confusion or disorientation | 97 (11.3%) | 82 (76.6%) | 179 (18.5%) | 20 (2.1%) |
| Intoxication or sedation | 4 (0.5%) | 3 (2.8%) | 7 (0.7%) | 21 (2.2%) |
| Impaired gait | 409 (47.6%) | 78 (72.9%) | 487 (50.4%) | 21 (2.2%) |
| Mobility assistance device | 444 (51.6%) | 74 (69.2%) | 518 (53.6%) | 21 (2.2%) |
| Altered elimination | 133 (15.5%) | 54 (50.5%) | 187 (19.3%) | 22 (2.3%) |
| ***ED visit characteristics*** | | | | |
| First systolic blood pressure | 142 (126, 160) | 143 (119, 159) | 142 (125,160) | - |
| First diastolic blood pressure | 76 (67, 86.2) | 76 (64, 92) | 76 (66, 87) | - |
| First temperature (°F) | 98.1 (97.9, 98.4) | 98.1 (97.7, 98.6) | 98.1 (97.8, 98.4) | 33 (3.4%) |
| First heart rate | 77 (67, 89) | 78 (68, 94) | 78 (67, 90) | 7 (0.7%) |
| First respiratory rate | 18 (16, 20) | 18 (16, 22) | 18 (16, 20) | 27 (2.8%) |
| First oxygen saturation | 100% (90%, 100%) | 100% (90%, 100%) | 100% (90%, 100%) | - |
| Arrival via EMS† | 356 (41.4%) | 70 (65.4%) | 426 (44.1%) | - |
| Chief complaint of altered mental status | 24 (2.8%) | 42 (39.3%) | 66 (7.0%) | |
| ESI level 1 | 2 (0.2%) | 1 (0.9%) | 3 (0.3%) | - |
| ESI level 2 | 137 (15.9%) | 31 (29.0%) | 168 (17.4%) | - |
| ESI level 3 | 654 (76.0%) | 75 (70.1%) | 729 (75.4%) | - |
| ESI level 4 | 66 (7.7%) | 0 (0.0%) | 66 (6.8%) | - |
| ESI level 5 | 1 (0.1%) | 0 (0.0%) | 1 (0.1%) | - |
| ***Delirium Subtype**** | | | | |
| Hyperactive | --- | 27 (25.2%) | --- | |
| Hypoactive | --- | 80 (74.8%) | --- | |

†Includes both ground and air ambulances.

*We used the Richmond Agitation Sedation Scale (RASS) recorded along with the delirium screening to define delirium subtype. Patients with an initial RASS score between +1 and +4 were considered to have hyperactive delirium. Patients with a RASS score between 0 and −3 were considered to have hypoactive delirium.

*Table 2* provides the list of selected variables along with the LASSO-penalized regression estimates. The strongest predictors were a triage chief complaint of altered mental status and the presence of confusion or disorientation identified during the nurse fall risk assessment. The REDEEM risk score included 10 different variables (7 based on triage information and 3 obtained during early history taking) with a score ranging from -3 to 66. (*Table 2*) A logistic regression model using this risk score found that a 10-unit increase in risk score was associated with more than 3 times the odds of ED delirium (odds ratio [OR] = 3.11, 95% CI: 2.63 to 3.69, $p < .0001$), while a 1-unit increase in risk score increased the odds of delirium by 12% (OR = 1.12, 95% CI: 1.10 to 1.14, $p < .0001$). *Figure 1* illustrates the AUC for the REDEEM risk score, which was estimated at 0.901 (95% CI 0.864 to 0.938).

**Figure 1.** Receiver operating characteristics (ROC) curve for the REDEEM model that derives the risk score.

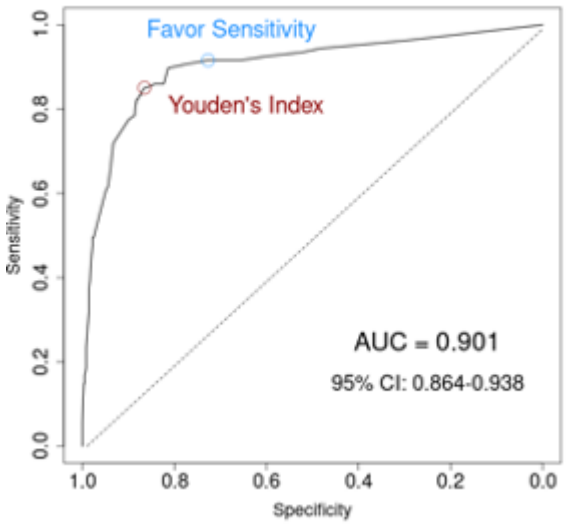


**Table 2.** REDEEM and its selected variables from LASSO-penalized logistic regression with model estimates.

| Predictor | Model Estimate† | Assigned Scores |
|---|---|---|
| **Triage information** | | |
| Arrival via EMS (ambulance) | 0.036 | +1 |
| Triage chief complaint of altered mental status | 1.804 | +18 |
| ESI level ≥ 3 | -0.266 | -3 |
| Low oxygen saturation (< 92%) | 0.205 | +2 |
| Low systolic blood pressure (< 111 mmHg) | 0.235 | +2 |
| High diastolic blood pressure (>99 mmHg) | 0.114 | +1 |
| Respiratory rate | | |
| Low respiratory rate (<16 breaths per minute) | 0.299 | +3 |
| High respiratory rate (> 24 breaths per minute) | 0.583 | +6 |
| **Early history taking** | | |
| Confusion or disorientation identified during fall risk assessment* | 2.464 | +25 |
| Altered elimination identified during fall risk assessment* | 0.826 | +8 |
| History of seizure disorders | 0.436 | +4 |
| **REDEEM Risk Score:** ranges from -3 (lowest) to +66 (highest) | | |

ESI, Emergency Severity Index.

†These estimates give an idea of relative variable importance within the data. Positive values indicate a positive relationship with ED delirium and negative values indicate a negative relationship. The absolute magnitude of the model estimate indicates the strength of the association and importance of the predictor.

*These two variables were part of the ED fall risk assessment and can be interpreted as being part of early history taking by ED nurses right after patients were roomed in the ED. Altered elimination is flagged by nurses in the presence of urinary or fecal signs or symptoms.

Youden's index found the optimal cutoff to be 11; patients with a risk score of 11 or greater were classified as high-risk whereas patients with a risk score less than 11 were classified as low risk. Using this cut-off, we found an overall accuracy of 86.3% (835 of 967 patients, 95% CI 84.0 to 88.4%) with a sensitivity of 84.1% (90 of 107 ED delirium patients, 95% CI 75.5% to 90.2%) and a specificity of 86.6% (745 of 860 non-ED delirium patients, 95% CI 84.1% to 88.8%). *Table 3* is a two-by-two contingency table and *Table 4* summarizes prediction characteristics. A Hosmer-Lemeshow test for the goodness of fit of a logistic model using this risk score to predict ED delirium found that the model was a good fit for the data ($p = 0.959$).

**Table 3.** Two-by-two contingency tables of the REDEEM risk score for the two selected optimal cutoffs.

| | **ED delirium assessment** | |
|---|---|---|
| **Model Predictions** | **With ED Delirium** | **Without ED Delirium** |
| **Youden's Index (cutoff ≥ 11)** | | |
| High Risk (≥ 11) | 90 | 115 |
| Low Risk (< 11) | 17 | 745 |
| **Favoring Sensitivity (cutoff ≥ 5)** | | |
| High Risk (≥ 5) | 98 | 235 |
| Low Risk (< 5) | 9 | 625 |

Because of the important consequences of missing delirium, an alternative cut-off that favors detecting a higher proportion of delirium cases at the cost of more false positives would be 5. If patients with a risk score of 5 or greater were considered high-risk and patients with a score below 5 were considered low risk, the overall accuracy would be lower at 74.8% (723 of 967 patients, 95% CI 71.9% to 77.5%). However, sensitivity would be increased to 91.6% (98 of 107 ED delirium patients, 95% CI 84.2% to 95.8%) with a corresponding

specificity of 72.7% (625 of 860 non-delirium patients, 95% CI 69.5% to 75.6%). (*Tables 3* and *4*) Accuracy characteristics of other alternative cutoffs are available in *Appendix 4*.

**Table 4.** REDEEM risk score performance for the two selected optimal cutoffs.

| Cut-offs | REDEEM ≥ 11 | REDEEM ≥ 5 |
|---|---|---|
| **Accuracy (95% CI)** | 86.3% (84.0%, 88.4%) | 74.8% (71.9%, 77.5%) |
| **Sensitivity (95% CI)** | 84.1% (75.5%, 90.2%) | 91.6% (84.2%, 95.8%) |
| **Specificity (95% CI)** | 86.6% (84.1%, 88.8%) | 72.7% (69.5%, 75.6%) |
| **PPV (95% CI)** | 43.9% (37.0%, 51.0%) | 29.4% (24.7%, 34.7%) |
| **NPV (95% CI)** | 97.8% (96.4%, 98.7%) | 98.6% (97.2%, 99.3%) |
| **LR (+) (95% CI)** | 6.29 (5.21, 7.60) | 3.35 (2.96, 3.79) |
| **LR (-) (95% CI)** | 0.18 (0.12, 0.28) | 0.12 (0.06, 0.22) |

PPV, positive predictive value; NPV, negative predictive value; LR (+), likelihood ratio of a positive result; LR (-), likelihood ratio of a negative result.

*Figures 2* and *3* are a visual representation of these 2 cutoffs in a hypothetical scenario of 1,000 patients. Using a score of ≥ 5 means that among 1,000 older adults presenting to the ED, 338 patients would need to be screened to find 92 delirious patients. A total of 662 patients would be considered low risk and not screened, including 8 patients that would be delirious and therefore potentially missed. (*Figure 2*) Using a cutoff of ≥ 11 would translate to 205 screenings to find 84 delirious patients while erroneously labeling 16 delirious patients as low risk. (*Figure 3*)

**Figure 2.** Pictogram of a hypothetical scenario of 1,000 older adults in which only those at high-risk (defined as REDEEM score ≥ 5) undergo targeted delirium screening in the ED.

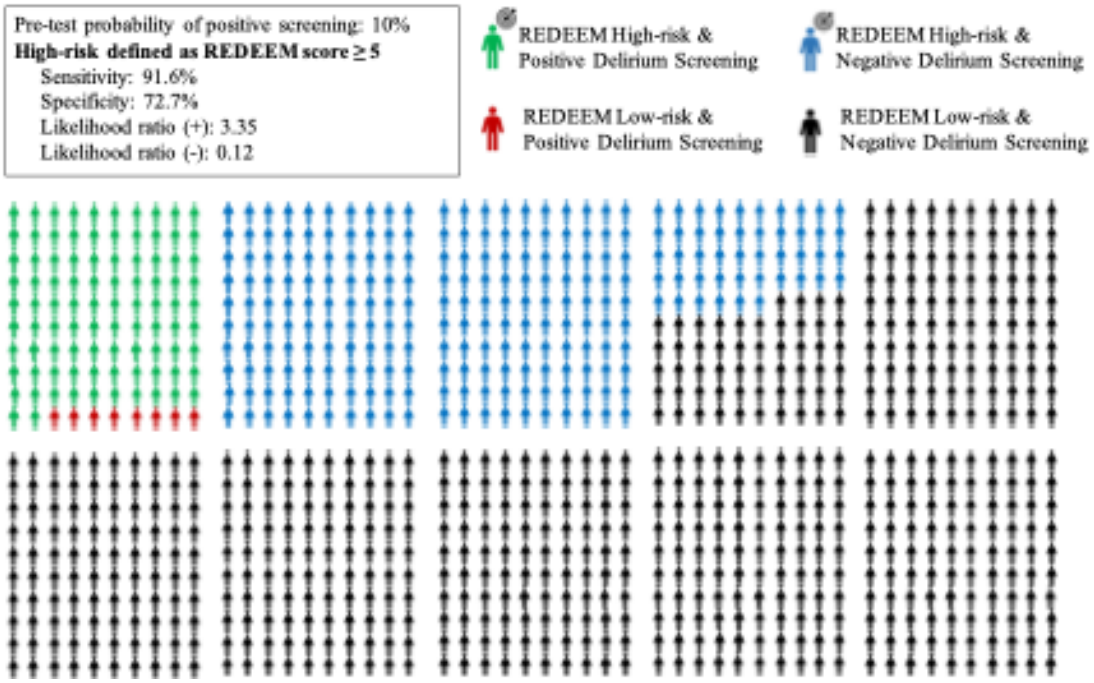
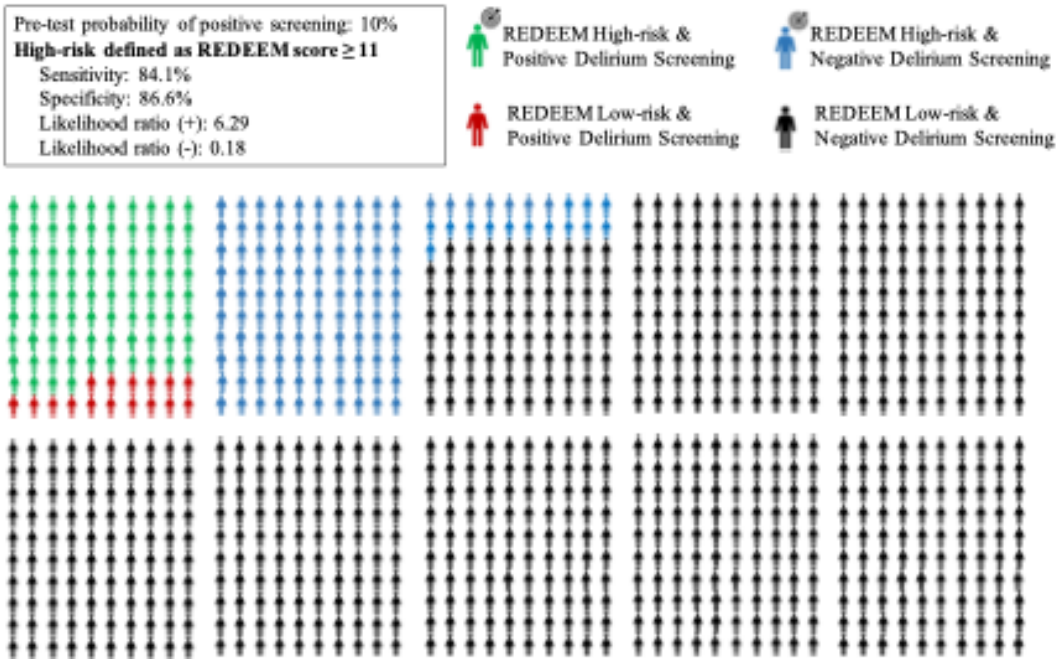



**Figure 3.** Pictogram of a hypothetical scenario of 1,000 older adults in which only those at high-risk (defined as REDEEM score ≥ 11) undergo targeted delirium screening in the ED.



The target sign along with the green and blue dummies represents the patients who would be targeted for screening.

## LIMITATIONS

First, this was a retrospective study from a single academic ED and our findings may not be replicable at other centers. For example, our cohort was composed mostly of White Non-Hispanic patients, with a lack of racial and ethnic diversity. Second, the prediction model and score require external validation and evaluation of its impact on patient-oriented outcomes prior to adoption into clinical practice. Third, only a small proportion (8.6%) of all adults aged 75 years or older who presented to the ED were screened for delirium during the study period, and the selection is almost certainly not random despite nurses not being aware of the study, and for this reason selection bias cannot be ruled out. Nevertheless, our rate of delirium was similar to prior ED literature (around 10%).[30] Moreover, most delirium episodes in our study were hypoactive, which is also consistent with prior ED studies. Fourth, although the 2-step approach has been reported to have good diagnostic performance,[17] its performance in daily practice when used by nurses may be different. However, ED nurses spend considerable time at the bedside and are in optimal position to recognize features of delirium.[31] Fifth, the chart review method developed by Inouye and colleagues was originally developed to be used in the inpatient setting and its diagnostic accuracy might be different when applied to identifying delirium retrospectively in a particular point in time (i.e., the ED). Sixth, due to the use of data routinely collected for clinical purposes, variables such as history of dementia, for example, may have been underestimated if not included as a diagnosis in the medical history. Lastly, this study did not aim to evaluate independent risk factors for ED delirium but rather to derive the most optimized risk stratification system using variables available early in the ED course. For this reason, the fact that other important risk

factors such as history of dementia or history of stroke, for example, are not included in the final model does not mean they are not important but rather means that the selected variables using LASSO-penalized logistic regression provided similar or better information for the prediction of ED delirium in our dataset.

## DISCUSSION

We found that approximately one in ten adults 75 years of age or older presenting to the ED will screen positive for delirium. We derived the REDEEM risk score, a risk stratification tool that includes 10 easily obtained variables with relatively good accuracy to predict risk of ED delirium. The score ranges from -3 to 66, and two different cutoff scores can be used to define high-risk patients. All the variables included in this score are structured in the EHR and available early in the ED course. This will facilitate external validation and its potential implementation for prioritization of delirium screening in geriatric ED patients. REDEEM is not intended to "rule in" or "rule out" delirium, but rather it is a risk stratification tool to assist on a targeted screening strategy in the ED. Even patients deemed as very high risk by REDEEM will require a formal delirium assessment to confirm such diagnosis. REDEEM should *not* be used as a delirium-specific diagnostic or screening tool, and it does *not* replace the validated 2-step diagnostic approach for delirium (DTS followed by bCAM). Rather, it may be a useful system to risk stratify patients and avoid unnecessary delirium screenings by rapidly identifying high-risk patients. Screening all patients may not be feasible in the ED, but a risk stratification tool like REDEEM could allow us to focus our efforts on those who need the most. Also, the variables are simple enough that the score can be built into the medical record as an automated alert system.

Several prior studies have evaluated risk factors for ED delirium.[11,12] However, none have attempted to create a risk stratification system that could allow for targeted screening

through the identification of a high-risk group early in the ED course. Han and colleagues created a 3-point risk score that included the following: history of dementia, Katz activities of daily living (ADL) index, and presence of hearing impairment.[4] Kennedy and colleagues created a 17-point risk score that included age, history of dementia, history of stroke or TIA, respiratory rate, suspected infection, and ED diagnosis of intracranial hemorrhage.[14] Lastly, Sri-on and colleagues created a prediction model that included history of dementia, hearing impairment, and ED diagnosis of metabolic derangement.[15] Despite having relatively adequate predictive ability (AUCs between 0.77 and 0.82), these prediction models have selected variables that are often not available in the early ED course, making them difficult to stratify patients for targeted screening. An ADL assessment, for example, is rarely available in the ED, and the diagnoses of conditions such as intracranial hemorrhage or metabolic derangement will frequently be available after comprehensive work-up. ED diagnoses are mostly helpful for inpatient providers who are focused on predicting those who may develop delirium during hospitalization. The REDEEM score overcomes many of the limitations in previously derived models by using variables routinely available in the EHR at the beginning of the ED visit. This allows care providers to identify patients who are high risk for delirium while in the ED, to deploy early active targeted screening, and to initiate immediate prevention strategies.

The variables included in REDEEM are aligned with known delirium risk factors. For example, mode of arrival (via ambulance vs other), ESI triage level, and initial vital signs are all correlated with severity of illness, a classic delirium risk factor.[12,32,33] Also, a chief complaint of altered mental status in geriatric patients has previously been identified as a very strong risk factor for delirium during the ED stay.[12,21] History of seizures was also included in our score, and has been associated with a higher risk of ED delirium.[12] Similar to cognitive impairment and history of stroke, prior seizures likely represent brain insult, which increases

the probability of delirium. Lastly, two elements of REDEEM came from information obtained through the fall risk assessment that was routinely performed by nurses including confusion/disorientation and altered elimination.[22,34] Documented history of dementia, a well-known strong risk factor for delirium,[12] was not retained in the final model. Its absence in REDEEM is partly explained by the fact that our cohort was exclusive of patients 75 years or older. Derivation of this score in a younger cohort might have retained dementia as a significant predictor. Nevertheless, the variable of "confusion and/or disorientation" captures most if not all patients with significant dementia as one would expect that these patients would inevitably have some sort of confusion and/or disorientation at baseline. For this reason, this variable is not only capturing patients with documented dementia but also other cognitive impairments that have not been previously identified in the medical records. A geriatric patient with confusion or disorientation (independent of how this information is obtained) is at high-risk of being delirious and should therefore be actively screened for delirium

To decipher an optimal cutoff to define the high-risk group (i.e., identify those who would receive targeted screening), we presented 2 options: a cutoff of $\geq 5$ or $\geq 11$. A cutoff of $\geq 5$ has greater sensitivity and minimizes false negatives (patients who would not be screened but in fact are delirious), while a cutoff of $\geq 11$ has greater specificity and minimizes false positives (patients who would be screened but in fact are non-delirious). Delirium is very important to diagnose and missing it can have important prognostic implications,[10] so one may think that a lower cutoff is better because of its increased sensitivity. However, in a hypothetical scenario of 1,000 geriatric patients presenting to the ED, the balance between "false negatives" and "false positives" is not as straightforward. In aggregate, for every 1,000 patients, when using the lower cutoff ($\geq 5$), one would need to perform 133 more screenings to detect 8 more delirious patients. Independent of the approach chosen, targeted screening in

general would decrease unnecessary screenings (654 and 778 patients assigned as low risk who would not have delirium in the scenarios of *Figures 2* and *3*, respectively). It is important to recognize that these figures assumed that delirium screening has excellent diagnostic accuracy, which is not true given limitations of existing diagnostic tools.[7,35]

External validation is necessary to determine a prediction model's reproducibility in different settings.[36,37] Despite the strengths of REDEEM including prior systematic review to inform data collection,[12] use of variables routinely available in the EHR during early ED course, and variable selection for the model using penalization methods, this was a derivation study, and external validation is required prior to its implementation into practice. This is important because there are several examples in the medical literature of models with good predictive ability in their derivation that were not confirmed to be adequate in subsequent validation studies. Further studies should also evaluate if a targeted screening strategy using REDEEM (or other risk stratification system) is feasible in the ED flow and if it improves patient-oriented outcomes, such as incidence of falls, functionality at discharge, and in-hospital mortality, when compared to screening without risk stratification (usual care). In the meantime, clinicians can use the findings of our study to augment their judgment for the recognition of high-risk patients who probably require delirium screening in the ED, and in whom early preventive interventions may be beneficial.

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Artigo 3

(OLIVEIRA J E SILVA et al., 2022a)

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**ABSTRACT**

Study objective: To evaluate the association between potential emergency department (ED)-based modifiable risk factors and subsequent development of delirium among hospitalized older adults free of delirium at the time of ED stay.

Methods: Observational cohort study of patients aged ≥ 75 years who screened negative for delirium in the ED, were subsequently admitted to the hospital, and had delirium screening performed within 48 hours of admission. Potential ED-based risk factors for delirium included ED length of stay (LOS), administration of opioids, benzodiazepines, antipsychotics, or anticholinergics, and the placement of urinary catheter while in the ED. Odds ratios (OR) and mean differences (MD) with 95% confidence intervals (CIs) were calculated.

Results: Among 472 patients without delirium in the ED (mean age 84 years, 54.2% females), 33 (7.0%) patients developed delirium within 48 hours of hospitalization. The ED LOS of those who developed delirium was similar to those who did not develop delirium (312.1 vs 325.6 min, MD -13.5 minutes, CI -56.1 to 29.0). Patients who received opioids in the ED were as likely to develop delirium as those who did not receive opioids (7.2% vs 6.9%: OR 1.04, CI 0.44 to 2.48). Patients who received benzodiazepines had a higher risk of incident delirium, the difference was clinically but not statistically significant (37.3% vs 6.5%, OR 5.35, CI 0.87 to 23.81). Intermittent urinary catheterization (OR 2.05, CI 1.00 to 4.22) and Foley placement (OR 3.69, CI 1.55 to 8.80) were associated with a higher risk of subsequent delirium. After adjusting for presence of dementia, only Foley placement in the ED remained significantly associated with development of in-hospital delirium (adjusted OR 3.16, CI 1.22 to 7.53).

Conclusion: ED LOS and ED opioid use were not associated with higher risk of incident delirium in this cohort. Urinary catheterization in the ED was associated with an increased

risk of subsequent delirium. These findings can be used to design ED-based initiatives and increase delirium prevention efforts.

## INTRODUCTION

Delirium is a serious condition of acute brain dysfunction that frequently occurs in hospitalized older adults and is associated with considerable morbidity and mortality.[1,2] Its presence is associated with a decline in cognition[3] and function[4], and it is linked with increased mortality.[5] As there are no effective medications which significantly alter the duration or severity of delirium,[6] management of delirium largely involves treatment of the underlying medical precipitants. Research and clinical practice have been focused on primary prevention strategies, and robust evidence suggests that nonpharmacologic, multicomponent interventions targeted at high-risk patients are cost-effective to preventing delirium.[7–10]

Several modifiable risk factors for delirium have been identified in hospitalized older adults.[11] However, studies evaluating emergency department (ED)-based modifiable factors and its association with subsequent delirium risk are scarce.[12] Longer ED stay has been linked with an increased risk of incident delirium,[13–16] but it is unclear whether this association holds in institutions with relatively short ED length of stay (LOS). Other conflicting evidence comes from ED studies evaluating urinary catheterization as well as short-term administration of drugs such as opioids and benzodiazepines in the ED.[13,14,17,18] The identification of modifiable risk factors for delirium can inform actionable interventions to mitigate the risks and tailor ED-based prevention strategies.

In this study, we aimed to evaluate the association between potential ED-based modifiable factors and subsequent development of delirium in hospitalized older adults who initially screened negative for delirium in the ED.

## METHODS

This was a preplanned analysis of an observational study of older adult patients who were screened for delirium in the ED at a single academic center. This report adhered to the STrengthening of the Reporting of OBservational studies in Epidemiology (STROBE) guidelines.[19] This study was approved by our Institutional Review Board and only patients who provided research authorization for medical records review were included.

### Study design, setting, and participants

We used a retrospective cohort study design. Older adults aged ≥ 75 years who presented to an academic ED, screened negative for delirium during their ED stay, and were subsequently admitted to an inpatient hospital unit were included. Both medical and surgical populations were considered eligible. Patients had to be screened for delirium within 48 hours of admission to meet inclusion criteria. There was no restriction to the type or level of inpatient unit (floor, monitored unit, or critical care unit), but patients needed to have delirium assessed with the same tools that were used for screening in the ED. Patients that did not meet these criteria were excluded. All patients screened for delirium presenting to the ED during a 14-month period (December 2$^{nd}$, 2019, through February 1$^{st}$, 2021) were considered eligible; we excluded those deemed not assessable for delirium (e.g., stuporous [RASS -4], or comatose patients [RASS -5]). Per our ED practice guidelines during the study period, delirium screening was recommended for all patients aged 75 years or older presenting to the ED, but the decision to screen each individual patient was left to the discretion of bedside nurses.

### Delirium ascertainment

To meet eligibility criteria for inclusion, patients had to have both a) at least one delirium screening during the ED stay and b) at least one delirium screening in the first 48 hours of admission as an inpatient. Screening for delirium had to be performed by bedside nurses with the sequential 2-step approach using the Delirium Triage Screen (DTS) followed by the brief Confusion Assessment Method (bCAM).[20] Delirium screening is standardized across the ED and the general medical floors with the same measurement tools[20] allowing longitudinal comparisons in our institution.

For those patients who had an unclear screening (e.g., positive DTS with incomplete bCAM, or both DTS and bCAM initiated but incomplete), individual medical record review was performed through a previously validated method.[21] For the assessment of delirium during the first 48 hours of hospitalization, 34 (7.2% of our sample) patients required individual chart review. To check reliability of these assessments, 8 out of these 34 patients were reviewed independently by two investigators (L.O.J.S. and F.B.), with 100% agreement on the presence or absence of delirium.

For the patients in our cohort who received more than one screening during the ED evaluation, if one of the screenings was positive, we classified them as having delirium in the ED. All patients who screened positive for ED delirium were excluded from this analysis.

The final cohort included all patients who screened negative for delirium in the ED, were admitted to the hospital and had at least one delirium screening using the DTS/bCAM approach in the inpatient setting. Patients who had at least one positive delirium screening within 48 hours of ED departure were classified in the delirium group. The 48-hour boundary was used with the assumption that delirium that occurs after 2 days of admission is unlikely related to interventions performed in the ED.

Potential ED-based modifiable factors

We collected data on variables related to the ED care that could be potential modifiable risk factors for subsequent delirium during hospital admission. To decide which variables to extract, we used findings from a prior systematic review.[12,22] These factors included ED LOS, administration of opioids, benzodiazepines, antipsychotics, or anticholinergics in the ED, and the performance of an in-out (intermittent) urinary catheterization or placement of a Foley (indwelling) urinary catheter while in the ED. For benzodiazepines, and anticholinergics we identified all medications included by the American Geriatrics Society 2019 Beers list.[23] A full list of medications is provided in *Appendix 1*.

Other baseline characteristics

Data were collected regarding the following variables: age, sex, ethnicity, race, residence status (private residence, assisted living, or skilled nursing facility), prior comorbidities including dementia, stroke/TIA, history of delirium, depression, anxiety, seizures, visual and hearing impairment, and ED visit characteristics including arrival via ambulance and ESI triage level. Comorbidities were measured with International Classification of Disease (ICD) codes[24,25] available in the electronic health record up to two days prior to the index ED visit.

Data analysis

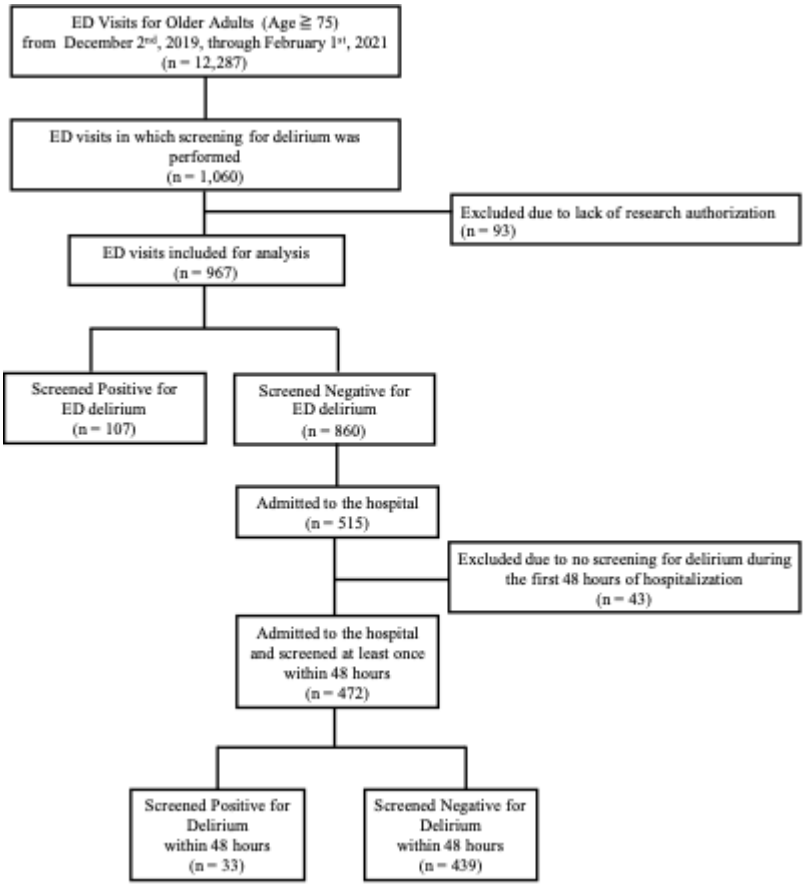
All statistical analyses were conducted using BlueSky Statistics (Version 7.0.746.34007) GUI for R. For descriptive statistics, continuous features were summarized as means and standard deviations (SD) while categorical features were summarized as counts and percentages. To evaluate the association between ED LOS and subsequent positive delirium screening within 48 hours, we calculated difference in means with 95% confidence intervals (CIs). To evaluate the association between administration of medications in the ED

(opioids, benzodiazepines, antipsychotics, and anticholinergics), use of intermittent urinary catheterization, or Foley (indwelling) urinary catheterization and subsequent development of delirium within 48 hours, we calculated odds ratios (OR) with 95% CIs. When appropriate, statistical adjustment was performed by fitting a logistic regression where we included history of dementia as a covariate. The small sample size precluded us from doing further statistical adjustments. All tests were 2-sided, and statistical significance was set at alpha less than 0.05.

**RESULTS**

A total of 967 patients were screened for delirium in the ED, and 107 (11.1%) screened positive for ED delirium. Among 860 who screened negative for ED delirium, 472 were admitted to the hospital with at least one delirium screening recorded within 48 hours of admission and comprised our final cohort of interest. The mean number of screenings per patient was 3.2 (SD 1.9) within the first 48 hours after being admitted to the inpatient setting. Within this cohort, 33 patients (7.0%, 95% CI 4.9% to 9.7%) developed delirium within 48 hours of hospital admission. (*Figure 1* cohort flowchart). Our cohort had a mean age of 84 years, 54.2% were female, and most were White (96.6%). (*Table 1*)

**Figure 1.** Flowchart of study cohort.




Patients who screened positive for delirium during the hospitalization were different from those who screened negative in several aspects including age, comorbidities, and mode of arrival to the ED. Most remarkably, patients in the delirium group were more likely to have a prior documented history of dementia (60.6% vs. 24.6%, p <.0001). (*Table 1*)

**Table 1.** Baseline characteristics of the cohort stratified by delirium screening within 48 hours of ED departure.

| | **Screened Negative for Delirium Within 48 Hours (N=439)** | **Screened Positive for Delirium Within 48 Hours** | **P-value* for the difference between groups** | **Total** |
|---|---|---|---|---|

| | | (N=33) | | (N=472) |
|---|---|---|---|---|
| ***Age and sex*** | | | | |
| Age (years) | 83.84 (5.95) | 86.58 (5.12) | 0.0105 | 84.03 (5.93) |
| Female | 239 (54.4%) | 17 (51.5%) | 0.7448 | 256 (54.2%) |
| ***Ethnicity*** | | | | |
| Hispanic, or Latino | 2 (0.5%) | 1 (3.0%) | 0.1958 | 3 (0.6%) |
| Not Hispanic or Latino | 429 (97.7%) | 32 (97.0%) | 0.7823 | 461 (97.7%) |
| Unknown Ethnicity | 8 (1.8%) | 0 (0.0%) | ‡ | 8 (1.7%) |
| ***Race*** | | | | |
| White | 425 (96.8%) | 31 (93.9%) | 0.3794 | 456 (96.6%) |
| African American | 3 (0.7%) | 0 (0.0%) | ‡ | 3 (0.6%) |
| Asian | 5 (1.1%) | 1 (3.0%) | 0.3542 | 6 (1.3%) |
| Other Race | 5 (1.1%) | 1 (3.0%) | 0.3542 | 6 (1.3%) |
| Unknown Race | 1 (0.2%) | 0 (0.0%) | ‡ | 1 (0.2%) |
| ***Residence status*** | | | | |
| Private residence | 333 (76.4%) | 21 (65.6%) | 0.1715 | 354 (75.6%) |
| Assisted living | 60 (13.8%) | 6 (18.8%) | 0.4339 | 66 (14.1%) |
| Skilled nursing facility | 43 (9.9%) | 5 (15.6%) | 0.2997 | 48 (10.3%) |
| Unknown | 3 (0.7%) | 1 (3.0%) | 0.2524 | 4 (0.8%) |
| ***Prior history and comorbidities*** | | | | |
| Dementia | 108 (24.6%) | 20 (60.6%) | <.0001 | 128 (27.1%) |
| History of stroke or TIA | 103 (23.5%) | 7 (21.2%) | 0.7681 | 110 (23.3%) |
| History of delirium | 51 (11.6%) | 10 (30.3%) | 0.002 | 61 (12.9%) |
| History of depression | 127 (28.9%) | 4 (12.1%) | 0.0428 | 131 (27.8%) |
| History of anxiety | 124 (28.2%) | 6 (18.2%) | 0.212 | 130 (27.5%) |
| History of seizures | 13 (3.0%) | 2 (6.1%) | 0.2825 | 15 (3.2%) |
| Visual impairment | 38 (8.7%) | 3 (9.1%) | ‡ | 41 (8.7%) |
| Hearing impairment | 66 (15.0%) | 8 (24.2%) | 0.1606 | 74 (15.7%) |
| ***ED triage characteristics*** | | | | |

| | | | | |
|---|---|---|---|---|
| Arrival via EMS† | 219 (49.9%) | 23 (69.7%) | 0.0281 | 242 (51.3%) |
| ESI level 1 | 1 (0.2%) | 0 (0.0%) | ‡ | 1 (0.2%) |
| ESI level 2 | 78 (17.8%) | 9 (27.3%) | 0.1744 | 87 (18.4%) |
| ESI level 3 | 346 (78.8%) | 22 (66.7%) | 0.1044 | 368 (78.0%) |
| ESI level 4 | 14 (3.2%) | 2 (6.1%) | 0.3095 | 16 (3.4%) |
| ESI level 5 | 0 (0.0%) | 0 (0.0%) | † | 0 (0.0%) |

†Includes both ground and air ambulances.

*Obtained either through a t-test, chi-square test, or Fisher exact test according to type of data and number of patients in each cell of the 2x2 table.

‡Fisher's test yielded p value equal to 1.

†Not estimable.

The ED LOS for those who screened positive was not significantly different than those who screened negative (difference in means: -13.52 minutes, 95% CI -56.05 to 29.01). Both groups had a mean ED LOS between 5 and 6 hours. (*Table 2*)

**Table 2.** Association between ED-based modifiable risk factors and subsequent positive delirium screening within 48 hours of ED departure.

| | **n (%) or mean (SD)** | | |
|---|---|---|---|
| | **Screened Negative for Delirium Within 48 Hours (N=439)** | **Screened Positive for Delirium Within 48 Hours (N=33)** | **Effect Estimates (95% CI)** |
| **ED LOS (SD) minutes** | 325.6 (143.8) | 312.1 (114.3) | Difference in means: -13.52 (-56.05 to 29.01) |
| **ED opioids** | | | |
| Yes (n = 97) | 90 (92.8%) | 7 (7.2%) | Unadjusted OR: 1.04 (0.44 to 2.48) |

| | | | |
|---|---|---|---|
| No (n = 375) | 349 (93.1%) | 26 (6.9%) | |
| **ED benzodiazepines** | | | |
| Yes (n = 11) | 8 (72.7%) | 3 (37.3%) | Unadjusted OR: 5.35 (0.87 to 23.81)<br>Adjusted* OR: 3.85 (0.77 to 15.19) |
| No (n = 461) | 431 (93.5%) | 30 (6.5%) | |
| **ED antipsychotics** | | | |
| Yes (n = 2) | 2 (100%) | 0 (0.0%) | Not estimable |
| No (n = 470) | 437 (93.0%) | 33 (7.0%) | |
| **ED anticholinergics** | | | |
| Yes (n = 5) | 4 (80.0%) | 1 (20.0%) | Unadjusted OR: 3.38 (0.07 to 35.54) |
| No (n = 467) | 435 (93.2%) | 32 (6.8%) | |
| **In-out catheterization** | | | |
| Yes (n = 130) | 116 (89.2%) | 14 (10.8%) | Unadjusted OR: 2.05 (1.00 to 4.22)<br>Adjusted* OR: 1.64 (0.77 to 3.44) |
| No (n = 342) | 323 (94.4%) | 19 (5.6%) | |
| **Foley catheterization** | | | |
| Yes (n = 43) | 35 (81.4%) | 8 (18.6%) | Unadjusted OR: 3.69 (1.55 to 8.80)<br>Adjusted* OR: 3.16 (1.22 to 7.53) |
| No (n = 429) | 404 (94.2%) | 25 (5.8%) | |

OR, odds ratio.

*Derived from a logistic regression with delirium screening as the dependent variable, and urinary catheterization and history of dementia as independent variables.

Patients who received opioids in the ED were as likely to develop delirium in the hospital as those who did not receive opioids (7.2% vs 6.9%: unadjusted OR 1.04, 95% CI 0.44 to 2.48). Patients who received benzodiazepines in the ED had a higher incidence of delirium than those who did not receive benzodiazepines, but the difference was not statistically significant with a wide confidence interval (37.3% vs. 6.5%: unadjusted OR 5.35,

95% CI 0.87 to 23.81). The point effect estimate was attenuated after adjusting for presence of documented dementia (adjusted OR 3.85, 95% CI 0.77 to 15.19). Due to a small number of patients receiving antipsychotics and anticholinergics, there was large uncertainty regarding these associations. (*Table 2*)

As for urinary catheterization, intermittent catheterization was significantly associated with an increased risk of subsequent positive delirium screening (OR 2.05, 95% CI 1.00 to 4.22). This association was not statistically significant after adjustment for presence of documented dementia, but it showed a relatively wide confidence interval (adjusted OR 1.64, 95% CI 0.77 to 3.44). Foley catheterization was significantly associated with a higher risk of delirium even after adjustment for the presence of documented dementia (adjusted OR 3.16, 95% CI 1.22 to 7.53). (*Table 2*)

## DISCUSSION

In this cohort study, the rate of delirium during the first 48 hours of admission was 7% among older adult patients who initially screened negative for delirium in the ED. ED LOS and the use of opioids in the ED were not associated with a subsequent higher risk of delirium. Use of other medications assumed to increase the risk of delirium—anticholinergics, antipsychotics, and benzodiazepines—was not common enough in this cohort to determine with confidence whether their use was associated with a higher risk of delirium. Urinary catheterization in the ED was associated with a higher risk of subsequent delirium. This association remained after adjustment for the presence of dementia.

Opioid exposure and the risk of delirium in older adults has had mixed evidence in prior studies. Both uncontrolled pain and pain medications are known precipitating risk factors for delirium, which makes pain management in the ED challenging.[26–29] Very few

studies, however, evaluated the impact of opioid use during the ED stay on the subsequent risk of delirium among patients being hospitalized. In our study, we found that judicious use of opioids in carefully selected patients does not appear to be associated with an increased risk of developing delirium within the first 48 hours of hospitalization. Like our findings, Daoust and colleagues found in a Canadian cohort of older adult patients that opioid use in the ED was not associated with a higher risk of subsequent delirium.[17] In their cohort, 31.9% received opioids while in our cohort 20.6% received opioids while in the ED. It seems that adequately treating the pain of older adults in the ED is more important than avoiding opioid use. Nevertheless, it is important that providers minimize opioid use when other alternatives can adequately control the pain (for example, the use of femoral nerve or fascia iliaca blocks for older adults with hip fractures,[30,31] or the use of a single dose of ketorolac[32]).

The type of opioid appears to play a role on the subsequent risk of delirium.[33] One study[26] comparing the incidence of delirium among cancer patients receiving parenteral opioids found that fentanyl was associated with the lowest delirium risk when compared to morphine and oxycodone. In our cohort, fentanyl was the most used opioid (approximately 75% of those who received opioids), likely because of his shorter half-life when compared to other opioids. This could partly explain why we did not find an association between ED opioid use and subsequent delirium risk. Also, meperidine is an opioid that has shown in prospective studies to increase the risk of delirium,[34–36] and none of our patients received this medication in the ED.

The association between benzodiazepines and delirium risk has previously been reported.[29] Most clinical studies in the ICU setting, for example, support such association.[37] Benzodiazepines alter the inhibitory tone by increasing GABA activity in the brain. This has been hypothesized to be a trigger for a breakdown network connectivity,

ultimately provoking delirium.[38] Our small sample size precluded us from having more precise results, but it is possible that the exposure to benzodiazepines in the ED is associated with a higher risk of subsequent delirium during early hospitalization. Future larger ED-based studies, however, will be needed to confirm or refute this finding.

Invasive procedures are known to increase the risk of delirium in older adults. We found that Foley urinary catheterization in the ED was associated with a higher risk of delirium within 48 hours of hospital admission. Although we were not able to adjust for other potential confounders such as severity of illness or presence of underlying infection, this association has been consistently shown in other studies despite adjustments for confounders.[16,39–43] Furthermore, a recent meta-analysis including 2 ED-based studies with 666 patients found a significant association between urinary catheterization in the ED and increased subsequent delirium.[12] In contrast to most prior studies, we separated those who received an intermittent (in-out) catheterization from those who had a Foley urinary catheter placed in the ED, showing that the delirium risk is likely higher with indwelling catheterization. While placing a Foley catheter in the ED can be appropriate in several clinical scenarios, it is important that ED care team members recognize its associated delirium risk in older adults. These findings call attention to the need of better evaluation of the risks and benefits of urinary catheterization in older ED patients. This is a potential feasible target for ED-based initiatives that aim to reduce incident delirium. One study by Fakih and colleagues, for example, had marked reduction in utilization of unnecessary urinary catheters after the implementation of institutional guidelines for appropriate use coupled with emergency physician education.[44]

Lastly, the ED has been traditionally viewed as an overcrowded and under-resourced setting where the geriatric-specific needs of older adults are unlikely to be met. In this context, the association between longer ED LOS and increased delirium risk has been

previously demonstrated in well-designed studies. Inouye and colleagues, for example, found that an ED LOS greater than 12 hours was associated with an increased risk of developing delirium during hospitalization.[16] Similarly, Bo and colleagues found that an ED LOS greater than 10 hours was associated with an increased risk of subsequent delirium.[13] Specific reasons behind such association are not well established but include immobility, noisy environment, lack of stimulation, and lack of food or hydration. Most recently, a study reported boarding in the ED hallway could increase the risk of delirium.[15] Despite relatively consistent evidence to support the association between long ED stays and subsequent delirium risk during hospitalization, studies that looked at lower cutoffs (> 4 hours[45] and > 5 hours[13]) have not shown a significant association. By evaluating ED LOS as a continuous variable and comparing the means between patients with and without delirium during the first 48 hours of admission, our study did not find a significant association. We suspect that this is in the context of a relatively short average ED LOS in our institution. For example, in our cohort, the mean ED stay in both groups were between 5 and 6 hours, and only 16 out of 472 (3.4%) patients had an ED LOS greater than 10 hours. It is likely that a short ED LOS does not substantially impact the risk of having delirium after hospital admission. Also, not finding a difference in means between the two groups in our study does not rule out that longer hours in the ED increase the risk of delirium as shown by Inouye[16] and Bo[13]. A proposed solution to decrease the risk associated with long ED stays includes the creation of geriatric EDs with focused care for seniors awaiting admission, as well as efforts to avoid hospital admissions.[46] Our ED, for example, has been incorporating more geriatric-friendly care by implementing non-pharmacological comfort-enhancing interventions[47,48] among other changes, and we hope this has been effective on decreasing delirium rates.

## LIMITATIONS

First, this was a single center US-based study, and its external generalizability might be limited. Its predominance of Non-Hispanic White patients also decreases its generalizability to other populations. Second, although the sequential delirium screening has had good diagnostic performance,[20] its performance in daily practice with nurses could be different. However, nurses typically provide frequent patient reassessments and are in an optimal position to recognize subtle delirium features. The use of structured screening instruments by nurses is likely associated with better recognition of delirium as compared to usual care without screening where providers often miss delirium.[49] Third, not all patients who presented to the ED during the study period were screened for delirium, yielding a potential selection bias. Delirium screening had been recently implemented in our ED and the relatively low rate of screening in the ED might represent that screening is a new care process. Nevertheless, among patients eligible for this analysis who were admitted to the hospital after being delirium-free in the ED only 43 out of 512 (8.4%) were excluded due to absent screening during hospitalization. Lastly, our small sample size precluded us from doing further statistical adjustment of potential confounders in the associations evaluated. For example, there was large uncertainty regarding the use of antipsychotics and anticholinergics as potential risk factors for delirium as very few patients received these medications in the ED. Also, the placement of an urinary catheter in the ED could be a marker of frailty, illness severity, and decrease in kidney function, variables that we did not control for in this analysis. Moreover, we did not control for other modifiable factors that could have occurred after admission from the ED. For these reasons, there is almost certainly some residual confounding.

## CONCLUSION

Urinary catheterization in the ED was associated with an increased risk of developing delirium within the first 48 hours of hospitalization in older adult patients admitted through the ED that were delirium-free during the ED stay. ED length of stay and opioid use were not associated with increased risk of delirium in this cohort. There was large uncertainty regarding the use of other drugs such as benzodiazepines, antipsychotics, and anticholinergics in the ED due to our small sample size. These findings can be used to design ED-based initiatives and increase delirium prevention efforts.

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Artigo 4

(ARNESON et al., 2023)

Arneson ML, **Oliveira J E Silva L**, Stanich JA, Jeffery MM, Lindroth HL, Ginsburg AD, Bower SM, Mullan AF, Bellolio F. Association of delirium with increased short-term mortality among older emergency department patients: A cohort study. Am J Emerg Med. 2023 Apr;66:105-110. doi: 10.1016/j.ajem.2023.01.040. Epub 2023 Jan 26. PMID: 36738568; PMCID: PMC10038894.

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**ABSTRACT**

Study objective: To evaluate the association between delirium and subsequent short-term mortality in geriatric patients presenting to the emergency department (ED).

Methods: This was an observational cohort study of adults age ≥ 75 years who presented to an academic ED and were screened for delirium during their ED visit. The Delirium Triage Screen followed by the Brief Confusion Assessment Method were used to ascertain the presence of delirium. In-hospital, 7-day, and 30-day mortality were compared between patients with and without ED delirium. Odds ratios with 95% confidence intervals (CIs) were calculated through logistic regression after adjusting for confounders including age, sex, history of dementia, ED disposition, and acuity.

Results: A total of 967 ED visits were included for analysis among which delirium was detected in 107 (11.1%). The mean age of the cohort was 83 years (IQR 79, 88), 526 (54.4%) were female, 285 (29.5%) had documented dementia, and 171 (17.7%) had a high acuity Emergency Severity Index triage level 1 or 2. During the hospitalization, 5/107 (4.7%) of those with delirium and 4/860 (0.5%) of those without delirium died. Within 7 days of ED departure, 6/107 (5.6%) of those with delirium and 6/860 (0.7%) of those without delirium died (unadjusted OR 8.46, 95% CI 2.68-26.71). Within 30 days, 18/107 (16.8%) of those with delirium and 37/860 (4.3%) of those without delirium died (unadjusted OR 4.50, 95% CI 2.46-8.23). ED delirium remained associated with higher 7-day (adjusted OR 5.23, 95% CI 1.44-19.05, p= .008) and 30-day mortality (adjusted OR 2.82, 95% CI 1.45-5.46, p= .002).

Conclusion: Delirium is an important prognostic factor that ED clinicians and nurses must be aware of to optimize delirium prevention, management, disposition, and communication with patients and families.

## INTRODUCTION

Delirium is an acute physiological disruption in the brain networks that support cognition resulting in fluctuating changes in the level of consciousness, attention, and cognition.[1] Delirium is poorly detected in the emergency department (ED)[2,3] but is important to recognize as it has been associated with decreased long-term functioning[4] and increased mortality,[5] especially following prolonged episodes.[6] Moreover, delirium is a common presentation in the ED, with studies showing prevalence in geriatric ED patients of around 10%.[7,8]

Multiple validated screening tools are available that can be administered in less than 5 minutes.[9–11] Nonetheless, delirium continues to be undetected in as many as 83% of ED cases,[2,3] mostly due to the predominance of hypoactive presentations,[8,12] time constraints limiting testing, and missed opportunities to recognize a fluctuating course.

While previous ED-based studies have reported an increased risk of death at 30 days[5,13,14] and at longer follow-up periods,[5,14] less is known about shorter term mortality (less than 30 days). This has created a gap in knowledge surrounding short-term mortality for patients diagnosed with delirium in the ED. The ED is the frontline for emergent medical care and often the first opportunity to diagnose delirium. A better understanding of the short-term mortality of this condition may increase the urgency for consistent delirium screening, improve ability to communicate prognosis with patients and families, and allow timely medical interventions to potentially reduce morbidity and mortality rates. There is also evidence that delirium that goes undiagnosed in the ED is likely to be unrecognized by the admitting provider as well.[12]

In this cohort study, we aimed to evaluate the association between delirium and subsequent short-term mortality (in-hospital, within 7 days, and within 30 days) in geriatric patients presenting to the ED.

## METHODS

This manuscript adheres to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) reporting guidelines for an observational cohort study.[15] It was approved by our center's institutional review board. All patients included in this study had consented to research authorization for medical records review.

### *Study design, setting, and participants*

This was a pre-planned analysis of an observational cohort study of older adults aged ≥ 75 years who presented to a quaternary academic ED in Minnesota with approximately 80,000 annual ED patient visits including 30,000 ED visits for older adults. Other analyses derived from this cohort have been published elsewhere.[8,16] Patients presented to the ED between December 2nd, 2019 and February 1st, 2021. All study participants were screened by a bedside nurse for delirium during their ED visit through a validated sequential two-step approach: the Delirium Triage Screen (DTS) and the brief Confusion Assessment Method (bCAM).[17,18]

### Delirium measurement

During the study period, delirium screening through DTS/bCAM[17,18] was recommended for all patients aged ≥ 75 years as part of standard of care, with the exception of comatose or stuporous patients (both populations deemed not assessable for delirium).

Nevertheless, it was at the discretion of nurses to decide which individuals to screen. Nurses received training on how to apply these tools including educational videos.

The DTS screening tool, which has a 98% sensitivity,[17] was used first. If the DTS was negative, patients were ruled out from having delirium, and no further screening was performed. If the DTS was positive, patients would then be screened with the bCAM tool (84% sensitivity, 96% specificity)[17] for further assessment of delirium. If the bCAM was negative, patients were ruled out from having delirium. Patients were deemed positive for delirium if they had a positive DTS and bCAM. If they had no DTS on record but a positive bCAM, they were also considered positive for delirium. Patients with multiple delirium screenings performed throughout the duration of their ED visit were deemed positive for delirium if at least one instance of screening was positive. Finally, if delirium screening was equivocal, 2 investigators reviewed the electronic health record in order to assess for the presence of delirium using a previously validated chart review-based method.[19]

**Primary outcome (short-term mortality)**

All ED visits were reviewed for in-hospital, 7-day, and 30-day mortality through electronic health record review.

**Potential confounders**

Data regarding potential confounders in the association between delirium and subsequent short-term mortality were also extracted including age, sex, ED disposition, history of dementia, and triage ESI level 1 or 2 (surrogate variable for severity of illness). Inconsistencies in the data were manually reviewed by 2 investigators and resolved by a senior investigator.

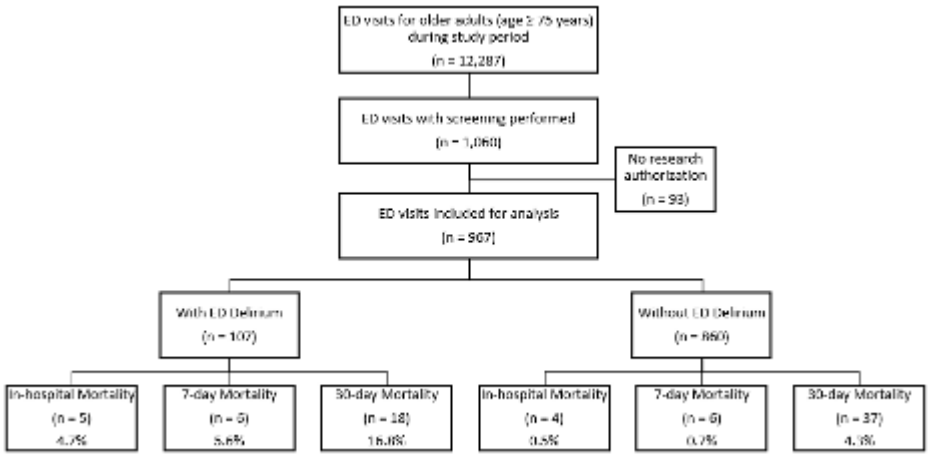
**Data analysis**

Statistical analysis was conducted by a biostatistician. Continuous features were summarized with quartiles. Categorical features were summarized with frequencies and percentages. The association between delirium and short-term mortality was evaluated using logistic regression. Odds ratios (OR) with 95% confidence intervals (CIs) were calculated to estimate the strength and direction of each association. Models were both unadjusted and adjusted for patient age, sex, ED disposition, history of dementia, and triage ESI at level 1 or 2. Due to the low number of mortality events captured, multivariable models implemented a LASSO penalty to reduce the risk of overfitting. The optimal penalization parameter was determined using 10-fold cross validation. Multiple ED visits from individual patients were not excluded from analysis. To account for the potential correlation between repeat ED visits, a sensitivity analysis was performed using mixed effects logistic regression with a random intercept at the patient level. Finally, a Kaplan-Meier curve was plotted to visually depict the survival differences between those with and without delirium. All statistical tests were 2-sided, and statistical significance was set at alpha less than 0.05.

## RESULTS

From 12,287 eligible ED visits, 1,060 (8.6%) underwent delirium screening during the study period. Ninety-three had no research authorization on file and were excluded from the analysis. Ultimately, 967 ED visits were included, with delirium present in 107 (11.1%). The flow chart is viewable in **Figure 1**.

**Figure 1.** Flowchart of study participants.




There were 897 unique patients comprising the 967 ED visits identified for this study. A mixed effects logistic regression model assessing the risk of 30-day mortality found no significant effect for within-patient correlation, so standard logistic regression was used for analysis. **Table 1** summarizes patient demographics for the cohort stratified by presence of ED delirium.

**Table 1.** Patient and ED visit characteristics stratified by presence of ED delirium.

| | **No ED Delirium** (N = 860) | **ED Delirium** (N = 107) | **Overall** (N = 967) |
|---|---|---|---|
| **Age,** median (Q1, Q3) | 83 (79.0, 88.0) | 85 (79.5, 89.5) | 83.0 (79.0, 88.0) |
| **Sex – Male**, n (%) | 394 (45.8%) | 47 (43.9%) | 441 (45.6%) |
| **Race,** n (%) | | | |
| African American | 8 (0.9%) | 1 (0.9%) | 9 (0.9%) |
| Asian | 8 (0.9%) | 0 (0.0%) | 8 (0.8%) |
| White | 831 (96.6%) | 104 (97.2%) | 935 (96.7%) |
| Other | 11 (1.3%) | 2 (1.9%) | 13 (1.3%) |
| Unknown | 2 (0.2%) | 0 (0.0%) | 2 (0.2%) |
| **Ethnicity**, n (%) | | | |
| Not Hispanic or Latino | 841 (97.8%) | 104 (97.2%) | 945 (97.7%) |
| Hispanic or Latino | 6 (0.7%) | 2 (1.9%) | 8 (0.8%) |
| Unknown | 13 (1.5%) | 1 (0.9%) | 14 (1.4%) |
| **Triage ESI**, n (%) | | | |
| Level 1 | 2 (0.2%) | 1 (0.9%) | 3 (0.3%) |
| Level 2 | 137 (15.9%) | 31 (29.0%) | 168 (17.4%) |
| Level 3 | 654 (76.0%) | 75 (70.1%) | 729 (75.4%) |
| Level 4 | 66 (7.7%) | 0 (0.0%) | 66 (6.8%) |

| | | | |
|---|---|---|---|
| Level 5 | 1 (0.1%) | 0 (0.0%) | 1 (0.1%) |
| **ED Benzodiazepines**, n (%) | 16 (1.9%) | 4 (3.7%) | 20 (2.1%) |
| **ED Disposition**, n (%) | | | |
| Hospital Admit | 387 (45.0%) | 72 (67.3%) | 459 (47.5%) |
| Hospital Observation | 87 (10.1%) | 14 (13.1%) | 101 (10.4%) |
| Send to OR | 5 (0.6%) | 0 (0.0%) | 5 (0.5%) |
| ICU Admit | 36 (4.2%) | 9 (8.4%) | 44 (4.6%) |
| Discharge | 340 (39.5%) | 11 (10.3%) | 351 (36.3%) |
| Transfer to Health Care Facility | 2 (0.2%) | 0 (0.0%) | 2 (0.2%) |
| Left AMA | 0 (0.0%) | 1 (0.9%) | 1 (0.1%) |
| Eloped | 1 (0.1%) | 0 (0.0%) | 1 (0.1%) |
| Expired in the ED | 1 (0.1%) | 0 (0.0%) | 1 (0.1%) |
| Unknown Disposition | 1 (0.1%) | 0 (0.0%) | 1 (0.1%) |
| **Medical History**, n (%) | | | |
| History of Dementia | 226 (26.3%) | 59 (55.1%) | 285 (29.5%) |
| History of Stroke | 206 (24.0%) | 37 (34.6%) | 243 (25.1%) |
| History of Delirium | 119 (13.8%) | 17 (15.9%) | 136 (14.1%) |
| History of Depression | 233 (27.1%) | 41 (38.3%) | 274 (28.3%) |
| History of Anxiety | 247 (28.7%) | 38 (35.5%) | 285 (29.5%) |
| History of Seizures | 27 (3.1%) | 11 (10.3%) | 38 (3.9%) |
| History of Visual Impairment | 22 (2.6%) | 7 (6.5%) | 29 (3.0%) |
| History of Auditory Impairment | 345 (40.1%) | 37 (34.6%) | 382 (39.5%) |
| **Patient Outcomes**, n (%) | | | |
| In-hospital Mortality | 4 (0.5%) | 5 (4.7%) | 9 (1.0%) |
| 7-day Mortality | 6 (0.7%) | 6 (5.6%) | 12 (1.2%) |
| 30-day Mortality | 37 (4.3%) | 18 (16.8%) | 55 (5.7%) |

ED = emergency department; ESI = emergency severity index; OR = operating room; ICU = intensive care unit; AMA = against medical advice

## In-hospital and 7-day mortality

During the hospitalization 5/107 (4.7%) of those with delirium and 4/860 (0.5%) of those without delirium died. Within 7 days of ED departure, 6/107 (5.6%) of those with delirium and 6/860 (0.7%) of those without delirium died (unadjusted OR 8.46, 95% CI 2.68 to 26.71, $p < .001$). **Table 2** describes the associations between delirium and 7-day mortality. After accounting for key confounders, ED delirium remained significantly associated with a more than 5-fold increase in the odds of 7-day mortality (adjusted OR 5.23, 95% CI 1.44 to 19.05, p=0.008).

**Table 2.** Association between ED delirium and 7-day mortality in univariable and multivariable logistic regression.

| | Univariable | | Multivariable[1] | |
|---|---|---|---|---|
| | **OR (95% CI)** | **P-value** | **OR (95% CI)** | **P-Value** |
| **ED Delirium** | 8.46 (2.68 – 26.71) | **< .001** | 5.23 (1.44 – 19.05) | **.008** |
| **History of Dementia** | 3.41 (1.07 – 10.83) | **.038** | 1.71 (0.48 – 6.09) | .25 |
| **Age** (per 5 years) | 1.25 (0.79 – 1.96) | .34 | 1.17 (0.69 – 2.01) | .56 |
| **Sex** | | | | |
| Female | *Reference* | --- | *Reference* | --- |
| Male | 1.68 (0.53 – 5.33) | .38 | 1.12 (0.33 – 3.85) | .77 |
| **ED Disposition** | | | | |
| Discharge | *Reference* | --- | *Reference* | --- |
| Hospital Admit[2] | 1.04 (0.5 – 4.36) | .96 | 0.61 (0.13 – 2.81) | .53 |
| ICU Admit | 8.29 (1.62 – 42.37) | **.011** | 5.22 (1.12 – 24.29) | **.044** |
| **Triage ESI** | | | | |
| ESI Level 3, 4, or 5 | *Reference* | --- | *Reference* | --- |
| ESI Level 1 or 2 | 3.39 (1.06 – 10.83) | **.039** | 2.13 (0.58 – 7.83) | .25 |

**30-day mortality**

Within 30 days, 18/107 (16.8%) of those with delirium and 37/860 (4.3%) of those without delirium died (unadjusted OR 4.50, 95% CI 2.46 to 8.23). (**Figure 2**) **Table 3** describes associations between ED delirium and 30-day mortality. After accounting for patient age, sex, triage ESI, ED disposition, and history of dementia, ED delirium was significantly associated with approximately a 3-fold increase in the odds of 30-day mortality (OR 2.82, 95% CI 1.45 to 5.46, p = 0.002**)**.

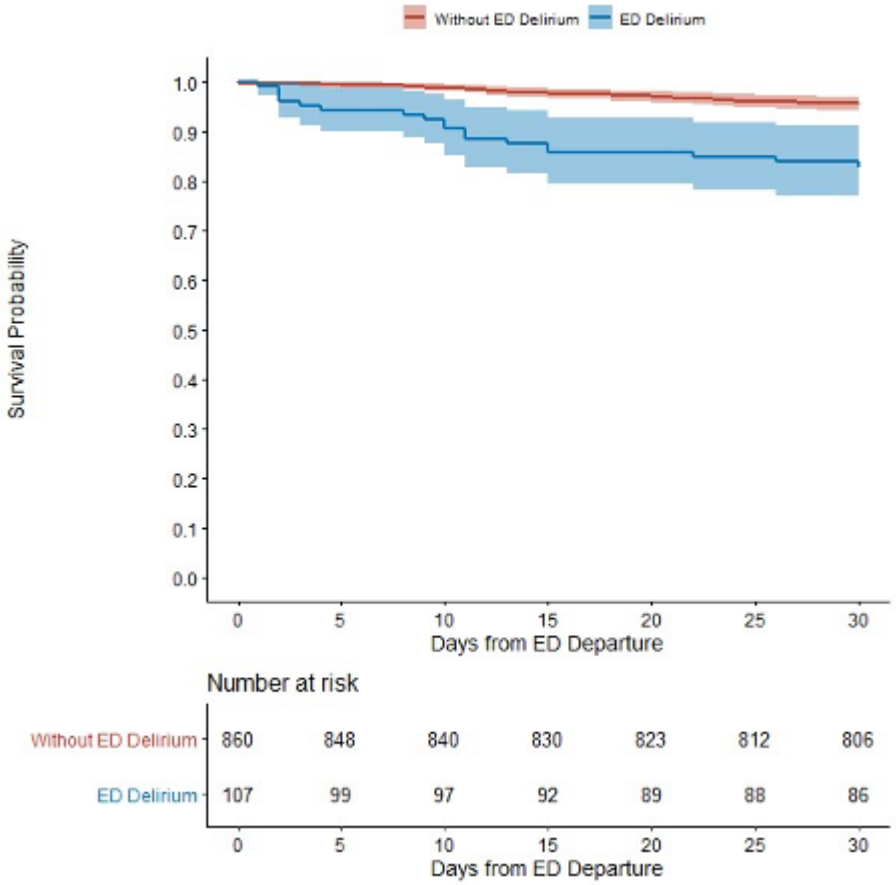
**Table 3.** Association between ED delirium and 30-day mortality in univariable and multivariable logistic regression.

| | Univariable | | Multivariable[1] | |
|---|---|---|---|---|
| | **OR (95% CI)** | **P-value** | **OR (95% CI)** | **P-Value** |
| **ED Delirium** | 4.50 (2.46 – 8.23) | **< .001** | 2.82 (1.45 – 5.46) | **.002** |
| **History of Dementia** | 1.77 (0.91 – 3.46) | .092 | 2.70 (1.48 – 4.91) | **.001** |
| **Age** (per 5 years) | 1.41 (1.14 – 1.75) | **.002** | 1.33 (1.04 – 1.70) | **.021** |
| **Sex** | | | | |
| Female | *Reference* | --- | *Reference* | --- |
| Male | 2.18 (1.24 – 3.84) | **.007** | 2.53 (1.37 – 4.70) | **.003** |
| **ED Disposition** | | | | |
| Discharge | *Reference* | --- | *Reference* | --- |
| Hospital Admit[2] | 2.74 (1.31 – 5.74) | **.008** | 1.94 (0.90 – 4.18) | .093 |
| ICU Admit | 7.00 (2.47 – 19.87) | **< .001** | 3.98 (1.31 – 12.10) | **.015** |
| **Triage ESI** | | | | |
| ESI Level 3, 4, or 5 | *Reference* | --- | *Reference* | --- |
| ESI Level 1 or 2 | 2.41 (1.34 – 4.35) | **.003** | 1.61 (0.84 – 3.06) | .15 |

[1]Multivariable model included all variables listed in this table.

[2]Hospital admission includes non-ICU admissions and admissions for hospital observation.

**Figure 2**. Kaplan-Meier curve comparing survival rates between those with and without ED delirium.




**Mortality rates and ED disposition**

Despite low event numbers, patients discharged from the ED with delirium had higher 7-day mortality than those discharged without delirium (7-day mortality: 1/11, 9.1% vs 2/340, 0.6%, p = 0.0255). Also, patients discharged from the ED with delirium had worse prognosis than those admitted to the hospital without delirium. (**Table 4**)

**Table 4.** Mortality rates with subgroups based on admission status.

| | 30-day Mortality | 7-day Mortality | In-Hospital Mortality |
|---|---|---|---|
| All Without ED Delirium **(n = 860*)** | 37 (4.3%) | 6 (0.7%) | 4 (0.5%) |
| **Admitted** Without ED Delirium (n = 516)** | 29 (5.6%) | 4 (0.8%) | 4 (0.8%) |
| **Discharged Without ED Delirium (n = 340)** | 8 (2.4%) | 2 (0.6%) | - |
| All With ED Delirium **(n = 107†)** | 18 (16.8%) | 6 (5.6%) | 5 (4.7%) |
| **Admitted With ED Delirium (n = 95)** | 17 (17.9%) | 5 (5.3%) | 5 (5.3%) |
| **Discharged With ED Delirium (n = 11)** | 1 (9.1%) | 1 (9.1%) | - |

*4 visits were left out from the two categories of admission vs discharged (2 were transferred to another health care facility, 1 left against medical advice, and 1 had unknown disposition).
**Admitted includes admissions from ED to the hospital floor, hospital observation unit, intensive care unit, and operating room.
†1 patient left against medical advice.

## DISCUSSION

We found that 11% of adults 75 years of age and older presenting to the ED screened positive for delirium, which is consistent with the published literature on delirium rates. For this cohort of 967 geriatric ED patients, there was increased in-hospital, 7-day, and 30-day mortality for patients with delirium in the ED compared to those without delirium. These data suggest that ED delirium is an important prognostic factor and may be considered as a form of acute brain failure.

We found a 30-day mortality rate of 16.8% compared to a mortality rate of 4.3% in those without ED delirium. Mortality was also higher for delirious patients who were discharged home from the ED (9.1% mortality for those who went home with delirium compared to those discharged home without delirium at 0.6%). In this study, the 30-day delirium mortality rate was higher than other ED-based research that assessed 30-day outcomes. Prior studies included patients aged 65 and older, while our study included those 75 and older, who have a greater comorbidity burden and baseline mortality rate. Kennedy et

al.[13] reported 6% 30-day mortality among those with ED delirium (vs 1% without delirium); Han et al. [5] reported 10.2% 30-day mortality (vs 2.2% without ED delirium); and Israni et al.[14] had a mortality of 11.9% (vs 2.9% without delirium). The difference in mortality might be explained by several factors but most likely age (our cutoff was higher), comorbidity burden (our population had more comorbidities) and perhaps severity of acute illness. Nevertheless, all available evidence from ED-based studies points towards delirium in the ED being an important prognostic factor. Moreover, prior meta-analyses looking at the association between delirium in any type of hospital setting and subsequent mortality confirm this finding.[20,21]

Our study found a 7-day mortality rate of 5.6% among patients with ED delirium (compared to a mortality rate of 0.7% in those without diagnosed ED delirium). To our knowledge, no other studies have specifically analyzed mortality rates of ED-diagnosed delirium at 7 days. A study by Stanich et al.[24] looked at the mortality rates of patients with altered mental status at 7 days (3.2% mortality rate) and 30 days, finding them to be higher than other common chief complaints (generalized weakness, abdominal pain, chest pain, and headache) presenting to the ED. Delirium is a type of altered mental status, so these patients represent a group to focus on for targeted screening.[7,8]

**Clinical significance & future directions**

While other studies have focused on long-term mortality greater than one month,[20,21] we aimed to highlight the short-term mortality risks of delirium. Our findings indicate an increased risk of short-term mortality for patients who screen positive for delirium in the ED. This enforces the importance of delirium being viewed as an important prognostic factor (and perhaps called as an ***acute brain failure***), and management in the ED should be adjusted accordingly.

It has been shown that patients presenting with altered mental status (with delirium being a subtype of altered mental status) had a significantly higher mortality rate at 7 and 30 days compared to patients with a chief complaint of chest pain.[24] While patients with chest pain typically (and correctly) receive extensive workups to further assess their mortality risk, those with altered mental status may receive less targeted care, despite their higher risk. While chest pain is typically a patient-reported chief complaint, patients with altered mental status often have vague and non-specific complaints. It is therefore necessary to screen for causes of altered mental status. Knowing that short-term mortality is increased for delirium should prompt initiation of more consistent screening to reduce missed diagnoses and improve opportunities to intervene with treatment. As treatment is often based on treating the underlying delirium precipitant (e.g., infection), it is imperative for ED providers to work diligently to find the underlying cause(s). Shorter durations of delirium have been shown to improve outcomes,[6] so timely diagnosis and treatment are crucial. Improved treatment and prevention options should be further explored[26] to potentially improve patient outcomes and reduce mortality. Reducing the amount of unnecessary urinary catheterization in the ED, for example, is one possibility.[16]

Additionally, knowing the short-term mortality risk of patients with delirium can allow for development of a more comprehensive follow-up plan once the patient is discharged from the ED or hospital. This should prompt further discussions with patients and families about return precautions and the importance of attending follow-up appointments with their primary care provider or specialists. Careful review of medications with special attention to those that are deliriogenic[27] must be completed. Also, almost as important as treating the underlying cause of the delirium, providers must identify other symptoms that could continue to trigger a delirium like urinary urgency in the setting of infection or pain. Once delirium is

diagnosed providers have an obligation given the heightened risks associated to do all that is possible to treat it. This presents a potential opportunity to reduce short-term mortality rates.

Finally, understanding the increased risk of short-term mortality allows for ED providers to better communicate potential severity of illness with patients and their families. Delirium indicates the patient is critically ill and should prompt providers to engage in a goals of care discussion. Understanding the patient's values and goals of care can allow providers to tailor care recommendations to meet the patient's wishes. Detecting delirium in the ED also provides an opportunity to educate the patient's family and/or care partners on nonpharmacologic measures to reduce delirium[28] such as reorientation, cognitive stimulation, and sleep hygiene. These strategies can also be communicated during hand-off to the admitting team to provide a continuity of delirium care.

**LIMITATIONS**

First, our study focused on patients aged 75 and older while most other studies have included patients aged ≥ 65 years. This leads to differences when comparing rates across populations. Second, our findings may not be replicable at non-academic centers such as rural or community hospitals that have a different patient population compared to our academic ED. Third, our population lacked racial and ethnic diversity, as it was composed of mostly non-Hispanic White patients that represent the population of the communities that live in MN. Fourth, patients were selected for delirium screening at the discretion of the bedside nurses (8.6% of all visits by people aged 75 and older had EHR evidence of screening) with risk of introducing selection bias to the study. Nevertheless, everyone who was screened during the study period was included in this analysis. Fifth, the method of chart review that was used for equivocal delirium cases was originally designed to be used in an inpatient setting, so it is possible there could have been differences in applicability to our ED setting.[19]

Sixth, as with all research that relies on medical records, it is possible that patients' medical records do not list up-to-date medical history diagnoses, and if that was the case for any of our participants, there could have been underestimations of certain comorbidities (like history of dementia) that could affect the ability to control for these variables. Eight, we had a low sample size for our 7-day analysis, so we used penalized regression in the multivariable analysis to avoid overfitting our data. Despite this, there is low statistical power with wide confidence intervals for the 7-day analysis, and its results should be interpreted with caution. Lastly, and most importantly, there is unmeasured confounding in our estimate of association between delirium and short-term mortality. For example, we did not account for all comorbidity burden but rather focused on a few comorbidities such as dementia. ESI was used as a marker for severity of illness, but is more of a marker of resource utilization.

## CONCLUSIONS

Older adult patients who screen positive for delirium in the ED have increased risk of short-term mortality (in-hospital, at 7-days, and at 30-days) compared to those without delirium. Delirium is a very important prognostic factor, and ED management (screening, treatment, patient and family communications) should be adjusted accordingly.

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## 8. CONSIDERAÇÕES FINAIS

O delirium é uma disfunção aguda que afeta as redes cerebrais que suportam a cognição, resultando em mudanças flutuantes no nível de consciência, atenção e cognição. Infelizmente, essa condição não é bem detectada em DEs, o que pode causar prejuízos na funcionalidade a longo prazo e aumento da mortalidade. Para combater esse problema, a identificação de fatores de risco em idosos na emergência pode ajudar a criar estratégias de reconhecimento precoce e prevenção do delirium.

No primeiro trabalho desta tese, realizamos uma revisão sistemática com meta-análise de 27 estudos que avaliaram fatores de risco para o delirium prevalente na emergência em mais de 13 mil pacientes. Após análise qualitativa e quantitativa desses estudos, identificamos algumas variáveis fortemente associadas a um aumento de risco de delirium, como: morar em instituições de longa permanência, comprometimento cognitivo prévio, comprometimento auditivo e histórico de AVC. Além disso, também analisamos 7 estudos que avaliaram fatores de risco modificáveis para o delirium que ocorre durante a hospitalização, incluindo o tempo de permanência no DE e a presença de dor intensa. Com base nesses achados, desenvolvemos a coorte do REDEEM (Recognizing Delirium in Emergency Medicine) para o desenvolvimento dos subsequentes trabalhos desta tese, incluindo a criação de um escore de predição e estudo de fatores de risco modificáveis para o delirium.

Em nosso segundo trabalho, incluímos quase 1000 pacientes idosos com idade igual ou superior a 75 anos e detectamos o delirium em cerca de 10% deles. Desenvolvemos o escore REDEEM, que inclui 10 variáveis - 7 baseadas em informações obtidas na triagem da emergência e 3 obtidas na história inicial - com um escore que varia entre -3 e +66. Demonstramos que é possível fazer uma triagem direcionada usando diferentes pontos de corte, o que pode diminuir a quantidade de rastreios para delirium, priorizando indivíduos de maior risco. É importante ressaltar que antes de implementar o protocolo institucionalmente,

é necessário validar o escore REDEEM.

Após a criação do escore, nosso terceiro trabalho focou na identificação de fatores de risco modificáveis, estudando a mesma coorte, mas focando em pacientes que não estavam em delirium na chegada à emergência, mas o desenvolveram nas primeiras 48 horas de internação. Foi demonstrado que a cateterização urinária no DE foi associada a um aumento do risco de desenvolver delirium nas primeiras 48 horas de internação em pacientes idosos admitidos pelo DE que estavam livres de delirium na chegada. O tempo de permanência no DE e o uso de opioides não foram associados a um aumento no risco de delirium nessa coorte. Os resultados da pesquisa geraram incertezas quanto ao uso de outras drogas, como benzodiazepínicos, antipsicóticos e anti-colinérgicos, devido ao tamanho reduzido da amostra estudada. É importante notar que a ausência de associação entre o tempo de permanência no DE e um maior risco de delirium em nossa coorte pode ser explicada pelo curto tempo que os pacientes idosos permaneceram na emergência (menos de 6 horas em média). No entanto, é preciso considerar que a coorte americana estudada pode diferir da realidade brasileira.

Por fim, é importante ressaltar a relevância do reconhecimento precoce do delirium em pacientes idosos na emergência, uma vez que a detecção e tratamento adequados podem reduzir as consequências negativas a longo prazo, como o aumento da mortalidade e a diminuição da funcionalidade. Como demonstrado em nossa coorte REDEEM, pacientes com resultado positivo para delirium na emergência apresentaram um risco aumentado de mortalidade a curto prazo em comparação com aqueles sem delirium. Portanto, é fundamental que os profissionais de saúde estejam cientes dos fatores de risco para delirium em idosos na emergência, a fim de criar estratégias de prevenção e detecção precoce dessa condição. Os achados de nossos estudos podem ser usados para desenvolver iniciativas de melhoria na emergência e aumentar os esforços para prevenir e tratar o delirium em idosos, melhorando assim a qualidade de vida e a sobrevida desses pacientes.

## 9. PERSPECTIVAS FUTURAS

O trabalho desta tese trouxe diversas conquistas e perspectivas futuras importantes para a prevenção do delirium na emergência. Primeiramente, foi possível resumir a evidência disponível sobre os fatores de risco para o delirium na emergência e publicar uma revisão sistemática na revista com o maior fator de impacto mundial em Medicina de Emergência. Além disso, três estudos originais (além da meta-análise) foram publicados em revistas também de alto fator de impacto, com o objetivo de aumentar a base de conhecimento sobre fatores de risco para o delirium e sua relação com a emergência.

Todos esses estudos foram usados para fins educacionais e para promover a conscientização dos médicos emergencistas da Mayo Clinic em relação ao risco de delirium. Participamos ativamente de uma iniciativa de melhoria na identificação de delirium no Departamento de Emergência do Sainty Marys Hospital da Mayo Clinic, a fim de reduzir a janela de tradução do conhecimento. Através do uso de nossos dados de pesquisa para comunicar com comitês de prática, a triagem de delirium agora é obrigatória para pacientes geriátricos na emergência da Mayo Clinic Rochester. Em um futuro próximo, planejamos validar o escore de estratificação de risco REDEEM para ajudar na identificação precoce de pacientes com alto risco de delirium. Nesse sentido, nossos esforços de pesquisa foram traduzidos em tempo real para a prática, permitindo uma abordagem alinhada com o objetivo de um sistema de saúde centrado no paciente, onde as necessidades dos pacientes vêm em primeiro lugar.

Com relação às perspectivas futuras, acreditamos que a criação de um sistema automatizado no prontuário eletrônico, que identifique já na chegada os pacientes idosos de alto risco para delirium, será fundamental. Além disso, um sistema que durante a internação do paciente na emergência identifique aqueles que se beneficiem mais de estratégias de prevenção, com vistas a evitar que os pacientes desenvolvam o delirium durante a internação,

também será muito útil.

Outra perspectiva importante seria mostrar aos gestores os dados de fatores modificáveis para convencê-los da necessidade de diminuir o tempo de permanência dos idosos na emergência ou transformar a sala de emergência em um ambiente menos "deliriogênico" e mais amigável para os idosos. Essas estratégias serão fundamentais para a prevenção do delirium na emergência e para a melhoria da qualidade do atendimento prestado aos pacientes idosos.