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Outcomes associated with older patients who present or develop delirium in the emergency department: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Delirium is commonly observed in older patients who are admitted to the emergency department (ED). Previous systematic reviews have identified poor outcomes associated with delirium in surgical, intensive care and other hospital settings, yet none have specifically considered the ED. This systematic review aims to examine associations between older patients who present or develop delirium in the ED and adverse outcomes within the hospital and after discharge.

Methods and analysis Searches will be conducted in MEDLINE, Embase, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Library. There will be no date or language restrictions. Key terms will include concepts related to delirium, the ED and older adults. Observational studies or non-intervention clinical studies will be included that compare outcomes in older patients (ie, ≥65 years) with and without delirium. Outcomes of interest will include length of hospital stay, non-home discharge (eg, nursing home/residential aged care facility), cognitive impairment, decreased physical function, mortality, readmission to hospital and quality of life measures. Two reviewers will independently screen the studies. Data extraction and quality assessment will be extracted by one reviewer and checked by a second reviewer, with any disagreements resolved by discussion or by a third reviewer. Where appropriate, data will be combined in a meta-analysis and a GRADE assessment will be made for each outcome. All methods will be guided by the Cochrane Handbook and the Centre for Reviews and Dissemination and reported following the Preferred Reporting Items for Systematic Review and Meta-Analysis statement as well as the recommendations set out by the Meta-analysis Of Observational Studies in Epidemiology group.

Ethics and dissemination As this systematic review will use published data, ethical approval is not required. The results will be disseminated through a peer-reviewed publication and conference presentations.

PROSPERO registration number CRD42024594975.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A rigorous systematic review methodology will be used to address the research question.
⇒ There will be no language or date restrictions to the search strategy.
⇒ The review includes observational studies, which are subject to bias and confounding.
⇒ Heterogeneity among the studies is expected and careful consideration of discrepancies will be needed to mitigate spurious conclusions.

INTRODUCTION

Delirium is a syndrome that is characterised by an acute decline in cognitive functioning and can present as hypoactive (eg, drowsy, lethargic, etc), hyperactive (eg, agitated, anxious, etc) or a fluctuating mix of these psychomotor subtypes. It has been estimated that almost one in four older acute medical hospital patients present or develop delirium.[1] Delirium is also commonly observed in the emergency department (ED),[2] with a recent systematic review reporting a prevalence rate of 15.2% in this setting (95% CI 12.5% to 18.0% (pooled crude rate based on 30 studies)).[3] Given that delirium is often unrecognised (eg, see El Hussein *et al*,[4] Lee *et al*,[5] Meged-Book *et al*,[6] and Barron and Holmes[7]), it is likely that some reported prevalence rates could represent underestimations.

Delirium is of concern because it has been associated with poorer outcomes in hospital settings, including mortality,[8] long-term cognitive decline,[9 10] and longer hospital stays and costs.[11] Previous systematic reviews (SRs) have been conducted that assess outcomes associated with delirium in surgical patients,[12] intensive care units[13–15] and hospitalised patients,[16 17] but none have specifically addressed the older ED patient, despite several new primary studies on this topic. A SR will be conducted by the Trondheim Emergency Department Research Group to examine associations between older patients who have a positive delirium diagnosis in the

ED and short- and long-term adverse outcomes. This SR specifically focuses on ED patients as they represent a distinct and vulnerable population. They often present with more acute medical or environmental stressors (eg, sepsis, polypharmacy) than those who develop delirium postoperatively or during a hospital stay. Moreover, the ED is a critical entry point for early delirium recognition—which could potentially improve prognosis and thus hospital length of stay. The ED thus presents specific challenges and opportunities for delirium research and interventions. By evaluating effect sizes of several outcomes derived from comparisons of older patients with and without delirium, it will be possible to assess the magnitude of the current problem in the ED context. This SR will be of relevance to clinicians and researchers who aim to prevent, detect and manage delirium in acute care patients.

METHODS AND ANALYSIS

The primary research question of this SR is: What short- and long-term adverse outcomes are associated with older patients (ie, ≥ 65 years) who present or develop delirium in the ED compared with those who do not? To address this question, a SR will be undertaken according to guidance presented in the Cochrane Handbook[18] and the Centre for Reviews and Dissemination (CRD)[19] and reported following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement[20] as well as the recommendations set out by the Meta-analysis Of Observational Studies in Epidemiology group.[21] This protocol was developed following the guideline of the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P)[22] and is registered with PROSPERO (CRD42024594975).

Inclusion and exclusion criteria

To be eligible for inclusion in the review, studies will have to meet all the following criteria in terms of population, exposure/intervention and comparator, outcomes, and study designs.

Studies that compare older patients (ie, ≥ 65 years) who are delirium positive (at ED arrival or during their visit) with those who are delirium negative will be eligible for inclusion. Delirium assessments must be made in the ED using a diagnostic tool or defined criteria (eg, Confusion Assessment Method, Brief Confusion Assessment Method, 3 min Diagnostic Interview for Confusion Assessment Method, 4AT, Diagnostic and Statistical Manual of Mental Disorder Criteria criteria etc). Patients with delirium tremens, drug-induced delirium or hepatic encephalopathy will be excluded. Studies that specifically assess delirium after an ED visit will not be included. Studies examining older patients undergoing emergency surgery and older patients with COVID-19 will not be included as other SRs have been conducted in these population groups/settings.

Studies reporting one or more of the following short- (ie, within 30 days) or long-term (ie, up to 1 year) outcomes will be eligible for inclusion: length of hospital stay (or a measure of prolonged hospital stay), non-home discharge (eg, nursing home/residential aged care facility), cognitive impairment, decreased physical function, mortality (in hospital and out of hospital), readmission to hospital, and other quality of life (QoL) measures or an overall QoL assessment.

Prospective and retrospective observational studies or non-intervention clinical studies that compare outcomes between patients with and without delirium will be included. Controlled clinical trials or other types of intervention studies will be excluded, as well as case series, commentaries and letters to the editor.

Conference abstracts will only be included if there is no associated full publication and if adequate data are reported (eg, detailed information on the population, diagnostic criteria, and clear results with numerical data reported for those with and without delirium).

Search strategy

The literature search will be conducted in MEDLINE, Embase, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Library. Key terms will include concepts related to delirium, the emergency department and older adults (online supplemental file 1). The search will not be limited by language or date. German, French and Scandinavian language papers will be assessed for inclusion and translated to English by members of the review team while Google Translate or DeepL will be used for all other languages. Grey literature will be searched in OAIster (OpenGrey, NYAM Grey Literature Report, and the British Library EThOS are not currently available for searching). Handsearching will also be conducted to check references of relevant papers and reviews identified by the search. In addition, a citation search will be carried out to identify subsequent publications which have cited any of the included studies.

Study selection and data extraction

The records retrieved from the searches will be de-duplicated in EndNote[23] and exported into Rayyan[24] for screening. During the first stage of study selection, titles and abstracts will be independently screened by two researchers against the inclusion/exclusion criteria. Full papers of all potentially relevant studies identified in the first stage will be screened by two reviewers working independently, with any discrepancies resolved by discussion between the reviewers or with the assistance of a third reviewer.

The number of studies identified by the search and excluded at various stages will be recorded and reported in a PRISMA study flow diagram.[20] After the second stage of screening, a table of excluded studies with detailed reasons for exclusion will be created.

Data to be extracted from each study will include information on the study (eg, study type, setting, country, objective, inclusion criteria, study methods including the delirium assessment tool used as well as who did the assessment and any information on their experience or training) and patient characteristics (eg, age, sex, main reason for ED visit, and for patients with delirium: subtype, severity), as well as the results and any potential confounding factors identified by the study authors. A data extraction form will be developed using Microsoft Excel[25] and piloted by two independent reviewers using a minimum of four studies. This process will also be used to check consistency in data extraction between the reviewers. The remaining studies will then be extracted by one reviewer and checked by a second reviewer. Any discrepancies will be resolved through discussion. If any relevant information is missing from the studies or if any data is unclear, the reviewers will attempt to contact the authors.

Critical appraisal

The observational studies will be assessed using the Joanna Briggs Institute critical appraisal tools.[26] One reviewer will conduct the quality assessment, and a second reviewer will check the assessment with any discrepancies resolved through discussion or with the assistance of a third reviewer.

Synthesis and analysis

Outcome comparisons between older patients with and without delirium will be presented.

Where possible and appropriate (ie, if the studies are clinically and statistically homogenous), data from the studies will be combined in a meta-analysis using Review-Manager (RevMan).[27] For continuous outcomes, means and SD will be collected and used to estimate study-specific and pooled mean differences with 95% CIs. For dichotomous outcomes, numerators and denominators will be collected, and Mantel-Haenszel risk ratios (RRs) or ORs and 95% CIs used to summarise effect sizes. If the scales/tools used to assess the outcomes differ between the studies, we will compute study-level standardised mean differences between comparison groups with 95% CIs. The results will be statistically pooled (where possible) using both fixed-effect and random-effects models and the results from these different models will be compared. Statistical heterogeneity will be assessed using the χ^2 test and the I^2 statistic, and by examining the random effects between study variance (Tau^2). If possible, sensitivity analyses will be performed to assess the robustness of results by excluding studies deemed to have a greater risk of bias. Comparisons between unadjusted and adjusted effect estimates will also be made. Funnel plots will be visually inspected to check for publication bias. For each outcome summarised, the GRADE system[28] will be used to provide an assessment of the quality of a body of evidence. One reviewer will rate the evidence using GRADEpro GDT[29] and a second reviewer will check the assessment, with any discrepancies resolved through discussion.

Exploratory subgroup analyses will be performed where possible by date of publication, study type, delirium assessment method used in the study, assessor and training (if reported) and age of the study participants (if outcomes are categorised by age groups in the included studies). If there are any studies conducted in specific patient groups (eg, older patients with fractures), subgroup analysis may also be conducted by patient type.

A narrative synthesis of the studies will be performed if the studies are too diverse to perform a meta-analysis, or if only one study reported on an outcome and pooling cannot be undertaken.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

As this systematic review will use published data, ethical approval is not required. The results will be disseminated through a peer-reviewed publication and conference presentations. If any minor amendments are made to this protocol during the review process, they will be reported in the final results of the paper.

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