INPLASY PROTOCOL

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None declared.

Effectiveness of non-pharmacological interventions in the prevention of delirium in adult hospitalized. An overview of systematic review and meta-analyses

Opazo, Y[1]; Gutierrez-Arias, R[2]; Seron, P[3].

Review question / Objective: **The aim of this overview is to determine the effectiveness of non-pharmacological interventions in terms of incidence of delirium, in-hospital mortality, length of hospital stay, and other secondary outcomes, in hospitalized adults.**
Information sources: **The databases to be consulted will be MEDLINE, Embase, Cochrane Library, Epistemonikos and CINAHL. In addition, the protocol registers of the SRs (PROSPERO and INPLASY) will be searched, and the list of references of the SRs included in this overview will be reviewed.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 August 2021 and was last updated on 07 August 2021 (registration number INPLASY202180023).

INTRODUCTION

Review question / Objective: **The aim of this overview is to determine the effectiveness of non-pharmacological interventions in terms of incidence of delirium, in-hospital mortality, length of hospital stay, and other secondary outcomes, in hospitalized adults.**

Rationale: **Currently, research aimed at evaluating the effectiveness of health interventions has experienced exponential growth, which can be considered both a benefit and a problem simultaneously, as the amount of published information makes it difficult for clinicians to keep up to date with the best available evidence. In this**

context, delirium, considered as a complex neuropsychiatric syndrome, with high associated costs and requiring an approach from different disciplines, is no stranger to this problem, as the publication of systematic reviews (SRs) aimed at evaluating the effectiveness of different non-pharmacological intervention strategies has increased exponentially in recent years. However, these reviews present different scopes and methodologies, with different conclusions on the effectiveness of interventions in this condition, which could limit the creation of optimal delirium prevention protocols derived from non-pharmacological strategies in the hospital context. Considering that overviews represent one of the highest levels of scientific synthesis of the evidence available for a specific condition or problem, it is necessary to conduct this type of study to summarise and evaluate the evidence reported from SRs of different non-pharmacological interventions in the prevention of delirium in hospitalized adults.

Condition being studied: Delirium is considered as a syndrome of acute brain failure in direct consequence of an underlying medical treatment or toxic exposure. This condition reflects the pathophysiological consequences of an acute medical illness or the effects of medication and should therefore be perceived by health professionals as a warning sign. The main hypotheses associated with the aetiology of delirium focus on neuroinflammatory processes, an aberrant stress response, neurotransmitter imbalances, and neural network alterations. Several risk factors for the development of delirium have been identified, establishing that this syndrome has a multifactorial aetiology, including advanced age, sensory deficits, sleep deprivation, social isolation, use of physical restraint, periods of immobilization, presence of comorbidities, dehydration, among others. In relation to the older adult population, the evidence determines it as a marker of poor prognosis, as it hinders communication with the treatment team, and is also associated with a greater number of adverse events, the most frequent being falls, decubitus ulcers, urinary incontinence and the accidental removal of catheters. This condition should be considered an important health problem, especially because of its contribution to in-hospital mortality and longer hospital stays, as well as increased costs of inpatient care, since the presence of delirium is not only a complication in the hospital setting, but patients with delirium are also at high risk of post-discharge neuropsychological dysfunction, associated with cognitive and functional impairment, and even increased long-term mortality.

METHODS

Search strategy: The controlled (e.g., Mesh and EMTREE) and natural language will be adjusted according to the database and platform used. The search strategy considers two groups of terms, one referring to the health condition, and the second referring to the study design to be included in this overview. The following is the search strategy to be used in MEDLINE through the Pubmed platform: (((((((("Delirium"[Mesh]) OR ("Emergence Delirium"[Mesh])) OR ("Sepsis-Associated Encephalopathy"[Mesh])) OR ("Confusion"[Mesh])) OR ("Hallucinations"[Mesh])) OR ("Psychoses, Substance-Induced"[Mesh])) OR (deliri* OR "acute confusion*" OR "acute organic psychosyndrome" OR "metabolic encephalopathy" OR "acute psycho-organic syndrome" OR "clouding of consciousness" OR "exogenous psychosis" OR "toxic psychosis" OR "toxic confusion" OR obnubilat*)) OR ("acute brain" AND (dysfunction* OR failure* OR syndrome*))) AND ((((("Systematic Review" [Publication Type]) OR ("Systematic Reviews as Topic"[Mesh])) OR ("Meta-Analysis" [Publication Type])) OR ("Meta-Analysis as Topic"[Mesh])) OR ((systematic* OR comprehensive* OR integrative) AND (bibliographic* OR literature OR review* OR search*))) OR (meta-analy* OR metaanaly*)).

Participant or population: SRs will be included if they consider primary studies that have recruited adults (18 years or older) hospitalized in critical or non-critical units. Inclusion will not be limited by the medical conditions that led to the participants' need for hospitalisation, such as neurological, trauma, oncological, cardiovascular, surgical, and other conditions. SRs that consider delirium prevention interventions in non-hospital settings (e.g., institutionalized settings) will be excluded.

Intervention: All SRs involving at least one type or more of non-pharmacological interventions in the experimental arm of the primary studies will be included:1) Environmental management interventions, defined as any activity aimed to noise and light management, strategies to restore circadian rhythm and the inclusion of time orientation elements, among others.2) Interventions with active family involvement, defined as any strategy that considers the active involvement of family members in the hospital unit during the hospital stay.3) Cognitive stimulation interventions, defined as any activity aimed to cognitive stimulation, such as allo-psychic and auto-psychic reorientation, memory activities, attention, executive functions, among others. 4) Sensory stimulation interventions, defined as any activity aimed at the stimulation of the various sensory channels to maintain or increase the level of alertness, and in addition to those activities that reduce sensory deficits. 5) Mobilization or physical exercise interventions, defined as any mobilization strategy or exercise practice, such as functional mobilization of upper and lower limbs, transitions and transfers, aerobic exercise, among others. 6) Multi-component interventions: all interventions that involve an interdisciplinary team and consider 2 or more interventions described above.

Comparator: SRs that have considered in the control arm of the primary studies, no intervention, a sham intervention, or usual care will be included. In addition, SRs comparing 2 or more non-pharmacological interventions will also be included.

Study designs to be included: SRs, with or without meta-analyses, that have clearly specified their eligibility criteria, and that have assessed the risk of bias (RoB) of the included primary studies, will be included. Such primary studies must be of randomized clinical trial (RCT) design. In the case of SRs that include primary study designs other than RCT (e.g., observational studies), they will only be included if they report information in a disaggregated form, and that allow data derived from studies with RCT design to be extracted. SRs protocols and conference presentations that do not have full text available will be excluded. The inclusion of SRs will not be limited by the date of publication.

Eligibility criteria: The SRs to be included must comply with the characteristics explained in the section "Participant or population", "Intervention", "Comparator" and "Study design to be included". In addition, SRs should report at least one outcome related to delirium (incidence, duration, or severity; see "primary outcomes" and "secondary outcomes").

Information sources: The databases to be consulted will be MEDLINE, Embase, Cochrane Library, Epistemonikos and CINAHL. In addition, the protocol registers of the SRs (PROSPERO and INPLASY) will be searched, and the list of references of the SRs included in this overview will be reviewed.

Main outcome(s): Three primary outcomes will be considered: 1) Incidence of delirium: measured with validated instruments used in the hospital setting, e.g., Confusion Assessment Method for the ICU (CAM-ICU); Confusion Assessment Method (CAM); Intensive Care Delirium Screening Checklist (ICDSC); Diagnostic and Statistical Manual of Mental Disorders (DSM-5); Delirium Observation Screening Scale (DOSS), among others. 2) In-hospital mortality: mortality reported for any medical condition during the hospital stay. 3) Length of hospital stay: measured as the

length of hospital stay in a critical or non-critical care unit.

Additional outcome(s): Additionally, the following secondary outcomes will be considered: 1) Duration of delirium episode: measured in days. 2) Severity of delirium: measured with validated instruments, e.g., Memorial Delirium Assessment Scale (MDAS); Delirium Rating Scale (DRS); among others. 3) Post-discharge cognitive impairment: measured with validated and diagnostically used instruments, e.g., Mini Mental State Examination (MMSE); Montreal Cognitive Assessment (MOCA); Diagnostic and Statistical Manual of Mental Disorders (DSM-5); among others. 4) Functionality: defined as the ability to perform actions or activities that respond to the demands of daily living that provide functional independence, and measured with validated instruments, e.g., Functional Independence Measure (FIM); The Barthel Index; among others. 5) Health-related quality of life: defined as the person's perception of his or her position in life, considering physical, social, and psychological aspects of health that are influenced by the cultural context in which the person lives, and measured with validated instruments or questionnaires, e.g., 36-Item Short Form Survey (SF-36). 6) Incidence of falls: reported during hospital stay in the critical or non-critical care unit. 7) Adverse events: measured through the incidence of any adverse effects directly related to the application of the non-pharmacological intervention.

Data management: Two reviewers will read the titles and abstracts of the studies identified through the search strategy and determine whether they meet all eligibility criteria, and rate them as "included", "excluded" or "maybe". Studies classified as "included" or "maybe" will be reviewed in full text to finally determine if they are included in the overview. For this stage of the study, the Rayyan® application will be used. The extraction of information from the studies will also be performed by two reviewers, using a standardized form to obtain basic information from the SRs, and the RCTs included in them, such as population, intervention and comparator characteristics, and outcome data, as well as the information necessary to assess the methodological quality of the SRs, and the assessment of the RoB reported by the SRs. If more than one publication exists for a SR, these will be grouped together, and the most complete version will be selected for final analysis and extraction of outcome data. Both the study selection and data extraction stages will be conducted independently and blinded. Disagreements will be resolved by consensus or, ultimately, by the decision of a third reviewer.

Quality assessment / Risk of bias analysis: The second version of the "A measurement tool for evaluating systematic reviews" (AMSTAR 2) will be used, which has been designed to assess the methodological quality of SRs of interventions. This tool considers 16 questions to evaluate the suitability of the methods used during the SR process. In addition, the risk of bias of the primary studies will be reported according to the evaluation of the authors of each SR. Finally, the certainty of the evidence will be reported for each primary and secondary outcome according to the GRADE approach, selecting the SRs with the best methodological quality for information extraction.

Strategy of data synthesis: Strategy of data synthesis: The results of the study selection will be communicated through the updated version of the PRISMA flowchart. In addition, summary tables will be used to describe the included SRs and, in addition, the reasons for exclusion of SRs that do not meet any eligibility criteria will be presented as supplementary material. Tables and figures will be used to visualise and quantify the presence of overlapping primary studies in the different SRs. Finally, summary of findings (SoF) tables will be used to report the certainty of evidence for each primary and secondary outcome.

Subgroup analysis: A subgroup analysis will be performed, presenting information separately by type of unit in which primary

study participants were hospitalized (e.g., critical care unit vs. non-critical care unit), type of disease or health condition causing hospitalisation (e.g., neurological, surgical, trauma, palliative), and by age range as reported by the SRs included in the overview.

Sensitivity analysis: **This overview does not aim to perform a meta-analysis of the primary studies included in the SRs; therefore, a sensitivity analysis will not be performed.**

Language: **Inclusion of SRs is not limited by language of publication.**

Country(ies) involved: **Chile.**

Other relevant information: **This overview is the thesis work of Yoselyn Opazo for her master's degree in Physical Therapy at the Universidad de La Frontera, Temuco, Chile.**

Keywords: **Delirium; Non-pharmacological intervention; Inpatients; Systematic review**

Dissemination plans: **Once this overview has been completed, it is intended to present its findings at congresses or meetings related to rehabilitation, as well as to publish it in a scientific journal related to the different disciplines aimed at the prevention and management of patients with delirium, such as occupational therapy, physiotherapy, nursing care or comprehensive rehabilitation.**

Contributions of each author:

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