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STUDY PROTOCOL

REVISED Effectiveness of interventions to reduce adverse

outcomes among older adults following emergency

department discharge: Protocol for an overview of systematic

reviews [version 2; peer review: 2 approved]

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Abstract

Background: Older adults are frequent users of Emergency departments (ED) and this trend will continue due to population ageing and the associated increase in healthcare needs. Older adults are vulnerable to adverse outcomes following ED discharge. A number of heterogeneous interventions have been developed and implemented to improve clinical outcomes among this cohort. A growing number of systematic reviews have synthesised evidence regarding ED interventions using varying methodologies. This overview aims to synthesise the totality of evidence in order to evaluate the effectiveness of interventions to reduce adverse outcomes in older adults discharged from the ED. Methods: To identify relevant reviews, the following databases will be searched: Cochrane Database of Systematic reviews, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports, Databases of Abstracts of Reviews of Effects, PubMed, MEDLINE, Epistemonikos, Ageline, Embase, PEDro, Scopus, CINAHL and the PROSPERO register. The search for grey literature will include Open Grey and Grey Literature Reports. Systematic reviews of randomised controlled trials will be analysed to assess the effect of ED interventions on clinical and process outcomes in older adults. Methodological quality of the reviews will be assessed using the Assessment of Multiple Systematic Reviews 2 tool. The review will be reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Summary of findings will include a hierarchical rank of interventions based on

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Open Peer Review

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estimates of effects and the quality of evidence. **Discussion:** This overview is required given the number of systematic reviews published regarding the effectiveness of various ED interventions for older adults at risk of adverse outcomes following discharge from the ED. There is a need to examine the totality of evidence using rigorous analytic techniques to inform best care and potentially develop a hierarchy of treatment options. **PROSPERO registration:** CRD42020145315 (28/04/2020)

Keywords

Older adults, aged, Emergency department, adverse outcomes, interventions, systematic reviews, evidence synthesis, overviews

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REVISED Amendments from Version 1

Many thanks to the reviewers for their useful feedback and suggestions. We have reflected on the feedback received and have revised the manuscript in line with this. Specifically, this updated version provides more detail on the algorithm to GRADE and the unit of analysis in an overview being a systematic review.

Any further responses from the reviewers can be found at the end of the article

Introduction

Population ageing is increasing in most countries worldwide¹. Across Organisation for Economic Co-operation and Development (OECD) countries, the proportion of the population aged over 65 years has increased from less than 9% in 1960 to 17% in 2015 and is expected to rise to 28% in 2050^{2,3}. This change in demographics presents both opportunities and challenges⁴ Longer life is a valuable resource and presents many opportunities to older adults to have productive and healthy years⁵. Although increased life expectancy is assumed to be accompanied by an increase in healthy life years, there is little evidence that older adults living today are living with an enhanced health status than their parents did at the equivalent age¹. Older adults (aged \geq 65 years of age) are the main users of health care services⁶ and account for a substantial amount of health care

Multimorbidity (the co-existence of ≥ 2 chronic conditions) is common in older adults^{1,9} and affects more than half of those aged 60 and over^{10,11}, with increasing prevalence in those aged over 80 years^{1,4}. Multimorbidity is also correlated with increased health care utilisation and subsequent health care costs¹⁰ as multimorbidity can cause problematic clustering of certain morbidities¹², and affect treatment of one morbidity and management of another¹. The combination of population ageing, multimorbidity and physiological changes in older age¹³ mean that older adults account for some of the highest percentage of acute care services use¹⁴ and have been described as "frequent users" of emergency departments (ED)^{15,16}, accounting for 12-24% of all Emergency department (ED) attendees^{17,18}. The reasons why more older adults are seeking ED services are numerous including shortage of aged-care facilities, barriers to accessing primary care services and changes in family demographics¹⁹.

Older adults experience longer lengths of stay while in the $ED^{18,20}$ and the visits require a high level of urgency and require more resources^{18,21,22}. In terms of community support services, international estimates demonstrate that between 45% to 60% of older adults presenting to the ED will be discharged directly home to the community²³. A growing body of evidence demonstrates high rates of adverse outcomes post discharge from the $ED^{13,24}$ as older adults encounter a period of increased vulnerability following presentation to, and subsequent discharge from, the ED^{15} . A systematic review of 32 prospective and retrospective cohort studies concluded that approximately 20% of older people discharged from the ED return within 30 days, while 17% experience functional

decline²⁵. Older adults, who return to the ED early following initial presentation, or index visit, are reported to return for the same complaint again¹⁸ indicating concerns that a lack of continuation of appropriate care may contribute to this form of health care utilisation²⁴. There is a high rate of nursing home admission following ED discharge and older adults have a higher rate of mortality than younger age groups following ED discharge^{18,26}.

The number of adverse outcomes reported following an index visit has led to the development of a number of interventions described in the literature to improve the health status of older adults^{22,27}. These interventions include single strategies such as ED staffing, modifications strategies to improve ED care delivery such as risk profiling, nurse led interventions, comprehensive geriatric assessments, case management within the ED and post-discharge and discharge planning14,22,28,29. A systematic review of nine studies focusing solely on ED-based interventions reported that interventions that extended beyond referral and those with an integrated model of care (multifaceted interventions) may lead to improved outcomes including nursing home admission, ED revisits, hospitalisation and death²⁹. The authors also reported that the use of a clinical risk screening tool in the ED could potentially allow for identification of older adults most likely to benefit from interventions, but this was not consistent for all outcomes. On the contrary, a systematic review of nine studies by Lowthian et al.²² in 2015, reviewed the effectiveness of ED -community transitional strategies such as geriatric assessment, community-based referral, and GP liaison on post-discharge outcomes. This review reported no evidence of the effectiveness of the ED transitional strategy intervention for unplanned revisits, hospitalisation 30 days post discharge or mortality 18 months follow up. A systematic review by Hughes et al. (2019) evaluated the effectiveness of ED interventions aimed at improving clinical, patient experience and health care utilisation included 15 studies (9 randomised controlled trials)²⁷. This review explored the impact of interventions that were delivered during the ED visit, following discharge and across the ED-primary care interface using a variety of strategies (case management, discharge planning, and management/ medication safety). The authors reported that interventions were heterogeneous with a mixed pattern of effects on clinical and process outcomes.

Given the diverse findings across these systematic reviews, there is a need to conduct an overview of systematic reviews to synthesise the evidence relating to the impact of ED interventions on a number of outcomes for older adults. An overview can highlight gaps in the literature^{30,31} and this method of evidence synthesis³² is timely to evaluate the effectiveness of ED interventions on reducing adverse outcomes for older adults following ED discharge. The objectives of this overview are:

1. To identify, appraise and synthesise all relevant systematic reviews of ED based interventions, transitional interventions from the ED to the community and ED initiated interventions to reduce adverse outcomes (clinical outcomes, healthcare utilisation, and patient care experience) in older adults following ED discharge. 2. To identify commonalities and differences between these ED interventions with attention focusing on the characteristics of interventions, the quality of the evidence, the absolute risk difference and other pertinent factors such as heterogeneity (clinical and methodological) within and across reviews.

Methods

Protocol

An overview of systematic reviews will be conducted to identify systematic reviews (with/without meta-analysis) investigating the effectiveness of interventions to reduce adverse outcomes in older adults following index visit to the ED. In line with recommendations to improve transparency and reduce potential bias, the authors developed this protocol to outline the key objectives of this overview and what methodology will be employed³³. There is an absence of specific reporting guidelines for overviews of reviews of healthcare interventions with the Preferred Reporting Items for Overviews of Reviews (PRIOR) guidelines currently under development³⁴. This protocol was designed in accordance with the methodological framework provided by the Joanna Briggs Institute (JBI) Reviewer's Manual³⁵, and using the guidance of the relevant items of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) standardised reporting guidelines³⁶.

This protocol has been prepared with guidance from the PRISMA-Protocols (PRISMA-P) statement³⁷. The PRISMA-P checklist was developed to standardise the conduct and reporting of protocols of systematic reviews that synthesise accumulated data from primary studies, in particular studies that evaluate the effects of interventions and thus not all PRISMA-P items will be applicable for this overview. The relevant sections of the checklist will be used for this protocol in the absence of specific guidelines for the conduction and reporting of overviews of reviews. This methodology has been recommended in the absence of specific guidelines for reporting overviews³². The protocol was registered with PROSPERO on 28th April 2020 (CRD42020145315).

Search strategy

The authors developed a comprehensive search strategy which has been peer reviewed by a dedicated Education and Health Sciences academic information specialist librarian using the Peer Review of Electronic Searches Model³⁸. The aim of the search strategy is to locate all pertinent research, both published and unpublished systematic reviews, in accordance with best practice for conducting a search strategy for an overview³⁵. A three-step search strategy will be utilised in this overview to ensure a comprehensive search of the literature³⁵. The authors conducted an initial search limited to EMBASE and PubMed databases to identify systematic reviews relevant to the overview research question. Following this, key words within the titles and abstract were identified and analysed and finally index terms for the systematic reviews were analysed in line with the recommendations for conducting a search strategy for an overview³⁵. These steps guided the development of a search strategy including the identified keywords and index terms which will be adapted for each database for the second step of the search strategy³⁵. To illustrate, the full electronic database search strategy for the Embase database is detailed in Table 1.

The third step will involve a manual search for systematic reviews via a search of the reference lists of all included systematic reviews selected for critical appraisal³⁵.

NUMBER	QUERY	RESULTS
1	'aged'/exp OR 'aged	4,503,863
2	'older adults':ti,ab OR 'older adult':ti,ab OR 'older people':ti,ab OR 'older patient':ab,ti OR 'older patients':ab,ti OR 'very elderly' OR senior:ti,ab OR seniors:ab,ti OR 'aged':ti,ab OR 'geriatric patient':ab,ti OR 'geriatric care'/exp OR 'geriatric care' OR 'geriatrics'/exp OR 'geriatrics' OR geriatric:ti,ab OR 'geriatric assessment'/exp OR 'geriatric assessment' OR 'elderly care':de OR 'gerontology':ab,ti	1,276,936
3	'very elderly'/exp OR 'very elderly'	191,476
4	'emergency health service'/exp OR 'emergency health service'	100,904
5	'emergency department':ab,ti OR 'emergency departments':ab,ti OR 'emergency ward':ab,ti OR 'emergency treatment':ab,ti OR 'emergency health service' OR 'emergency room':ab,ti OR 'hospital':ab,ti OR 'emergency unit':ab,ti OR 'trauma unit':ab,ti OR 'emergency nursing':ab,ti OR 'emergency care':ti,ab OR 'acute medical unit':ab,ti OR 'emergency medicine':ab,ti	1,695,708
6	'systematic review':ab,ti	184,484
7	#1 OR #2 OR #3	4,676,994
8	#4 OR #5	1,696,511
9	#7 AND #8	497,954
10	#6 AND #9	355

Table 1. Search strategy for Embase Database.

To identify relevant systematic reviews, the following electronic databases will be searched following recommendations from the JBI Reviewers Manual³⁵: the Cochrane Database of Systematic Reviews, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports, Databases of Abstracts of Reviews of Effects, PubMed, 1966 to date; OVID Medline, 1996 to date; Embase, 1974 to date; Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO Host), 1981 to date; Epistemonikos; AGELINE, 1978 to date; PEDro, 1999 to date; Scopus and the PROSPERO register³⁹. A comprehensive search will encompass a search of the grey literature, reports from governments and non-government organisations as per best practice in conducting an overview^{35,39}.

Study selection

Screening. A two-stage process will be utilised to examine the results of the search strategies of all databases. Citations from each database will be exported by MC to a master reference management library, EndnoteX8 (Clarivate Analytics, PA, USA) and duplicates will be removed by MC. Stage 1 will involve screening of titles and abstracts in this master database by two independent reviewers (MC and RG) against the inclusion criteria for the overview as per best practice³⁵. In Stage 2, full text articles will be retrieved for all systematic reviews that meet the inclusion criteria for the overview identified in the initial screening (Stage 1) and also for studies where there is a query on based on the Stage 1 screening of title and abstract.

A comparison of these systematic reviews will be conducted by the same two independent reviewers (MC and RG) and discrepancies will be resolved by consensus or by a third reviewer (SL). The process of the entire search and selection processes will be presented in a PRISMA flow diagram.

Inclusion and exclusion criteria

Types of studies. The unit for analysis will be quantitative systematic reviews with or without meta-analysis, and research synthesis that investigates the effectiveness of ED interventions delivered to older adults following discharge from the ED. Eligible systematic reviews will be appraised by two independent reviewers (MC and RG) for methodological quality prior to inclusion in the overview, using a standardised critical appraisal tool, JBI Critical Appraisal Checklist for Systematic Reviews and Research Synthesis³⁵. Any disagreements that arise between the two reviewers will be resolved through consensus or discussion or guidance from a third reviewer (SL) will be employed³⁵. A narrative summary of the results of the critical appraisal of systematic reviews will be presented supported by relevant supporting tables and/or figures³⁵. Following discussion between authors, the quality of each systematic review will be based on the predetermined criteria^{35,40,41}.

A score of 0–3 representing very low-quality score; a score of 4–6 representing a low quality score; a score of 7–9 representing a moderate-quality score; and a score of 10–11 will be considered a high-quality score. A score of 0–3 indicates a very low-quality systematic review, and thus a systematic review will be excluded if it does not meet >3 of the 11 criteria³⁵.

This overview of systematic reviews will include systematic reviews published in any language. If a systematic review is an update of a previous systematic review, the most recent and highest quality systematic review will be considered and the lower quality systematic review will be excluded from the overview³⁹.

Eligibility criteria using PICOT framework

Population. This overview will consider existing systematic reviews that include older adults (65 years and over) following an index visit to the ED or Acute Medical Unit (AMU) discharged within 72 hours of index visit.

Interventions. Systematic reviews that analyse the effect of ED based interventions, transitional interventions and ED initiated interventions on outcomes for older adults who present to the ED with an index complaint.

Comparator:

All comparators will be considered.

Outcomes

Primary clinical outcome. Functional status/decline

• Systematic reviews reporting overall functional status including measures of functional ability assessed using a validated tool such as:

A measure of functional decline or ability (Activities of Daily Living):

Barthel's ADL Index (BI),

Functional Independence Measure (FIM),

Physical functioning aspect of the Health Related Quality of Life Short Form 36

Secondary outcomes

Secondary Clinical outcomes

- Health related Quality of life (EuroQol, EQ-5D)
- Mortality

Secondary outcomes

- Healthcare Utilisation: ED readmission, hospital admission rates (following ED discharge)
- Patient experience or satisfaction: studies reporting any validated measure of patient experience and satisfaction
- ED Length of stay (LOS)

Table 2 summarises the population, intervention, comparator,outcome and study design (PICOS) statement.

Public and patient involvement

Members of the public and patients will not be involved in this overview of systematic reviews. The authors anticipate that the findings of this review (which represents Phase 1 of the Medical Research Council framework for developing and evaluating complex interventions⁴²) will represent the first stage

STUDY CHARACTERISTIC	INCLUSION CRITERIA
Population	Systematic reviews including older adults aged 65 years and over who present to an ED for acute, urgent or emergency care.
Interventions	Any intervention strategy including: Comprehensive geriatric assessment within the ED Geriatric nursing assessment within the ED Interventions initiated in the ED used to guide appropriate follow-up and referral Discharge Planning Case Management Medication safety Strategies guided by 2014 Geriatric Emergency Department guidelines
Comparator	Systematic reviews that include studies that compare interventions to usual or enhanced care (e.g. information or educational control)
Outcomes	 Primary outcomes: Functional decline Overall functional status (or sub domains of physical or mental functioning), Secondary outcomes : health related quality of life; mortality; Patient satisfaction/experience (any validated measure of patient satisfaction/experience); Healthcare utilisation: ED readmission; unplanned hospital admission (following ED discharge)
Setting	Emergency departments
Study design	Quantitative systematic reviews of randomised controlled trials with or without meta-analysis
Timing	Time points that are logically affected by the intervention and are clinically relevant, including short (e.g. 30 days) and longer (e.g. 90 days) time points

Table 2. PICOTS Statement.

in the design of a pilot intervention to address the risk of adverse outcomes in older adults following discharge from the ED. The subsequent phases will have a strong public and patient involvement.

Data collection and extraction. Two independent reviewers (MC and RG) will extract data from the selected systematic reviews using the standardised data extraction tool in JBI SUMARI³⁹. This will be piloted to ensure that the content and mechanism of data recording is accurate. The following information will be extracted from each systematic review as recommended by the JBI Manual for the conduct of overviews³⁵:

- 1. Citation details (authors and year of publication)
- 2. Objectives of the included systematic review
- 3. Type of review
- 4. Study population
- 5. Setting and context
- 6. Number of databases searched
- 7. Date range of database searching
- 8. Publication date range of studies included in the review that inform each outcome of interest

- 9. Number of randomised controlled trials (RCTs) included and the country of origin of the RCT
- 10. Tool used to critically appraise the primary studies and their quality rating
- 11. Outcomes reported that are relevant to the overview research question with effect estimates, SE and CI as available.
- 12. Methods of analysis employed to synthesis the evidence
- 13. Comments of overview authors regarding any included study, including potential confounding variables

Should any disagreements arise between the two reviewers, these will be resolved through discussion or with guidance from a third reviewer $(SL)^{35}$. Should a systematic review present unclear, missing or incompletely reported data, we will endeavour to contact the authors of the systematic review to obtain the data and document same.

Methodological quality of included reviews

The methodological quality of the included systematic reviews will be assessed by two independent reviewers (MC and RG) using the Assessment of Multiple Systematic Reviews 2 (an update of AMSTAR) tool⁴³. The AMSTAR 2 is a 16-item

checklist utilised to assess the quality of systematic reviews that include randomised or non-randomised studies of healthcare interventions⁴³. The AMSTAR-2 includes 10 items from the original AMSTAR tool⁴⁴. Reviewers score each domain with 'yes' or 'no', or in some domains there is a third option of 'partial yes'. The quality of each systematic review will be rated as high, moderate, low and critically low. Any disagreements that may arise will be resolved through discussion or will be addressed by a third reviewer (SL).

Assessing the quality of evidence

An algorithm that assigns the Grading of Recommendations, Assessment, Development and Evaluation (GRADE)30,45,46 framework level of evidence will be used to grade the certainty of evidence. This algorithm is a new methodological approach to assessing the quality and certainty of evidence in overviews⁴⁶ and has been used in recent overviews^{47,48}. This approach will assess the quality of the evidence relating to the primary and secondary outcomes included in RCTs in systematic reviews as detailed above. Two independent reviewers (MC and RG) will assess the quality of evidence for each outcome in each systematic review independently. Any disagreements that may arise will be resolved through discussion or will be addressed by a third reviewer (SL). In this algorithm, each systematic review starts with a ranking of high certainty (no downgrade) and is downgraded one level per serious methodological concerns as outlined in Box 1 below.

Box 1. Algorithm for applying GRADE level of evidence in systematic reviews⁴⁶

A systematic review is downgraded 1 Level as per the following methodological concerns:

1. Number of participants within pooled analyses (100–199 participants)

2. Risk of bias in randomisation and blinding for <75% included studies

3: Heterogeneity as measured by a recognised measure of statistical heterogeneity, I^2 > than 75%;

4: 'No' to one of the AMSTAR 2 questions 2, 4, 5 and 6 (corresponding to a priori research design, search characteristics, independence of study design and data extraction).

A systematic review is downgraded two levels per very serious methodological concerns:

1: Number of participants within pooled analyses (1–99 participants)

2: 'No' to two or more of the AMSTAR 2 questions 2, 4, 5 and 6 (corresponding to a priori research design, search characteristics, independence of study design and data extraction).

Dealing with overlap. The issue of overlapping reviews (studies appearing in more than one review) is a challenge to authors of overviews. A matrix of evidence table will be collated and examined by two independent reviewers (MC and RG)

to assess the amount of overlap between systematic reviews. Should multiple systematic reviews exist investigating the population for the same outcome, the following will be applied:

- 1. If the primary studies are completely overlapping, the most recent, highest quality (based on the AMSTAR 2), most relevant, and most comprehensive systematic review will be selected.
- 2. If the primary studies partially overlap, both reviews will be retained if the lower quality review consists of more than one-third new studies.

Data synthesis and analysis

The results extracted from each systematic reviews will be presented both quantitatively and qualitatively to answer the objectives of this overview³⁵. The authors will present key quantitative results in tables accompanied by narrative interpretation as per best practice in presenting a summary of evidence in an overview³⁹. The results of the various sections of the overview will be presented in a Summary of Evidence table that will name the ED intervention (s), identify the systematic review(s) and provide a clear indication of the results³⁹. Given the anticipated heterogeneity, the findings will be summarised using a narrative synthesis approach.

The data contained within each systematic review (including effect estimates and 95% confidence intervals) will be reported in a narrative summary. Interventions will be ranked according to estimates of the absolute risk difference and the results of the methodological quality of the evidence³⁵. A summary of ED interventions will be developed with consideration of the certainty of the evidence and AMSTAR-2.

Discussion

This overview will employ robust methodology to present a synthesis of evidence from systematic reviews regarding the effectiveness of ED interventions and strategies on reducing adverse outcomes in older adults following index visit to the ED. Given the breadth of interventions and the diversity of the findings reported in systematic reviews, there is a need to conduct an overview to provide a broader and high-quality evidence synthesis. This overview will identify systematic reviews, and compare and contrast the results of several systematic reviews, as well as explore the reasons for the findings. As overviews are a new form of research synthesis, a number of challenges regarding the methodological conduct of an overview are described in the literature^{33,49,50}. These issues will be discussed when presenting the findings of the overview. To the best of our knowledge this is the first overview of systematic reviews published exploring this research question.

Dissemination of findings

The findings of this umbrella review will be disseminated through the publication of peer-reviewed manuscripts. Additionally, findings will be presented at both national and international conferences and via a Public and Patient Involvement group of older adults.

Study status

Searching and screening have been completed.

Data availability

Underlying data No data are associated with this article.

Reporting guidelines

Figshare: PRISMA-P checklist for 'Effectiveness of interventions to reduce adverse outcomes among older adults following emergency department discharge: Protocol for an overview of systematic reviews' https://doi.org/10.6084/m9.figshare. 12179022.v1⁵¹

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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Ruth McCullagh 匝

Discipline of Physiotherapy, School of Clinical Therapies, University College Cork, Cork, Ireland

Thank you very much for the opportunity to review your protocol. I have no other suggestions to make and wish you the very best of luck with the project.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Older adult rehabilitation and physiiotherapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 26 April 2021

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Michelle Gates 回

Alberta Research Centre for Health Evidence, Department of Pediatrics, University of Alberta, Edmonton, AB, Canada

Thank you for considering my earlier suggestions.

Abstract:

 Good overall. I would still strongly recommend not hierarchically ranking the interventions (other than potentially by strength of evidence). I think you have removed this from the text, so it would be good to remove here as well.

Methods:

- Please note that PRISMA is a reporting guideline, not a methodological standard. Therefore, it would be preferable to say that you will report the review according to PRISMA. I would say the same for PRISMA-P, it should not guide conduct, but reporting only. For conduct you may e.g., follow the Cochrane Handbook or other methodological guidance.
- I would say that GRADE is not a new approach, but indeed it has not yet been adapted for use in overviews. It therefore is useful that you have provided an algorithm.
- For GRADE, often 300 events is considered adequate for precision. For risk of bias, you may
 want to check how this impacts the results. Heterogeneity may also encompass the
 direction of effects that you see (and not just the I2).
- Note that a poor quality systematic review may still report data from good studies. This
 might be something to think about when applying GRADE based on AMSTAR score.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Evidence synthesis

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 15 March 2021

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Michelle Gates 问

Alberta Research Centre for Health Evidence, Department of Pediatrics, University of Alberta, Edmonton, AB, Canada

Thank you for the opportunity to review this protocol for an overview of reviews of interventions in the emergency department to reduce adverse outcomes among older adults following discharge (e.g., return to ED, among others). It seems generally well planned. I have listed some points below that could be addressed to improve the planned overview.

Introduction:

• Before 'longer life is a valuable' it looks like a new sentence should start.

- Could be more specific in the objective statement about which PICOTs are of interest (e.g., which interventions, in specific population, and specific outcomes).
- Can likely remove the paragraph describing overviews of reviews. Would then replace the earlier objective statement with one or all of the 3 specific objectives.
- I think that identification of the evidence is part of the overview process but should not be a specific objective.
- It would be good for the objectives to be in PICOT format.

Methods:

- Please note that the PRISMA and PRISMA-P are reporting guidelines, they are not meant to guide design.
- For the search I think it might be useful to include terms other than 'systematic review' as these are often named differently (e.g., review, meta-analysis, among others).
- It is not fully clear from the description how full text screening will happen. Please clarify.
- Why will pooled analyses (I am assuming this is from non-systematic reviews) be included?
- Are only high quality systematic reviews going to be included? It is not clear. If not, I am not sure why critical appraisal is happening at the selection stage.
- In the eligibility criteria, please indicate comparators of interest in the text.
- Are you including only reviews of RCTs? It seems like this from the data extraction section but I do not see this within the eligibility criteria.
- It is not clear why the quality of the systematic reviews is being assessed twice first the JBI criteria are listed at the selection stage, then later AMSTAR-2.
- Dealing with overlap if both reviews are kept, what will you do about the overlap? What will you do if the reviews appraised their primary studies differently?
- What will you do if reviews do not report an appraisal of the quality of their included studies? Will you appraise these yourself, or report them as missing?
- What will you do if all the information needed for GRADE is not available within the systematic reviews? For e.g. if quality appraisal is missing as above?
- Would it make sense (if not conducting new syntheses) to extract GRADE assessments directly from the systematic reviews?
- It looks like the evidence will be presented qualitatively only. Will there be meta-analysis? If not, I would not say there will be a quantitative synthesis.

 I would caution strongly against a hierarchical summary of results, as it is important to not make informal indirect comparisons across the findings of different systematic reviews.
 Please see Cochrane handbook Ch 5 for more information on this. It is difficult to assess the transitivity assumption in overviews of reviews.

Is the rationale for, and objectives of, the study clearly described? Partly

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others? Partly

Are the datasets clearly presented in a useable and accessible format? Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Evidence synthesis

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Mar 2021

Mairead Conneely, Faculty of Education and Health Sciences, Ageing Research Centre, Health Research Institute, University of Limerick, Limerick, Ireland

Many thanks for your time spent reviewing this protocol and for your constructive and insightful feedback and comments. We have reflected upon your feedback and made revisions to our manuscript in line with it. Please see below a detailed point by point response to all comments (reviewer's comments in **bold** and authors' responses in black).

SECTION: INTRODUCTION

Comment 1: Before 'longer life is a valuable' it looks like a new sentence should start. Response: Many thanks for this comment. This error has been amended

Comment 2: Could be more specific in the objective statement about which PICOTs are of interest (e.g., which interventions, in specific population, and specific outcomes). Response: Many thanks for this comment. The objectives have been edited for more explicit statement aligned to PICOT framework.

Comment 3: Can likely remove the paragraph describing overviews of reviews. Would then replace the earlier objective statement with one or all of the 3 specific objectives

Response: Many thanks for this comment. This section has been condensed to one sentence to link the previous paragraph to the objectives of the Overview.

Comment 4: I think that identification of the evidence is part of the overview process but should not be a specific objective.

Response: Many thanks for this comment. We have merged objectives one and 3 in the revised manuscript.

Comment 5: It would be good for the objectives to be in PICOT format

Response: Many thanks for this comment. The objectives have been edited to specify the PICOT statement.

SECTION: METHODS

Comment 1:Please note that the PRISMA and PRISMA-P are reporting guidelines, they are not meant to guide design.

Response: Many thanks for this comment. The wording has been edited for clarity.

Comment 2: For the search I think it might be useful to include terms other than 'systematic review' as these are often named differently (e.g., review, meta-analysis, among others).

Response: Many thanks for this comment. The JBI Manual of Evidence Synthesis Chapter 10 recommends the use of the term "systematic review" to broaden the search as far as possible and recommend not using terms such as meta-analysis as the return may be limited to meta-analysis and risk losing out of potentially relevant systematic reviews. We sought clarification on this also from the information specialist and she concurred with the process outlined by JBI.

Comment 3: It is not fully clear from the description how full text screening will happen. Please clarify.

Response: Many thanks for this comment. Further details have been added to this section for an explicit description of the screening process.

Comment 4: Why will pooled analyses (I am assuming this is from non-systematic reviews) be included

Response: Many thanks for this comment. The JBI Manual recommends including pooled analyses due to different terms used. For comprehensiveness, if there was a systematic review that did pooled analysis, that met our PICOT, it would be pertinent to include. However, we understand the confusion with different terminology and have deleted.

Comment 5: Are only high quality systematic reviews going to be included? It is not clear. If not, I am not sure why critical appraisal is happening at the selection stage Response: Many thanks for this comment. We have amended the updated manuscript to address this query. All relevant systematic reviews will be screened for inclusion using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Synthesis. A score of 0-3 indicates a very low-quality score and such studies will be excluded. This initial screening of quality using the JBI Checklist has been conducted in other overviews also and we have

referenced same in the manuscript.

Comment 6: In the eligibility criteria, please indicate comparators of interest in the text.

Response: Many thanks for this comment. Comparators have been added to the text as part of the PICOT.

Comment 7: are you including only reviews of RCTs? It seems like this from the data extraction section but I do not see this within the eligibility criteria.

Response: Many thanks for this comment. This is already outlined in the PICOT statement in Table 2.

Comment 8: It is not clear why the quality of the systematic reviews is being assessed twice - first the JBI criteria are listed at the selection stage, then later AMSTAR-2. Response: Many thanks for this comment. The sentence on the scoring of the JBI Critical Appraisal has been edited to make explicit the exclusion of a systematic review based on >3 of the 11 criteria as suggested in the JBI Manual for the conduct of systematic reviews. Thus only Systematic reviews that score higher than 3/11 will be included in this overview. Thus the JBI Critical appraisal tool will be used as a screening tool for a minimal acceptable

standard for a systematic review. The methodological quality of the included systematic reviews will be assessed using the AMSTAR 2 tool. The use of the AMSTAR 2 tool always informs the algorithm to GRADE for evaluation of the quality of evidence.

Comment 9: Dealing with overlap - if both reviews are kept, what will you do about the overlap? What will you do if the reviews appraised their primary studies differently? Response: Many thanks for this comment. In the presence of complete overlap between reviews, the highest quality review, as determined by the AMSTAR 2, will be included in data synthesis and analysis. In cases, where there is complete overlap and the reviews receive the same rating using the AMSTAR 2, then the most recently published review will be included. However, for this umbrella review our unit of analysis is the systematic review and consequently, we will not be performing a quality rating of the primary studies. This is described in Methods section, subsection "Dealing with Overlap" of the manuscript.

Comment 10: What will you do if reviews do not report an appraisal of the quality of their included studies? Will you appraise these yourself, or report them as missing? Response: Many thanks for this comment. We agree that the use of a predetermined tool to assess the quality rating of primary studies in included systematic reviews can strengthen the review. However, for this overview review our unit of analysis is the systematic review and consequently, we will not be performing a quality rating of the primary studies. As part of the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses, we will record and present whether systematic reviews completed critical appraisal by two or more reviewers independently. Additionally, as part of the AMSTAR 2 we will be recording if the authors of the systematic reviews used a satisfactory tool to assess for risk of bias.

Comment 11: What will you do if all the information needed for GRADE is not available within the systematic reviews? For e.g. if quality appraisal is missing as above Response: Many thanks for this comment. As per the recommendations outlined by Pollock et al 2017, which we have referenced, "If ROB for individual trials was not reported within the review, we

were conservative and assumed that less than 75% of participants had low ROB". We have added a box detailing the algorithm to GRADE for further details on the algorithm.

Comment 12: Would it make sense (if not conducting new syntheses) to extract GRADE assessments directly from the systematic reviews?

Response: Many thanks for this comment. Cochrane systematic reviews will have this Grade Assessment detail. However, non-Cochrane reviews will may not present an assessment of the quality of the evidence or may present many methods. For consistency, we will apply the GRADE algorithm to all systematic reviews as opposed to extracting the regular GRADE which would be a different tool.

The unit of analysis is a systematic review and the algorithm to GRADE is applied at the level of the systematic review.

Comment 13: It looks like the evidence will be presented qualitatively only. Will there be meta-analysis? If not, I would not say there will be a quantitative synthesis. Response: Many thanks for this comment. The wording has been edited to highlight qualitative only.

Comment 14: I would caution strongly against a hierarchical summary of results, as it is important to not make informal indirect comparisons across the findings of different systematic reviews. Please see Cochrane handbook Ch 5 for more information on this. It is difficult to assess the transitivity assumption in overviews of reviews.

Response: Many thanks for this comment. The JBI Manual recommends the use of a hierarchical summary of results. However, we understand the reservation with the use of the term and have edited this section accordingly.

Competing Interests: No competing interests were disclosed.

Reviewer Report 10 July 2020

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Ruth McCullagh 🛈

Discipline of Physiotherapy, School of Clinical Therapies, University College Cork, Cork, Ireland

Thank you for giving me the opportunity to review your protocol.

The abstract reports need for the study and the planned methods clearly.

The background explains clearly the conflicting outcomes of trials and existing systematic reviews, highlighting the complexity of the problem. An overview of systematic reviews is clearly justified.

The methods described are aligned with the recommended methods and show sound methodology, with a comprehensive search strategy, citeris that match the research question, methods to limit their bias and evaluation of methodological quality of the data.

Wishing you success and I look forward to reading the outcome of the study.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

Are the datasets clearly presented in a useable and accessible format? Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Older adult rehabilitation and physiiotherapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 10 Jul 2020

Mairead Conneely, Faculty of Education and Health Sciences, Ageing Research Centre, Health Research Institute, University of Limerick, Limerick, Ireland

Many thanks for reviewing our protocol Dr McCullagh Mairéad Conneely

Competing Interests: No competing interests were disclosed.