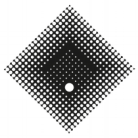
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BMJ Open

Efficacy of pressure ulcer prevention interventions in adult intensive care units: a protocol for a systematic review and network meta-analysis

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ABSTRACT

Introduction Pressure ulcers (PUs) are associated with substantial health burden. Patients in intensive care units (ICUs) are at high risk for developing PU. In the absence of large randomised controlled trials (RCTs) that compare commonly known interventions for preventing PU in ICUs, uncertainty remains around the best practice strategy for PU management in adult ICUs. This study, therefore, aims to identify the most effective interventions and combinations of interventions that prevent PU in adult ICU using systematic review and network meta-analysis (NMA).

Methods and analysis We will search for all published and unpublished RCTs evaluating interventions to prevent PU compared with other PU prevention measures or with usual care in adult ICU. The primary outcomes are the incidence of PUs and PU severity in critically ill patients in ICU. The secondary outcomes include number of PUs per patient and intervention-related harms caused by the prevention intervention or intervention-related harms. All data extraction will be performed by at least two independent reviewers on the basis of a priori developed extraction form. We will evaluate the risk of bias of the included RCTs in accordance with the Cochrane Collaboration's risk of bias tool, and assess the quality of evidence using Grading of Recommendations Assessment, Development and Evaluation. A standard pairwise meta-analysis and a Bayesian NMA will be conducted to compare the efficacy of different PU prevention interventions. A surface under the cumulative ranking curve will be used to rank the probabilities of each prevention intervention for various outcomes.

Ethics and dissemination This study will not require the ethics approval as it is a review based on published studies. The findings of this study will be submitted to a peer-reviewed journal for publication. We anticipate that the results of the study will provide the evidence to inform clinicians and guideline developers on determining the best interventions for the prevention of PU in ICU patients.

PROSPERO registration number CRD42018085562.

Strengths and limitations of this study

- To the best of our knowledge, this study will be the first network meta-analysis that comprehensively explores and compares the effectiveness of various pressure ulcer prevention interventions in adult intensive care unit (ICU) patients.
- The present study will ensure that both the risk of bias and the quality of evidence of the included randomised controlled trial is properly assessed by Cochrane risk of bias assessment tool and Grading of Recommendations Assessment, Development and Evaluation, respectively.
- The findings from this study may help guide healthcare providers to select appropriate prevention methods which may ultimately lead to a reduction in healthcare costs and improved patient outcomes in adult ICUs.
- Due to the retrospective nature of this study, the findings of this study are likely to be influenced by the quantity and quality of the studies included.

INTRODUCTION

Hospital acquired pressure ulcers (HAPUs) are a significant global challenge associated with considerable physical and economic burden.[1–3] Critically ill patients in intensive care units (ICU) are at high risk of developing HAPU due to their characteristics such as multiple comorbidities, unstable haemodynamics, bedridden, increased use of medical devices and special medications.[4–8] Estimates suggest that up to 49% of the ICU patients developed HAPUs.[9–14]

Previous research including systematic reviews and meta-analyses have failed to reach robust conclusions on the relative effectiveness of different PU prevention strategies due to the limitation of not allowing for indirect comparisons.[6 15–20] For instance, a recent systemic review of 25 studies on the effectiveness of PU prevention strategies in the ICU cautiously recommended a silicone foam dressing, however, no single superior strategy was identified in the intensive care context.[20] McInnes and colleagues conducted a meta-analysis with aims to assess the effects

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of supporting surfaces in preventing PUs. The authors selected 53 trials with more than 16 000 participants. They found several known surface supporting devices appear to have no clear benefits in practice.[21] Consequently, a variance continues to exist between recommended PU preventions and actual practice.[22]

Network meta-analysis (NMA) is a statistical methodology that compares multiple interventions simultaneously by analysing studies making different comparisons in the same analysis.[23] Contrary to the traditional meta-analysis, NMA incorporates direct and indirect evidence within a network of RCTs and enables comparison of multiple intervention and ranking of the interventions that have not been studies in a head to head fashion.[24] Despite that PU prevention programmes encompass a variety of measures such as education, training, repositioning, nutritional support, moisture management and support surfaces,[15 17–19 25–27] only the effectiveness of support surfaces was recently assessed by an NMA.[28]Up-to-date, no NMA has been conducted to systematically compare and rank the efficacy of the available prevention strategies in adult ICU patients, this study is therefore deemed a necessity. The objective of the study is to rank the effectiveness of PU prevention interventions in ICUs through a systematic review and NMA. The review question is, what are the most effective PU prevention interventions (or combinations of interventions) compared with usual care for reducing the incidence of PU in adult ICUs?

METHODS AND ANALYSIS

Eligibility criteria

Types of settings

Only studies conducted in adult ICUs will be included.

Types of participants

Patients aged 18 years or older in adult ICUs will be included. Patients will not be eligible if they have been diagnosed with PU prior to their admission to the ICU. No further restrictions will be made on participants' gender, ethnicity and nationality.

Types of studies

Only full articles of RCTs reporting comparisons of one prevention intervention with another or conventional care for adult ICU patients will be included. We will exclude editorials, opinion papers, reviews, qualitative studies and case reports. Quasiexperimental and non-experimental such as cohort, case–control and pre–post studies will also be excluded.

Types of intervention

We are interested in any intervention aimed at preventing PU in adult ICU patients. Both monofactorial and multifactorial interventions will be included, such as risk assessment, support surfaces, dressings, repositioning regiments, nutritional supplementation and educational or training programmes.

Comparators

We will make comparisons between the usual care and single prevention measure as well as between different PU prevention interventions.

Outcome measures

Primary outcomes

1. The incidence of PUs in critically ill patients in ICUs. This will be calculated based on the percentage of the participants who develop new PUs during the study period.[29]
2. The severity of PUs. This will be classified as per the National Pressure Ulcer Advisory Panel (NPUAP), European Pressure Ulcer Advisory Panel (EPUAP), and Pan Pacific Pressure Injury Alliance (PPPIA) Clinical Practice Guidelines.[30]

Secondary outcomes

1. Number of PUs per patient.
2. Adverse events caused by the prevention intervention or intervention-related harms.

The literature search will be limited to English and Chinese articles and no date restrictions will be applied. We are aware that overlooking non-English and non-Chinese articles may lead to biases and gaps in our understanding of the topic. However, the literature has shown the dominance of English in international scientific publications with almost 80% research findings reported in English.[31] Considering the dramatic increase in scientific publications in Chinese-language journals,[32] encompassing both English and Chinese articles may allow us to achieve a descent coverage. A draft eligibility form (online appendix 1) has been developed based on the relevant study.[33] This form will be further reviewed by a panel of experts comprising librarian, ICU clinical nurse specialists, wound care nurse specialists and subsequently piloted by the key investigators.

Search strategy

'Pressure ulcer', 'pressure sore', 'pressure injury', 'decubitus', 'decubitus ulcers' , 'bed sore', 'intensive care' and 'critical care' will be used as keywords or (and) MeSH terms. Searches will be undertaken in the following electronic databases: EMBASE, PubMed, the Cochrane Central Register of Controlled Trials, CINAHL, SinoMED to identify published studies. The databases will be searched from their inception to 31 January 2019. An experienced librarian will be invited to review the selected search strategy. A draft search strategy is summarised in online appendix 2. We will also contact organisations that produce clinical practice guideline of PU management (eg, NPUAP, npuap.org; EPUAP, epuap.org; PPPIA; Chinese Nursing Association; Japanese Society for Pressure Ulcers). In addition, we will manually search for the unpublished literature and check references of all included trials to ensure relevant articles are covered. Experts in the PU prevention and management field

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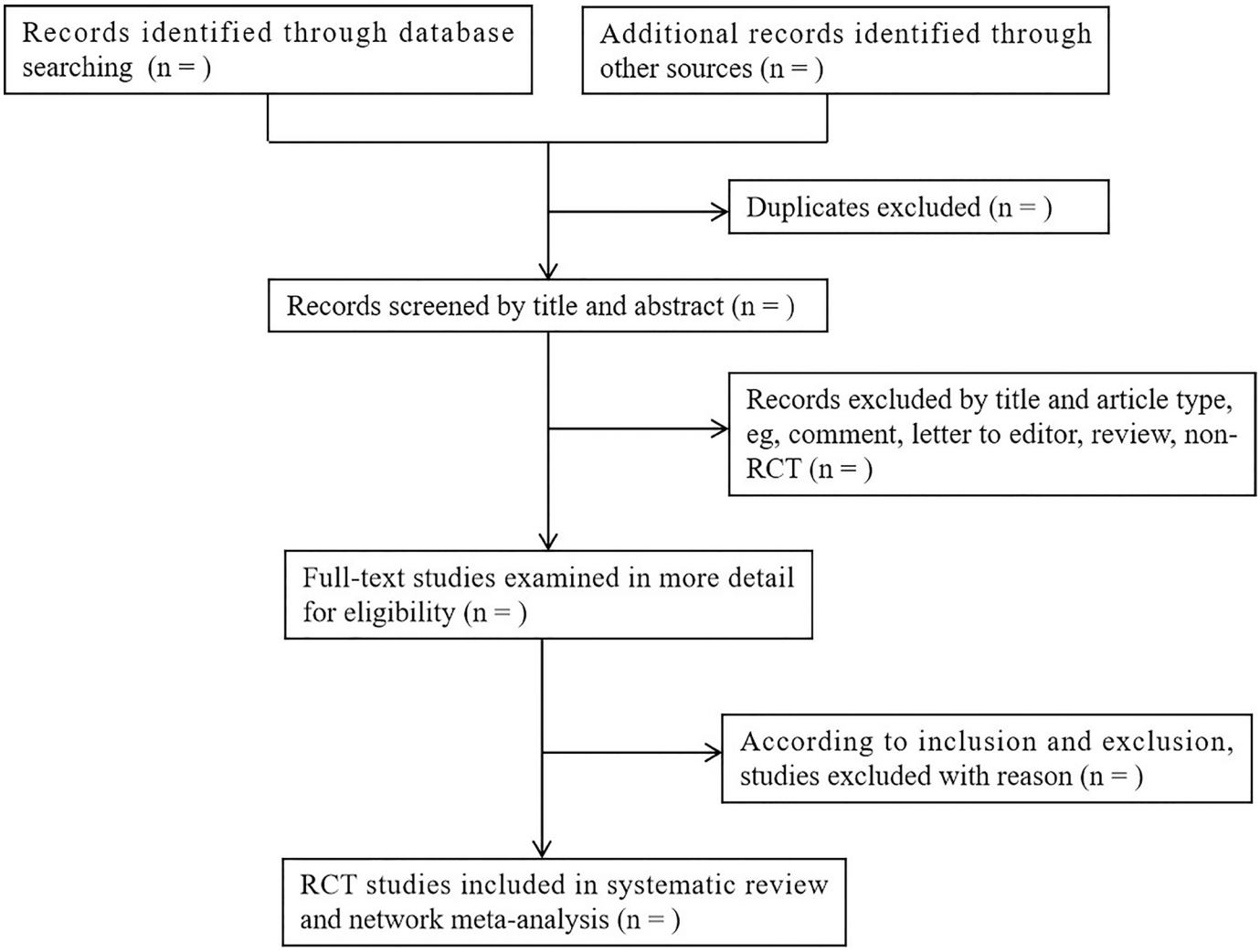

Figure 1 Study selection process. RCT, randomised controlled trial.

will also be contacted via email to locate non-published studies.

Study selection

All investigators will be properly trained prior to the commencement of the data screening. Rayyan online literature management software (https://rayyan.qcri.org) will also be introduced to screen and manage literature. After screening a random sample of 50 citations, Kappa test will be used to calculate the inter-observer agreement for all studies included. If Kappa value is less than 0.75, a second round of training will be implemented. Duplicate publications of original research will be excluded. The titles and abstracts of identifiable articles will be screened independently by two reviewers (YD and FW), to exclude reports that clearly do not meet the inclusion criteria. The same reviewers will then independently examine full-text articles to determine eligibility. When disagreements arise, the third author (WZ) will be asked to evaluate the full text and the discrepancy will be resolved by group discussions. Excluded trials and the rationale for exclusion will be recorded. Figure 1 depicts the study selection processes in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[34] flow diagram.

Data extraction

A rigorous process will be applied to the data extraction. First, a draft data extraction form will be developed through team discussions. The form will then be pilot tested by each member of the team prior to its usage. Two reviewers (YD and FW) will extract the data of interest independently using the data extraction form, and conflicts or disagreements will be resolved by team discussions. The following descriptive data will be extracted: country of origin, author(s), year of publication, intervention(s) and comparator(s), sample size, patient characteristics, setting, primary outcomes, secondary outcomes, outcome measurements and any adverse events caused by the preventive interventions. In case of insufficient information, wherever possible, authors of primary studies will be contacted by either telephone, email or post to obtain missing data. If a study presents incomplete primary outcomes it will only be included in the systematic review rather than the meta-analysis.

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Quality appraisal

Risk of bias appraisal

Cochrane Risk of Bias Assessment Tool will be used to appraise the risk of bias.[35] This tool includes: (1) random sequence generation (selection bias); (2) allocation concealment (selection bias); (3) blinding of outcome assessors (detection bias); (4) blinding of patients and personnel (performance bias); (5) incomplete outcome data (attrition bias); (6) selective reporting (reporting bias); (7) anything else, ideally prespecified (other bias). Authors of the original study will be contacted for more information if there are inadequate details of allocation concealment and other characteristics of trials. Each item will be classified into high risk or unclear risk or low risk with respect to the level of risk of bias by two independent reviewers (YD and FW). Any discrepancies will be resolved by a third reviewer.

Geometry of the network

The available evidence will be presented in a network plot to ensure it provides information on the relative effectiveness of PU prevention measures. The size of the nodes will reflect the sample size of each intervention and the thickness of edges will be associated with numbers of RCTs.

Data synthesis and statistical analysis

Pairwise meta-analysis

Data will be synthesised with a pairwise meta-analysis. Risk ratio (RR) and 95% CI will be used for dichotomous outcomes, mean differences or standardised mean differences (SMDs) with 95% CI will be used for continuous outcomes. We will evaluate clinical and methodological heterogeneity through examination of the population, methods and interventions of the included studies. Heterogeneity across trials will be assessed by estimating the variance between studies using the χ^2 test and I^2 statistic. For a p value ≥0.1 and I^2 ≤50%, no significant statistical heterogeneity exists and the Mantel-Haenszel fixed effect model will be employed; otherwise the Mantel-Haenszel random effects model will be used (p value <0.1 and I^2 >50%). The sources of heterogeneity will be explored by sensitivity analyses.[36] The potential for publication bias will be examined through the Begg's and Egger's test if more than 10 studies are available. The contour-enhanced funnel plot will be obtained additionally to distinguish asymmetry. The pairwise meta-analysis will be carried out in Stata V.13.

Evaluation of the transitivity assumption

Transitivity is one of the major assumptions that NMA relies upon.[24] We will assess the transitivity by checking whether time to occurrence of PUs is similar in the different RCTs and comparing the distribution of the potential modifiers such as age, and the risk scale of PU across the different pairwise comparisons.[23]

Network meta-analysis

We will perform Bayesian NMAs to compare the efficacy of selected PU prevention interventions. The NMA will be conducted in the WinBUGS V.1.43 software (Medical Research Council Biostatistics Unit, Cambridge, UK).[37] A complex statistical models will be built by a Bayesian software program, the Markov Chains Monte Carlo simulation technique will be used to generate samples. An initial burn-in period of 5000 iterations will be set to allow convergence, then posterior summaries will be produced based on a further 30 000 iterations. Both Kernel density and the auto-correlation plots will be used to assess model convergence.[38] We will calculate the summary RRs or SMD for all pairwise comparisons in a league table. The ranking probabilities of all prevention interventions for each outcome will be estimated via the surface under the cumulative ranking curve.[39] We will also compare stability using the frequentist approach.[40]

Assessment of inconsistency

The consistency between direct and indirect evidence will be assessed by a loop-specific approach within each loop of the network. The loop-specific approach separates direct evidence from indirect evidence for a specific comparison in the loop (inconsistency factor). I^2 and its 95% CI will be used to estimate the consistency within the entire network.[41] If the inconsistency is identified, subgroup analyses and multiple meta-regressions will be performed to determine the impact of the mean age of the participants, the risk score of PU, the length of ICU stay and blinding method on the PU incidence.

Rating the confidence in estimates of the effect in NMA

The quality of evidence that influences network estimates will be assessed using the Grading of Recommendations Assessment, Development and Evaluation.[42] On the basis of five domains including the study limitations, inconsistency, imprecision, indirectness and publication bias, the quality of evidence will be classified into one of the four levels, including high, moderate, low and very low quality.[42]

Patient and public involvement

Patients and the public were not involved in the conception and design of this protocol.

Ethics and dissemination

Ethical approval is not required for this study as it does not include any interventions with human or animal or confidential personal data. The findings of this study may assist clinicians and guideline developers in their efforts to prevent PU in ICU patients. The procedures of the study will be conducted in accordance with the PRISMA-compliant guidelines. The findings of the study will be reported according to the PRISMA-compliant guidelines and submitted to a peer-reviewed journal for publication.

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Contributors After conceptualising and designing of the study, FW and YD registered the protocol on the PROSPERO database. YD, FW and SL critically revised the protocol and contributed to the drafting of the final manuscript. YD, WZ, HW, RC, XL and YZ tested the feasibility of the study and involved in the revision of the protocol. YD, FW, WZ, HW and YZ will perform the data collection and analyses. All authors read and approved the final manuscript.

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