

BMJ Open Quality of reporting of outcomes in trials of therapeutic interventions for pressure ulcers in adults: a protocol for a systematic survey

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ABSTRACT

Pressure ulcers (PUs) have a high incidence, especially in hospital units. Randomised clinical trials (RCTs) of therapeutic interventions for PU should include a clear description of the outcomes and results to enhance transparency and replicability.

Objectives The primary objective of this study is to assess the completeness of the descriptions of the outcomes of therapeutic interventions in RCTs in adult patients with PU. The secondary objectives are to evaluate the types of reported primary outcomes, measurement methods or tools used to evaluate the outcomes and the results of reported outcomes.

Methods We will conduct a systematic survey of RCTs published from January 2006 to April 2018. The selection process of the studies will be done in two stages of screening: title and abstract, and full text revision, always by two researchers independently. The completeness of the outcome will be assessed according to five criteria: domain (outcome title), specific measurement or technique/instrument used, specific metric or format of the outcome data that will be used for analysis, method of aggregation (how data from each group will be summarised) and time-points that will be used for analysis. The quality of the results of the outcome will be classified as either complete, incomplete or unreported. We will conduct a descriptive analysis of the number, type and degrees of outcome specification in the included RCTs. The frequency of categories in each domain of the outcomes will also be reported. The median and IQR will be estimated for each element of the specified outcome (out of five).

Ethics and dissemination This will be the first systematic assessment of the outcomes of therapeutic interventions used for pressure ulcers. After completion, this review will be submitted to a peer-reviewed journals.

INTRODUCTION

Pressure ulcers (PUs) or pressure injuries are complex wounds requiring an overabundance of skills and knowledge to manage and care for¹ and are considered adverse events that cause suffering for patients² and costs

Strengths and limitations of this study

- This will be the first systematic survey to assess how the outcomes of efficacy or effectiveness of therapeutic interventions is described in reports of randomised clinical trials (RCTs) on pressure ulcers (PUs).
- Selected articles will be reviewed independently and in duplicate to evaluate the completeness of the descriptions of the outcomes and the quality of the results of reported outcomes.
- Limitations: Only RCTs published in English and Portuguese will be considered. Safety outcomes will not be analysed. Our findings will only be generalisable to the field of PUs in adults.

for society.³ According to published literature, clinical practice and expert opinion, most PUs are avoidable, but not all.⁴ While preventing PU is obviously a sign of better quality of care and is also cheaper than treating them, the preventive process is not easy because it involves numerous factors that need to be considered.⁵

Based on the results of several studies about prevalence and incidence of PU in intensive care settings, the prevalence varied from 4% to 49%, whereas the incidence ranged from 3.8% to 12.4%.⁶ The prevalence of PU in hospitalised patients in different care settings varied between 1.25% and 18.5%, but the majority of studies revealed more than 10%.^{7–10}

In Brazil, the prevalence of PU is 16.9%, similar to data from two other international studies in hospitals with similar inclusion criteria.^{11 12} There was no significant difference between the prevalence of PU in the seven Brazilian states studied, indicating that this also is a national health problem.¹³ Still in Brazil, an evaluation found that the cost of

treatment was US\$11.95 per day for material, while the cost of prevention was only US\$4.83.¹⁴

PU can be quite burdensome to patients causing considerable damage to their health, by hindering their functional recovery, causing pain and the development of severe infections associated with prolonged hospitalisations, sepsis and ultimately leading to premature mortality.¹⁵

In clinical trials, an outcome is an event or measure in study participants that is used to assess the effectiveness or safety of the intervention being studied, or sometimes adverse events.¹⁶ Systematic reviews of large, well-designed randomised clinical trials (RCTs) showing positive effects of given treatments are the foundation of good evidence-based clinical practice. For the evidence coming from primary RCTs to be useful, it needs to be based on well-defined outcomes that have good properties.^{17 18} Full pre-specification of outcomes can reduce the risk of outcome reporting bias.¹⁹

According to previous studies,^{19 20} a good description of RCT outcomes should present five key elements, namely:

- ▶ Domain or title of the outcome, for example, *wound healing*.
- ▶ Specific technique or instrument used to make the measurement, for example, *wound healing* will be defined as skin re-epithelisation without drainage or dressing requirements, confirmed at two consecutive study visits 2 weeks apart.
- ▶ Metric or specific format of the outcome data of each participant that was used for analysis, for example, *change in wound area* from baseline, in millimetres.
- ▶ Method of aggregation or how the data of each group were summarised, for example, *mean change in wound area from baseline*.
- ▶ Time points that were used for analysis, for example, at 4 weeks.

A systematic evaluation of outcomes of RCTs in venous ulcers published between 1998 and 2013, showed considerable heterogeneity: 78 different outcomes, evaluated at 12 different times, with poor reporting of the methods used to evaluate them.²¹ As far as we know, there are no studies that have evaluated the quality of outcomes and results used in RCTs involving patients with PU. Thus, this study will be filling an important knowledge gap and provide a better understanding of current practice regarding outcome definitions and descriptions in PU trials.

Objectives

The primary objective of this study is to analyse the completeness of the outcomes of efficacy or effectiveness of therapeutic interventions in RCTs in adults with PU according to the five elements (domain; specific technique; metrics of each participant's outcome data; aggregation method and time that were used for analysis).¹⁹

Secondary objectives include:

- I. Determining the proportion of RCTs that report primary outcomes.

- II. Determining the proportion of RCTs that report objective outcomes.
- III. Describing the measurement methods or tools used to evaluate the outcomes.
- IV. Evaluating the quality of the result of the reported outcome classified as complete, incomplete or unreported.

Hypothesis

It was found a great heterogeneity in study outcomes that investigated wound healing,²¹ then the hypothesis of this study is that heterogeneity of outcomes is also found in the studies of interventions for healing in PU and that these outcomes are with an incomplete report.

METHODS

Study design and eligibility criteria

This study will be a systematic survey of articles published from January 2006 to April 2018. This time-frame was chosen because it is part of the period during which there have been several published articles addressing the completeness of reporting or adherence to various reporting guidelines.²²

Inclusion criteria

RCTs of therapeutic interventions such as dressings, medications and care guidelines (eg, turn charts, turning regime, etc) for PU, published between January 2006 and April 2018, and studies in English and Portuguese. Only RCTs from stages 2 to 4 PU will be included. Stage 1 PU will not be included because interventions for this stage are more related to prevention of progression to open wound rather than treatment for ulcer healing, so the outcomes of these studies are different. The studies that do not clearly presented the PU stage will be evaluated in relation to the outcomes. Outcomes related to preventive strategies will be excluded.

Exclusion criteria

RCTs that include chronic ulcers of different aetiologies, studies whose primary objective is economic evaluations for prevention and treatment of PUs, not accessible in full or reporting prevention interventions will be excluded. We will also exclude PU-focused RCTs that were due to medical devices, such as catheters, tubes, probes, apparatus and dressings adhesives.

A study will be defined as a RCT if it is a prospective study to evaluate efficacy, effectiveness or safety of an intervention and if the intervention allocation is described by phrases such as 'randomly allocated', 'randomly assigned' or 'allocated by randomisation', and if there is a comparative group.²¹ The comparative group may be placebo, another treatment, a different dose of the same treatment, usual care, historical control or only lack of treatment.²³

Patient and public involvement

Patients and public were not involved as this study was a systematic survey of the published literature.

Search strategy and article selection

The search strategy will include terms such as ‘pressure ulcer’, ‘pressure injury’, ‘randomised clinical trials’, ‘treatment’ and ‘adults’ (online supplementary appendix A). The following databases will be searched: PubMed, Cochrane, Cinahl, Embase, Lilacs, Scopus and Web of Science. The number of articles identified in these databases was 801.

The studies will be selected in two stages: title and abstract screening, then full text screening. We will conduct screening in duplicate. Researchers will resolve any discrepancies by consensus or by consulting a third author.

Data extraction

Data extraction from each article will be done through a standardised Microsoft Excel worksheet. Two reviewers will summarise the data and any disagreement will be resolved through consensus. If consensus cannot be obtained, a third author will be contacted.

We will pilot the data extraction form on 10 randomly select trials before proceeding with full data extraction to ensure all reviewers extract data consistently and to ensure the data extraction form is unambiguous and free from errors.

The following data will be extracted.

General features of included RCTs

Bibliometric information and other details will be extracted from each RCT: author, year of publication, journal of publication, total number of patients recruited in the study, whether the study was sponsored by industry, journal impact factor (Journal Citation Reports website: <https://jcr.incites.thomsonreuters.com>), if the journal requires use of the Consolidated Standards of Reporting Trials and if the study was a single or multi centre trial and in which country or countries the study was performed.

Evaluation of the characteristics and quality of the outcomes reported in the RCTs

Outcomes will be defined as a measurable variable at a specific time to evaluate the efficacy or effectiveness or harm of an intervention.^{21–24} Outcomes of efficacy or effectiveness will be analysed. The following characteristics of outcomes will be assessed.

Presence or not of primary and secondary outcomes

In order to consider the outcomes, we will use the following criteria:

- ▶ Primary and secondary outcomes are those explicitly reported as such in the methods section of an RCT.²⁵
- ▶ When there is only one reported outcome, it will be considered primary.
- ▶ When several outcomes are reported with no designation as primary or secondary outcomes, the study will be considered to not have a primary or secondary outcome.
- ▶ When several outcomes are reported as primary, all of them will be considered primary.

Box 1 Domains of efficacy/effectiveness outcomes in chronic ulcers with some examples.

Healing outcomes:

1. Wound closure.
2. Healing time.

Non-healing outcomes (Intermediate or substitutes):

3. Reduction rate: decreased wound area.
4. Change in wound condition: debridement, increased granulation tissue, reduction of exudate and odour.
5. Biomarkers: biochemical components of non-healing wound exudate, physiological markers (wound surface pH, tissue oxygen measurement), tissue markers (histological examination, dermal collagen, neovascularisation).
6. Bacteriology: reduction of bacterial load.
7. Infection signs: control of infection, prevention of local, systemic infection and osteomyelitis.
8. Symptoms and signs: control or reduction of pain at the wound site, stabilisation of the wound, without worsening.
9. Dressing performance: reduction in the number of dressing changes.
10. Quality of life.

Completeness of outcome

We will read the methods section of the RCT to determine if the outcome is reported completely. A score of 0–5 will be given based on how many elements are reported. A ‘fully specified’ outcome will be considered if all five of the following elements are described.

Domain or title of the outcome

The domain or title of each outcome will be noted and will be classified into two groups: healing outcomes and non-healing outcomes (substitute or intermediate outcomes).²⁶ Healing outcomes are those that bring the greatest impact on the patient's life. Substitute outcomes are laboratory variables or physical signs that are used as substitutes for an objective outcome. Intermediate outcomes usually occur during the course of treatment and are intended to replace a significant clinical outcome. In chronic wounds, many intermediate or substituting outcomes have been used because of the complexity of wound healing; therefore, the substitute and intermediate outcomes are used as indicators of improvement in prognosis for such wounds.²⁶ The domains of efficacy/effectiveness outcomes will be classified according to the European Wound Management Association (EWMA) Patient Outcome Group Document (box 1).

In box 1, we present the domains of efficacy outcomes in chronic ulcers that will be classified according to EWMA Patient Outcome Group Document.²⁷

Specific technique or instrument used to make the measurement

The technique used will be considered as ‘specified’ if the RCT authors state with which instruments, tools, scales, scores and/or how the outcome was defined. They will be considered as ‘unspecified’ when they are not reported,

Table 1 Summary of the objectives, outcome, measurement, method of analysis and hypotheses

Objective	Outcome	Measurement	Methods of analysis	Hypotheses
Primary				
To analyse the completeness of reporting of outcomes of therapeutic interventions for pressure ulcers in adults.	Completeness of the outcome.	Count of number of elements reported (domain, specific technique, metrics, aggregation method and time points of analysis).	Median (IQR) elements reported proportion of studies with all five elements reported: count (%).	We hypothesise that completeness and quality of reporting will be sub-optimal.
Secondary				
To determine the proportion of RCTs with reported primary outcomes.	Primary outcome reported.	Count of the number of studies that reports a primary outcome.	Count (%).	We hypothesise that completeness and quality of reporting will be sub-optimal.
To determine the proportion of RCTs with reported objective outcomes.	Objective outcome reported.	Count of the number of studies that reports at least one objective outcome.	Count (%).	
To describe the measurement methods or tools used to evaluate the outcomes.	Measurement methods reported.	Count of the number of studies that reports the measurement method for the outcomes.	Count (%).	
To evaluate the quality of result of reported outcome.	Quality of outcome results reporting.	Count of the number of studies with complete, incomplete or unreported outcome.	Count (%).	

or relevant phenomena are not defined (eg, if ‘wound healing’ has not been defined).

For each outcome, the method or measurement tool used will also be evaluated. To measure outcomes adequately, a scale, scoring system, questionnaire, or other tool can be used. There may be a combination of more than one outcome within a domain of outcomes, such as scoring based on a variety of symptoms, for example, the McGill pain score and the Pressure Ulcer Scale for Healing (PUSH) tool.²¹

It will be verified if there are psychometric property studies for the methods (instruments, scales, among others) to evaluate the outcomes.

Specific metric or format of the data of the outcomes of each participant that will be used for analysis

A specific metric will be considered as ‘specified’ if the RCT authors describe how they would analyse the data, including change from baseline, time-point or time-to-event. If this information is not reported, it will be considered as an ‘unspecified’ metric. The type of metric used will also be noted.

Method of aggregation or how the data of each group were summarised

We will consider that the aggregation method was ‘specified’ if the RCT authors described how the data were summarised, including average, median, percentage or

proportion, or an absolute number. When the authors do not mention any method of aggregation, we will classify this as ‘unspecified’.

Time points that were used for analysis

We will check whether the authors specified the time points to be used in their analysis. When the authors declare the time of judgement of the outcome, it will be considered as ‘specified’.

Evaluation of the quality of result of reported outcome

The reported outcome quality rating of each RCT will be evaluated in the results section and reported on one of three levels, adapted from Chan *et al.*²⁴ In this way, reported outcome result will be considered ‘complete’ when there is enough data to determine the size of the effect (OR and relative risk) and the accuracy measure (CI) or ‘incomplete’ when only p values or qualitative data are reported. When there is no data in the results, although the outcome has been defined in the methods section, we will categorise this as ‘outcome not reported’.²⁴

Statistical analysis

For the primary objective, completeness of outcome reporting will be analysed in two ways. First, we will compute the median (IQR) number of elements reported. Second, we will compute the proportion (%) of studies with complete ‘fully specified’ outcome reporting (ie, all five elements

reported). For the secondary outcomes, proportions (%) will be computed for the number of studies that report a primary outcome, the number of studies that report at least one objective outcome, the number of studies that report the measurement method and the number of studies with complete, incomplete or unreported outcome. All percentages will be reported with 95% CIs.

A summary of the objectives, outcome, measurement, method of analysis and hypotheses is given in [table 1](#).

ETHICS AND DISSEMINATION

In a recent study on the pre-specification of outcomes in protocols of systematic reviews in wound care, the authors concluded that the outcomes were poorly pre-specified and that metric, aggregation and evaluation time elements were rarely properly specified.¹⁹

Quality and completeness of outcomes in published literature and the credibility of the results for decision-making are indispensable for good clinical practice. The use of inadequate, poorly defined or invalid outcomes can lead to waste of resources; or misleading information that overestimates, underestimates or completely negates the potential benefits of an intervention.²⁸ The use of clear outcomes would also improve synthesis of studies (eg, meta-analysis).

Many outcomes are reported in RCTs of PU. It is important to understand which are the most commonly used, especially as primary outcomes and how the outcomes are operationalised.

To emphasise the impact of the heterogeneity and poor quality of outcome, a review found that of 196 RCTs of non-steroidal anti-inflammatory drugs for rheumatoid arthritis, more than 70 outcomes were described.²⁹ In other review, 2000 studies on schizophrenia, 640 instruments were cited of which 369 were used only once, and 149 studies showed unpublished scales, which were a source of bias.³⁰ Only 45% of a cohort of 519 RCTs published in the year 2000 specified the primary outcome, compared with 53% for a similar cohort of 614 RCTs published in 2006.^{31 32}

Given the above, evaluating the quality of outcomes may highlight limitations and inform investigators on adequate approaches to describing and evaluating the outcomes to reduce inconsistencies and biases in the results of future trials.

This review will be disseminated in conference proceedings and peer-reviewed journals. The results will also be presented at scientific conferences.

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