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Early mobilization after skin graft for burn injury in adults (Protocol)

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[Intervention Protocol]

Early mobilization after skin graft for burn injury in adults

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of early mobilization after skin graft for burn injury in adults.

BACKGROUND

Description of the condition

Burn injuries are the fourth most frequent type of traumatic injury, accounting for approximately 180,000 deaths annually worldwide [1]. In 2004, an estimated 11 million people sought medical care due to burn-related injuries [2]. Burn injuries remain a major public health challenge, particularly in low- and middle-income countries (LMICs), where over 90% of burn cases occur [3]. Although burn incidence has declined in high-income countries, it increased in LMICs between 1990 and 2019, exacerbating existing disparities in prevention and treatment [4]. This trend underscores the urgent need for improved burn prevention and management strategies in resource-limited settings [5].

Burn incidence, severity, and mortality also vary across demographic groups. In 2019, younger and middle-aged men had a higher global incidence of moderate and severe burns, and presented the heaviest burden of serious injury in terms of years lived with disability, whereas older women had higher rates of severe and inhalation injuries [6]. Women in LMICs are particularly vulnerable, facing a greater risk of burn-related mortality (24% versus 15% in men) [7], primarily due to domestic hazards such as cooking over open flames [1]. Furthermore, women in these countries have less access to essential interventions, such as blood transfusion, nutritional support, and surgical procedures [7].

Burns can have a profound and lasting impact on survivors' quality of life, particularly in LMICs where access to specialized care is limited. Burns can result from thermal, chemical, electrical, radiation, or friction-related sources [8], and can cause coagulative destruction of various layers of the skin [9]. Burn diagnosis is based on the depth of the injury, the percentage of total body surface area (TBSA) affected, and its cause (etiology). These factors determine the severity and long-term consequences of burns [9, 10, 11]. While partial-thickness burns (first and second degree) typically heal within weeks, full-thickness burns (third and fourth degree) often require surgical intervention and may lead to permanent disability, amputation, or death [12, 13].

Pain management in people with burns is also a challenge due to the presence of multiple types of pain, including background, neuropathic, procedural, and breakthrough pain [14, 15]. Severe pain has been linked to rehabilitation resistance, emotional distress, and even increased suicide risk [16]. While the intensity of pain is the primary concern for immediate management, distinguishing the type of pain is crucial for selecting appropriate interventions [17]. However, current pain assessment tools remain largely unidimensional, emphasizing the need to use diverse instruments that can capture the multifaceted nature of burn pain [15, 18, 19, 20, 21].

Description of the intervention and how it might work

Severely burned adults (> 20% TBSA) commonly require specialized care that involves extended periods of hospitalization and the use of sedatives and analgesics to control pain [8, 22]. An additional concern in the treatment of burn survivors is skin graft failure, which may lead to the need for additional reconstructive surgeries, prolonged hospitalization, and an increased risk of hospital-acquired infections [23]. Skin graft failure can result from localized bleeding outside of blood vessels (hematoma); separation of the skin from underlying tissues (shearing); inadequate fixation to the wound bed (adherence), either in the fibrin-mediated phase (phase I) or in the revascularization-dependent phase (phase II); and death of the transplanted skin tissue (necrosis) [24, 25, 26], frequently resulting in prolonged immobilization [27]. However, immobility is associated with significant complications, including increased length of hospital stay, higher mortality risk, and exacerbation of common burn-related comorbidities, such as intensive care unit (ICU)-acquired weakness and inability to perform full joint range of motion (joint contractures) [28, 29, 30, 31, 32, 33]. To mitigate these effects, international guidelines recommend early mobilization as a key strategy to improve functional outcomes in people with burns [34, 35, 36]. A study analyzed the limitation of range of motion in joints of upper and lower limbs and movement planes after burns, tracking its evolution over time [37]. The results showed that, in the initial phase of recovery, the restriction was greater in the lower limbs, while at 12 months, the most significant limitation occurred in the upper limbs [37].

Early mobilization is characterized by a progression of functional activities, such as mobility exercises in bed, sitting, transfers, standing, and the ability to walk without the need for any kind of assistance (ambulation) [38], started in the first days of critical illness [39]. However, the optimal timing of early mobilization remains controversial. While one clinical guideline defines ‘early’ as within the first 14 days of injury, it also suggests that initiating early mobilization after 7 days may not provide sufficient clinical benefit [32]. Conversely, other studies indicate that mobilization within 48 to 72 hours may yield better outcomes, particularly in critically ill people [40].

The rehabilitation of individuals admitted to specialized burn treatment units is typically divided into three phases: the acute phase (from admission until the onset of wound closure, usually between days 12 and 14), the intermediate phase (lasting until full wound closure), and the long-term phase (continuing until the patient achieves the maximum benefit from rehabilitation, including any necessary reconstructive procedures) [41, 42]. Evidence suggests that initiating physical training during the acute phase may help prevent muscle mass loss and enhance muscle strength during hospitalization [43]. Previous studies report that people who undergo resistance and aerobic exercises during their stay in the burn center may experience greater muscle preservation in the anterior thigh region, compared to people who do not perform the exercises [43]. Evidence also suggests that early mobilization can help wound healing through the stimulation of fibronectin synthesis [44], during extracellular matrix formation, resulting in accelerated reepithelialization [45]. In other populations, such as severely ill adults with sepsis syndrome, early mobilization reduced systemic inflammation [46]. This finding is particularly relevant for people with burns, as burns trigger a persistent systemic inflammatory response, making healing more difficult and contributing to a hypermetabolic state (increase in metabolic rate in response to burn stress) [47]. The metabolic rate can increase by 40% to 80% in the first few months post-burn and may remain elevated for up to a year [47, 48]. This heightened metabolic demand accelerates protein breakdown, leading to muscle mass loss and functional decline [49, 50].

Why it is important to do this review

Clinical trials showed that people with burns who received skin grafts and underwent early ambulation presented longer walking

times and shorter hospital stays compared to people in the to those who underwent late ambulation [51, 52]. In a systematic review and meta-analysis conducted by Lagziel 2021, burn survivors receiving early mobilization had a shorter length of hospital stay compared to those receiving late ambulation or moving after skin grafts [53]. The authors also observed less pain and wound infection in people who walked or moved about (ambulated) earlier. However, the review did not follow standard Cochrane methodological guidance and presents some important methodological limitations, such as the absence of a protocol and the pooling of results from different study designs. Guidelines recommend that early mobilization should be initiated as early as possible in burn survivors [32, 54], with the aim of reducing ICU-acquired weakness and delirium, characterized by a severe disturbance in mental abilities resulting in confused thinking and reduced awareness [32]. Despite the existence of recommendations that suggest the use of early mobilization in people with burns after grafting, the effectiveness and feasibility of this intervention are still unclear [43].

OBJECTIVES

To assess the effects of early mobilization after skin graft for burn injury in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We will consider parallel randomized controlled clinical trials (RCTs) and cluster-RCTs, available in full-text, abstracts, or unpublished, with no restrictions on language or publication year. We will exclude quasi-randomized trials, defined as studies that do not use valid randomization methods to allocate people or groups of people to intervention arms, such as date of birth or day of the week [55]. We will also exclude other types of RCTs, such as cross-over studies, as they are unsuitable for our review question.

Types of participants

Adults (≥ 18 years old), regardless of race and gender, with acute burns due to any cause (e.g. hot solids or liquids, electricity, chemicals, flames), with any depth and percentage of TBSA burned (% TBSA). We will include people who have undergone skin grafting and were admitted to an ICU, or any unit in the hospital setting or a center specializing in burns.

We will consider studies involving a mixed population (e.g. adults and children) if separate data are available for eligible participants or if the study authors can provide them [56]. Otherwise, we will consider studies in which most of the participants are 18 years old or older [56]. Specifically, the mean or median age minus the standard deviation must be greater than 18; or if numerical data or interquartile ranges are provided, at least 50% of participants must be over 18 [57].

Types of interventions

We will consider early mobilization as outlined in Table 1.

We will also include studies that combine more than one intervention, as long as the effects of early mobilization can be evaluated separately (e.g. early mobilization plus usual care versus usual care alone).

We will consider the following comparators outlined in Table 2.

We will include studies involving these interventions and comparators, regardless of intensity, frequency, or duration of treatment.

Outcome measures

Critical outcomes

We will include the trials that meet the inclusion criteria of this review, regardless of outcomes reported.

We considered recommendations from the Core Outcome Measures in Effectiveness Trials (COMET) Initiative [58, 59, 60, 61], and Cochrane systematic reviews regarding people with burns [62, 63], and early intervention [64], to define the results potentially relevant to this review.

If the same outcome is measured using multiple scales or instruments, either within a single study or across different studies, we will apply a predefined hierarchy to select the measure to be reported in our results. We will report the remaining measures in the table of included studies. Below, we describe each outcome and list the relevant measures in order of priority.

Time to wound healing, including that of grafted site wounds

Considered as the period when the wound reached complete epithelialization or when the majority of epithelialization was achieved [60]. This outcome can be reported as time to event (wound healing) or time (in days), evaluated through planimetry or clinical assessment (e.g. photography) [60].

Pain

Pain intensity: assessed through:

- Burn Specific Pain Anxiety Scale (BSPAS) [15, 20];
- Critical Care Pain Observation Tool (CPOT) [21];
- Visual Analogue Scale (VAS), Numerical Rating Scale (NRS) or Verbal Rating Scales (VRS) [18];
- McGill Pain Questionnaire [20];
- Behavior Pain Scale (BPS);
- Breakthrough Pain Assessment Tool (BAT) [65]; or
- Brief Pain Inventory (BPI).

Pain classification: can be classified as:

- background pain (i.e. defined as constant resulting from direct injury to or inflammation of skin tissue);
- procedural pain (i.e. characterized by increased hyperalgesia during or immediately after a dressing change or rehabilitation efforts);
- neuropathic pain (i.e. caused by direct injury or inflammation of neural tissue in the peripheral or central nervous system, often persisting after burn wounds have healed); or
- breakthrough pain (i.e. transient worsening of pain, unrelated to procedures, due to insufficient analgesia or changes in pain mechanisms over time) [14].

We will consider the assessment of pain classification through any of the following methods:

- clinical evaluation (e.g. by assessing the characteristics of pain);
- validated tools (e.g. Douleur Neuropathique 4 (DN4) or PainDETECT, Neuropathic Pain Questionnaire (NPQ) [19]);
- imaging (e.g. Magnetic Resonance Imaging (MRI), or Positron Emission Tomography (PET) Scan); or
- inflammatory markers (e.g. cytokines).

Quality of life

Considered as the subjective perception of an individual's quality of life in relation to the physical, mental, and social aspects of health [66]. Assessed through the Burn Specific Health Scale (BSHS), Brisbane Burn Scar Impact Profile (BBSIP), Short Form-36 (SF-36) [60, 67].

Adverse events or prespecified complications

We will evaluate all serious adverse events collectively, as well as all non-serious adverse events. We will evaluate serious and non-serious complications using the same approach.

- **Serious adverse events:** defined as any undesirable occurrence related to the intervention that threatens life, requires hospitalization or results in persistent or significant disability (e.g. graft loss, sepsis, or wound infection) [61, 68]
- **Non-serious adverse events:** defined as any undesirable occurrences related to the intervention that do not threaten life [69] (e.g. temporary mild pain or redness)
- **Serious complications:** defined as undesirable occurrences not related to the intervention that threatens life (e.g. hypovolemic shock, compartment syndrome, acute kidney failure)
- **Non-serious complications:** defined as undesirable occurrences not related to the intervention that threatens life (e.g. blisters, itching, skin peeling)

We will group outcomes into the following sets of time points.

- **Short term:** up to 1 month after the start of the intervention (during hospitalization)
- **Intermediate term:** from more than 1 month to 6 months after the start of the intervention
- **Long term:** from more than 6 months to 1 year after the start of the intervention
- **Longer term:** more than 1 year

If we find a study that conducted two or more assessments in the short term, we will prioritize the longer segment.

Important outcomes

Physical function

- **Ability to do daily tasks:** defined as the ability for mobility, self-care, and performance of daily activities [60]. This is assessed through Functional Assessment for Burns — Critical Care (FAB CC), Functional Assessment for Burns (FAB score), Shortened Disabilities of the Arm, Burnt Hand Outcome Tool (BHOT), Lower Limb Functional Index — 10 (LLFI-10), Shoulder and Hand Questionnaire (QuickDASH), Sollerman Hand Function Test (SHT) or objective tests such Timed Up and Go test (TUG) [70], 30-Second Sit-to-Stand Test, or other walking tests (e.g. 10-Meter Walk Test).
- **Time to return to work, school, or previous occupation:** i.e. ability to remain the same prior to hospitalization, transitioning into a modified or new modality [71]. Reported as number of people returning to work (yes/no), number of days between hospitalization or any resumption of work [71].

Length of hospital stay (reported in days)

Death

- From the burn
- From any cause

Search methods for identification of studies

Electronic searches

We will carry out sensitive searches, without limitation of year of publication or language, of the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; latest issue), via the Cochrane Register of Studies;
- MEDLINE via PubMed (1996 to present);
- Embase via Elsevier (1947 to present);
- Literature Latin American and Caribbean Health Sciences (LILACS) via the Virtual Health Library (1982 to present);
- Physiotherapy Evidence Database (PEDro) (https://pedro.org.au/; latest issue).

To identify RCTs, we will apply Cochrane's highly sensitive filters for searching RCTs in MEDLINE via PubMed and Embase via Elsevier, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* [72].

To identify recently published, ongoing and unpublished studies, we will also search the following clinical trial platforms:

- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP); https://trialsearch.who.int/;
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (https://www.clinicaltrials.gov/).

We have listed all search strategies in Supplementary material 1.

Searching other resources

To identify additional potentially important studies, we will handsearch the reference lists of included studies.

We will handsearch conference abstracts and gray literature (i.e. literature that has not been formally published or studies not indexed in databases).

We will complement electronic searches with manual searches in congress and conference proceedings, such as the:

- International Society for Burn Injuries (ISBI) Congress (from inception to date of search);
- European Burns Association (EBA) Congress (from inception to date of search);
- Brazilian Burns Congress (from inception to date of search).

We will contact the authors of the primary studies to identify additional studies potentially important for this review and request additional information when necessary.

Data collection and analysis

Selection of studies

Two review authors (TSS and CFRS) will independently examine the titles and abstracts of the results identified by the search, using the Rayyan application [73]. The same authors will then independently examine the full text of potentially relevant reports. We will resolve any disagreement through discussion and, if required, we will consult a third review author (ACPNP).

We will identify and remove duplicates. After full-text assessment, we will gather multiple reports from the same study so that each study, rather than each report, is the unit of interest in the review. Where necessary, we will contact study authors for further information on eligibility criteria. We will document the selection process with sufficient detail to complete a PRISMA flow diagram and a table detailing the characteristics of excluded studies [74].

Data extraction and management

We will develop a data extraction form, which two review authors (TSS and RACJ) will pilot, with any discrepancies resolved by consensus and the form adjusted as necessary. After this stage, two review authors (TSS and RACJ) will independently extract the following data.

- **Identification of the study:** title, authors, country, and year
- **Methods:** study design, randomization, total study duration, details of any run in period (e.g. walking training before graft placement), study setting (e.g. ICU, specialized center for the care of people with burns), withdrawals, and date of study
- **Participants:** number of participants who were randomized, age, age group, sex, types of burns (e.g. hot solids or liquids, electricity, chemicals, flame), burn location (e.g. upper body, lower limbs, or whole body) and donor area, % TBSA burned, burn depth (e.g. depth partial or total or classified as by first, second, and third degree), graft characteristics (e.g. classified based on their origin as autografts, allografts, and xenografts, or other valid classification reported by the authors), allocation unit, if applicable (e.g. ICU, specialized burn center, hospital), comorbidities, inclusion criteria, and exclusion criteria
- **Interventions:** type of intervention (resistance exercises, range of motion exercises, walking exercises, among others); early mobilization details (equipment, duration, intensity, and frequency); details of the comparator group intervention and concomitant interventions
- **Results:** primary and secondary outcomes specified, collected and effectively reported, time points collected and reported, number of missing/not assessed participants for each outcome, method for handling missing participant data (example, analysis by protocol or by intention to treat), and number of participants analyzed
- **Notes:** occurrence of funding and potential conflicts of interest of the study authors

A third review author (NI) will resolve any disagreements. In the absence of information or incomplete information, we will contact the study authors for further information. One review author (TSS) will enter data into Review Manager (RevMan) [75], and a second review author (ACPNP) will check data entry.

Risk of bias assessment in included studies

Two review authors (TSS and RACJ) will independently assess the risk of bias for each result using the Risk of Bias tool 2.0 (RoB 2) outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [76]. In the event that any author of this review is also an author of studies included in the review, we ensure that the involved authors will not participate in the risk of bias assessment for their own studies. We will resolve any disagreements by consensus or, if necessary, by a third review author (ACPNP). The effect of interest will be the effect of assignment to the interventions [76].

We will assess the risk of bias for outcomes, considering the priority order defined in the outcome measures section, classifying them according to time points (short, intermediate, long, and longer term). Additionally, we will conduct risk of bias assessment based on the following domains:

- bias arising from the randomization process;
- bias due to deviations from intended interventions;
- bias due to missing outcome data;
- bias in measurement of the outcome; and
- bias in selection of the reported result.

As indicated in the *Cochrane Handbook for Systematic Reviews of Interventions*, to assess the risk of bias in cluster-randomized trials, we will use the specific RoB 2 tool for this type of study [76, 77].

We will judge each potential source of bias as either 'low risk of bias', 'some concerns', or 'high risk of bias', based on answers to the signaling questions in RoB 2. The overall risk of bias for each outcome will be determined based on the RoB 2 algorithm, following the guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* [76], and will be classified according to the domain considering the most unfavorable assessment across the different domains [76]. We will contact study authors to clarify any unclear or missing information regarding the domains evaluated. We will use the Excel tool to manage and record RoB 2 assessments [77], and to make consensus decisions for signaling questions. We will make the details of the judgments available as additional appendices.

Measures of treatment effect

For dichotomous outcomes, we will present the results as risk ratio (RR) along with their respective 95% confidence intervals (CI) [56]. For continuous outcomes, we will report results as mean differences (MD) or standardized mean differences (SMD), accompanied by their respective 95% CIs [56]. We will use MDs (pre- and post-intervention) when different studies measure the outcome with the same instrument. In the absence of results reported as MDs or in the absence of an appropriate correlation between individual measurements, we will resort to the data reported post-intervention. We will use SMDs when different studies measure the same outcome using different scales. If a study presents results across various time intervals, we will opt for the last time point, in accordance with the timeframes (short term, intermediate term, long term, and longer term) specified in this protocol.

If adjusted data are available (analysis of variance (ANOVA) or analysis of covariance (ANCOVA)), we will prioritize the use of these

data. Whenever possible, we will also prioritize the use of intention-to-treat (ITT) or full analyses when they are reported (i.e. those in which data are imputed by the trial authors for participants who were randomly assigned but did not complete the study), instead of completer or per protocol analyses. We will not undertake imputations in cases where this was not done by the primary study authors.

Unit of analysis issues

In RCTs with parallel groups, the unit of analysis will be the individual participant. In cluster-RCTs, the unit of analysis will be the ICU, specialized burn center, or hospital.

When participants have multiple burns, the unit of analysis will be the participant, not the individual burns. We will use the total body surface area burned (% TBSA) as a reference to determine the overall extent of the burn in participants.

If there are two comparisons of interest in a multiple-arm study (e.g. early mobilization A (early ambulation) versus C (bed rest) and early mobilization B (early active-assisted exercise in bed) versus C (bed rest) in a single study), and they are combined in the same meta-analysis, we will either combine the interventions (e.g. early mobilization A plus early mobilization B) or halve the data from the comparison group to avoid duplication of data. For dichotomous outcomes, we will use participants, rather than events, as the unit of analysis (e.g. the number of participants who experienced graft infection, instead of the number of occurrences of graft infection per person). However, if rate ratios are reported in a study, we will analyze them on this basis.

If we identify cluster-randomized trials, we will adjust sample sizes using an estimate of the intracluster correlation coefficient (ICC) obtained from the study itself, a similar study, or a similar population (if available), as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* [56]. If ICC from other sources are used, we will state this explicitly and conduct sensitivity analyses to examine the effect of variation in the ICC.

If we find both cluster-RCTs and individually randomized trials, we will synthesize the relevant information. We will combine the results of both if there is little heterogeneity between the study designs and if the interaction between the intervention effect and the choice of randomization unit is unlikely. We will perform a sensitivity analysis to investigate the effects of the randomization unit [78, 79, 80].

Dealing with missing data

We will contact study authors by email to request relevant data in cases of uncertainty about the data presented in the included studies. Also, we will reach out to authors of ongoing studies and, in cases where results are available only in abstracts, to obtain provisional or additional data. If, despite contacting the study authors, access to the requested data remains unavailable and if their absence is likely to introduce significant bias, we will attempt to estimate the missing values (e.g. standard deviation, effect size, P values, or CIs) using the available data. We will conduct this process using the RevMan calculator, following the guidelines outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [56]. We will explore the impact of including the study on the overall results through a sensitivity analysis, and we will present the results with and without studies that contain missing data. We will address the potential impact of missing data on the review's findings in the discussion section [56]. Furthermore, this scenario will be taken into account in the GRADE classification for the affected outcomes.

Reporting bias assessment

We will conduct comprehensive searches to identify eligible studies. If there are at least 10 studies included in a meta-analysis, we will assess the likelihood of publication bias through the funnel plot and Egger's regression test [81]. Also, we will attempt to identify any selective reporting in the included publications by comparing the study protocols with the final articles. In the absence of a protocol, we will seek information about the outcomes in study registration databases. Furthermore, we will compare the results listed in the 'Methods' section of the final article with those presented in the 'Results' section.

Synthesis methods

We will conduct the synthesis of all eligible studies in the primary analyses. If at least two studies are sufficiently homogeneous, that is, similar in terms of participants, interventions, comparisons, and outcomes, we will combine their results in a meta-analysis and ensure that data from rating scales are entered with a consistent direction of effect (e.g. lower scores indicating improvement in all included studies for that particular outcome result). We will conduct separate meta-analyses considering the % TBSA burned (i.e. early mobilization versus standard care in people with < 10% TBSA, 10% to 20% TBSA, or > 20% TBSA) [8, 82]. We will include all eligible studies in our primary analyses, regardless of their risk of bias. When conducting meta-analyses, we will use the inverse variance or Mantel Haenszel methods and the random-effects model.

If meta-analysis is not feasible, we will report the results by following the Synthesis Without Meta-Analysis (SWiM) guidance [83].

Investigation of heterogeneity and subgroup analysis

We will assess statistical heterogeneity through visual inspection of forest plots and using the I^2 statistic. We will interpret the I^2 statistic as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 75% may represent substantial heterogeneity; and 75% to 100% represents considerable heterogeneity [56]. We will explore possible reasons for heterogeneity through subgroup analysis should there be a sufficient number of studies available for the analysis. We will use the RevMan subgroup test to compare the differences between them. For subgroup analysis, we will consider the following data.

- Age: adults versus elderly (> 65 years)
- LMIC versus high-income country (as defined by the World Bank classification of countries [84]
- Early mobilization onset time (before and after 72 hours postoperatively of skin grafting)
- Graft recipient region (e.g. upper limb, trunk, or lower limb)

We will assess clinical heterogeneity by making qualitative comparisons of the populations, interventions, and outcomes. The subgroup analysis will be conducted based on primary and secondary outcomes, using the formal test for subgroup differences in RevMan Web [85].

If we cannot identify the cause of heterogeneity, we will downgrade the certainty of the evidence due to inconsistency during GRADE assessments.

Equity-related assessment

To assess the equity-related factors in the included studies, we will consider the PROGRESS-plus factors [86]. If data are available, we will analyze the difference in early mobilization effects between the PROGRESS-plus factors in subgroup analysis, specifically for the age and place of residence (LMICs versus high-income countries) items. Also, we will consider the gender/sex item, for which we will conduct a descriptive analysis and present the results in a table. We will discuss the possible reasons for the differences found [87].

Sensitivity analysis

We will conduct sensitivity analyses by excluding the following analyses from the critical outcomes.

- For assessment of the risk of bias, removing studies with an overall high risk of bias or unclear risk of bias in at least two domains of the risk of bias table
- Removing studies with missing data

If we include cluster-RCTs in meta-analyses with individually randomized trials, we will conduct a sensitivity analysis to investigate the effect of the randomization unit [78]. When ICCs from other sources are used in cluster-RCTs, we will conduct a sensitivity analysis to assess the variation in the ICC [56].

Certainty of the evidence assessment

We will assess the certainty of the body of evidence for each outcome using the GRADE approach [88]. For this purpose, we will use the following GRADE considerations:

- risk of bias;
- indirectness of evidence;
- inconsistency of results;
- imprecision of effect estimates; and
- publication bias

Two review authors (TSS and CFRS) will independently assess the certainty of the evidence, and classify it as either 'high', 'moderate', 'low', or 'very low', according to performance in relation to the five criteria listed above. In the event that any author of this review is also an author of studies included in the review, we will ensure that the involved members of the review team who authored the included studies will not participate in the GRADE assessments. A third review author (ACPNP) will resolve any disagreements.

We will use GRADEpro GDT software to summarize our judgments about the certainty of the evidence for each main outcome [89]. We will consider the overall risk of bias assessment, as determined by the RoB 2 tool, to support our GRADE decision on downgrading to risk of bias. The judgment and reasons for the judgment will be presented in a table containing the main findings for seven of the outcomes measurements assessed:

- time to wound healing (short-term): evaluated through planimetry;
- serious adverse events (medium-term);
- serious complications (medium-term);
- pain (medium-term): assessed through BSPAS;
- quality of life (longer-term): assessed through the BSHS;
- length of hospital stay reported in days (short-term): assessed in days;
- death from the burn or any cause (long-term).

In the absence of the instruments specified for assessing the mentioned outcomes, we will consider alternatives based on the priority order established in the Outcome measures section.

Consumer involvement

Our goal is to ensure that this Cochrane review is relevant and useful for both burn survivors and healthcare professionals involved in the care of people affected by burns. In developing this protocol, we sought evidence that emphasizes the importance of outcomes from the perspective of people with burns, based on the COMET initiative [58]. During the review process, we plan to involve people who have experienced the impact of burns, and healthcare professionals with extensive experience in the care of burn survivors. We will invite these contributors to provide feedback on the review findings. Their involvement will be crucial in ensuring that the plain language summary is clear, accessible, and accurately reflects the most relevant information for both lay people and professionals in the field.

SUPPLEMENTARY MATERIALS

Supplementary materials are available with the online version of this article: 10.1002/14651858.CD016109.

Supplementary material 1 Search strategies

ADDITIONAL INFORMATION

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Editorial and peer-reviewer contributions

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- Sign-off Editor (final editorial decision): Toby Lasserson, Cochrane Deputy Editor-in-Chief;
- Managing Editors (selected peer reviewers, provided editorial guidance to authors, edited the article): Hannah Payne and Gail Quinn, Cochrane Central Editorial Service;
- Editorial Assistant (conducted editorial policy checks, collated peer-reviewer comments and supported editorial team): Lisa Wydrzynski, Cochrane Central Editorial Service;
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TSS: none

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Data sharing is not applicable to this article as it is a protocol, so no datasets were generated or analysed.

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ADDITIONAL TABLES

Table 1. Interventions groupings with a description and eligible interventions

Intervention grouping	Description of intervention grouping	Eligibility criteria for interventions in the group
Early mobilization	Rehabilitation initiated as early as possible for people with burns after skin graft surgery [64], or planned to start earlier than the care received by the control group.	• Any combination of one or more of the types of active or active-assisted exercise, including but not limited to range of motion, bed mobility, transfer training, pre-gait exercises, ambulation, resistance exercises, aerobic exercise, exercises for independence in functional tasks. • With or without the aid of cycle ergometers, walking aids, elastic resistance bands, orthoses, compressive dressings or other resources reported by the studies' authors. • Conducted in specialized burn centers, intensive care units, or in any hospital setting. • Provided by physiotherapists or other healthcare professionals.

Table 2. Comparison groupings with a description and eligible interventions

Comparison grouping	Description of comparison grouping	Eligibility criteria for the comparison group
Mobilization delayed	Mobilization that commences later than the early mobilization group [64]	Mobilization equal to the intervention group
Usual care	Standard care that does not involve mobilization, and that is initiated at the same time as the mobilization [64]	Routine nursing care, positioning of the affected area, adjustment of orthoses, or other standard treatments reported in the RCTs
Other non-pharmacological therapies	Non-pharmacological therapies that do not involve mobilization, which begin at the same time as mobilization, and are not considered as usual care	For example, respiratory muscle exercises [64]
Pharmacological therapies	Any pharmacological agent used for burn treatment that is started at the same time as mobilization and is not considered as usual care	For example, topical antimicrobial agents [90]

Abbreviations: RCT: randomized controlled trial