Εικόνα που περιέχει κείμενο, σύμβολο, λογότυπο, γραμματοσειρά

Περιγραφή που δημιουργήθηκε αυτόματα

**ARISTOTLE UNIVERSITY OF THESSALONIKI**

**FACULTY OF HEALTH SCIENCES**

**SCHOOL OF MEDICINE**

Early Mobilization of ICU-Admitted Adult Patients: Overview of Systematic Reviews

A thesis submitted in fulfillment

of the requirements for the degree of

Master of Science in Health Statistics & Data Analytics

By

Andreas Polychronidis

Thessaloniki, April 2025

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At

The Faculty of Health Sciences

School of Medicine

Aristotle University of Thessaloniki

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Thessaloniki, April 2025

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**Word count: 8364**

Contents

[Table of Abbreviations 5](#_Toc194855762)

[Acknowledgments 6](#_Toc194855763)

[Abstract 7](#_Toc194855764)

[Introduction 8](#_Toc194855765)

[Study Design 9](#_Toc194855766)

[Inclusion & Exclusion Criteria 9](#_Toc194855767)

[Participants 9](#_Toc194855768)

[Interventions 10](#_Toc194855769)

[Control - Comparator 14](#_Toc194855770)

[Outcomes 14](#_Toc194855771)

[Methods 18](#_Toc194855772)

[Search Strategy 18](#_Toc194855773)

[Screening and Selection 18](#_Toc194855774)

[Data Extraction 18](#_Toc194855775)

[Quality Assessment 19](#_Toc194855776)

[Risk of Bias Assessment 19](#_Toc194855777)

[Data Synthesis & Analysis 19](#_Toc194855778)

[Statistical Analysis 20](#_Toc194855779)

[Ethical Considerations 20](#_Toc194855780)

[Results 21](#_Toc194855781)

[Study Selection 21](#_Toc194855782)

[Study Characteristics 22](#_Toc194855783)

[AMSTAR2 24](#_Toc194855784)

[Corrected Covered Area (CCA) 26](#_Toc194855785)

[ICU-Acquired Weakness 27](#_Toc194855786)

[ICU Length of Stay 27](#_Toc194855787)

[Hospital Length of Stay 29](#_Toc194855788)

[ICU Mortality 29](#_Toc194855789)

[Mechanical Ventilation & Weaning Duration 30](#_Toc194855790)

[Quality of Life 32](#_Toc194855791)

[Incidence & Duration of Delirium 32](#_Toc194855792)

[Adverse Events & ICU Complications 33](#_Toc194855793)

[Discussion 35](#_Toc194855794)

[Suggestions for Clinical Practice 36](#_Toc194855795)

[Challenges and Barriers to Implementation 37](#_Toc194855796)

[Future Directions and Research Priorities 37](#_Toc194855797)

[Conclusions 38](#_Toc194855798)

[Funding & Competing Interests 39](#_Toc194855799)

[References 40](#_Toc194855800)

[Appendix 52](#_Toc194855801)

# Table of Abbreviations

|  |  |
| --- | --- |
| **Abbreviation** | **Meaning** |
| EM | Early mobilization |
| ICU | Intensive care unit |
| MV | Mechanical Ventilation |
| ICU-AW | Intensive care unit – acquired weakness |
| NMES | Neuromuscular Electrical Stimulation |
| SR | Systematic review |
| AMSTAR | A measurement tool to assess systematic reviews |
| PICO | Population – Intervention – Control – Outcome |
| RCTs | Randomized Controlled Trials |
| RoB | Risk of bias |
| SBT | Spontaneous breathing trials |
| IMT | Inspiratory muscle training |
| SC | Standard care |
| UC | Usual Care |
| QoL | Quality of life |
| CT | Conventional therapy |
| CP | Conventional physiotherapy |
| PFT | Pulmonary function training |
| SEM | Standardized early mobilization |
| PT | Physical therapy |
| AAH | Artificial airway humidification |
| TENS | Transcutaneous electrical nerve stimulation |
| APWT | Air pressure wave therapy |
| MD | Mean difference |
| ST | Swallowing therapy |
| SMD | Standardized mean difference |
| WMD | Weighted mean difference |
| OR | Odds ratio |
| RR | Risk ratio |
| RD | Risk difference |
| CI | Confidence interval |
| LOS | Length of stay |

# Acknowledgments

This overview represents my thesis for the conclusion of my studies in the postgraduate program “Health Statistics & Data Analytics” of the School Medicine at the Aristotle University of Thessaloniki. Throughout my studies, my professors were always helpful and contributed a lot to the completion of my studies.

I would particularly like to express my deepest gratitude to my professor and supervisor of my thesis, Ms. Anna Bettina Haidich, Professor of Medical Statistics & Epidemiology, for scientific and advisory guidance during the preparation of my thesis, plus constructive and insightful feedback. I would also like to thank Dr. Dimitrios Lathyris for his scientific input, constructive discussions, and encouragement throughout the preparation of my thesis.

Finally, I would like to thank my family, who have supported me throughout my academic journey, including the last 2 years, and to whom I owe all my academic achievements to this day.

# Abstract

**Background:** Many critically ill patients admitted to the Intensive Care Unit (ICU) experience several problems from extensive bed rest and immobility, including ICU-acquired weakness (ICU-AW), and functional decline after their discharge (1). Early mobilization (EM) has advanced in the last decades as a capable intervention for critically ill patients, and this thesis will provide a comprehensive overview of systematic reviews evaluating the efficiency of early mobilization interventions in ICU-admitted adult patients. (2)

**Objectives:** The primary outcomes include ICU-acquired weakness, ICU length of stay, and hospital length of stay. Secondary outcomes involve possible ICU complications and adverse events, as well as ICU mortality, weaning duration, duration of mechanical ventilation, and health-related quality of life after hospitalization.

**Design:** Overview of systematic reviews and meta-analyses.

**Methods:** The databases searched were MEDLINE via PubMed, Epistemonikos, and CINAHL Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Library and CINAHL until January 2025. The quality of these reviews was assessed by the AMSTAR 2 tool (A Measurement Tool to Assess systematic Reviews) (3). Additionally, the Risk of Bias (RoB) Assessment from the authors of each review was considered.

**Results:** This overview synthesized findings from 21 systematic reviews and meta-analyses consisting of 241 primary studies where consistent evidence supported the benefits of early mobilization. Key findings indicated that early mobilization could lower significantly the duration of mechanical ventilation, reduced ICU and hospital length of stay, and mitigated the risk of long-term disability.

**Conclusions:** This overview discussed strategies to overcome these barriers, emphasizing the importance of patient care and evidence-based protocols to ensure effective mobilization. Future research directions may include the investigation of cost-effectiveness, long-term outcomes like functional status and activities of daily living, plus the integration of early mobilization into routine ICU practice.

**Keywords:** Early Mobilization, ICU, Length of Stay, Mortality, Delirium, Systematic Reviews, Meta-Analysis

# Introduction

Cases of critical illness often require admission to the Intensive Care Unit (ICU), where patients are subject to invasive procedures, prolonged immobility, and deep sedation (4). Prolonged ICU hospitalization may contribute to ICU complications and serious adverse events leading to severe issues such as ICU-acquired weakness (ICU-AW), functional disabilities, and impaired quality of life. ICU-AW is a critical disorder characterized by severe muscle weakness, related among others, to sepsis, and immobility, affecting a notable proportion of the patients with prolonged ICU stays and can persist for months or even years, impairing the patient’s quality of life after hospitalization. (5,6)

Early mobilization (EM) is the induction of passive or active physical activity within the first few days of ICU admission and has been proposed as a strategy to mitigate these adverse effects. There are various ways to involve patients in activities ranging from passive movements to sitting, transferring to the edge of the bed, seated balance activities, early standing activities (7), and walking (with or without mechanical/nursing assistance). The early mobilization treatment targets the physiological and the psychological consequences of immobility. Emerging evidence from randomized controlled trials (RCTs) and observational studies suggest that EM can enhance functional outcomes, shorten ICU and hospital stays, improve the recovery process, and minimize long-term issues for patients. (8,9)

The incorporation of early mobilization into ICU care marks a substantial change from the conventional medical approach of extended bed rest and heavy sedation (10). Nevertheless, implementing early mobilization comes with challenges, such as worries about patient safety, the need for healthcare staff training, and the allocation of resources. Furthermore, differences in protocols and a lack of agreement on best practices impede broader adoption.

This overview of meta-analyses of randomized control and observational studies that treat early mobilization (EM) in ICU patients aims at the evaluation of the effectiveness, safety, and implementation of early EM techniques for adult patients admitted at the ICU. We evaluated the existing evidence on the impact of early mobilization on ICU-AW incidence, on ICU and hospital length of stay, and on mortality and quality of life. We also estimated the quality of evidence and the potential influence of various early mobilization and usual care protocols on treatment effects. Finally, we reported and assessed the potential biases and adverse events that were reported in the included studies.

# Study Design

This thesis employed an overview of systematic reviews methodology, specifically focusing on systematic reviews and meta-analyses that examined the efficacy, safety, and feasibility of early mobilization (EM) in ICU-admitted adult patients. Study design joined a structured approach to identify, appraise, and synthesize findings from existing literature in a PICO format.

## Inclusion & Exclusion Criteria

Systematic reviews and meta-analyses were included if they focused on early mobilization interventions or treatments for adult ICU patients. We selected the appropriate reviews based on reported outcomes related to ICU-acquired weakness, ICU mortality, the duration of mechanical ventilation or weaning, incidents of delirium, adverse events, the length of ICU or hospital stay, and overall quality of life assessments following hospitalization. Additionally, we considered only those reviews that adhered to systematic review methodologies, such as the PRISMA guidelines.

The focus of this study was limited to interventions administered during the ICU stay. We have excluded interventions that involved rehabilitation outside the ICU or those aimed at the post-critical care phase. Additionally, reviews focusing on pediatric or adolescent populations or patients admitted for neurological, cardiac surgeries or strokes have been excluded. We also excluded any reviews that did not perform a meta-analysis or studies that did not include any empirical research. These criteria ensured that the reviews included focus on the efficiency of early mobilization for patients during their ICU admission period while considering a specific population group that is relevant to this thesis. The thesis will highlight the diverse and complex approaches to early mobilization and their impact on patients admitted to the ICU with the compilation of a diverse array of evidence-based interventions.

## Participants

This overview focused on adult ICU patients who had been admitted for any critical illness apart from neurological and cardiac surgeries, or stroke events. Systematic reviews and meta-analyses were included only if they specifically looked at early mobilization interventions during the ICU stay and performed meta-analysis on the data of the included studies. These interventions aimed to tackle issues like ICU-acquired weakness, ICU mortality, and the length of mechanical ventilation or weaning. The reviews also assessed the occurrence of delirium, adverse events, the ICU and hospital length of stay, and the quality of life after hospitalization.

## Interventions

Early mobilization (EM) encompasses a range of interventions designed to counteract the negative effects of immobility in ICU-admitted patients. These interventions aim to promote physical activity as early as clinically feasible during a patient’s ICU stay, improving functional outcomes and overall recovery. The interventions included in this study are as follows:

1. **Passive and Active Mobilization**

Passive mobilization discusses a series of clinical interventions protocols which can provide a suitable recovery process for a group of patients admitted in the ICU. There are various passive mobilization techniques such as passive joint mobilization (11), passive motion of the lower extremities (12), daily passive range of motion (PROM) (13), and the passive movement of the patient’s limbs (14). This technique is utilized for ICU-admitted patients who are either sedated, unconscious, or unable to initiate movement (15,16). Movements are manually performed by healthcare professionals who move the patient’s joints through their range of motion. The primary focus is placed on large joints to maintain joint flexibility and circulation, and the primary goals of the passive mobilization treatment are to prevent joint stiffness and contractures, improve muscle strength (17), and increase vascular function (18) even when the patient cannot engage actively. Safety is a priority, with vital signs and patient tolerance closely monitored to avoid overstimulation or stress and is adjusted according to patient-specific conditions such as fractures, edema, or surgical restrictions. (19)

Active mobilization requires the patient’s voluntary participation and is suitable for those who are prepared to engage in purposeful movement (6,20). Patients actively perform exercises such as arm and leg lifts, or grip-strength activities, either in bed or while seated. These activities gradually intensified to include sitting on the edge of the bed, standing with assistance, and walking when clinically feasible. The goals of active mobilization are the enhancement of muscle strength, the prevention of muscle atrophy, improvement of respiratory function and cumulative endurance and functional capacity to facilitate faster recovery (21,22). Safety and continuous monitoring are critical components, with continuous observation of physiological parameters such as heart rate, blood pressure, and oxygen saturation. Early mobilization is adjusted based on the patient’s hemodynamic and respiratory stability. (23)

Passive and active mobilization in the ICU requires that early interventions are based on the health profile of every patient, while balancing the benefits of activity with the risks of these activities may pose to a critically ill patient (24). Proper education and training for the ICU staff ensures the safe and effective implementation of these mobilization strategies, while the combination of passive and active mobilization helps ICU teams initiate the recovery process early, even for patients in the most critical stages, promoting better physical and functional outcomes while minimizing complications associated with immobility. (9,25,26)

1. **Early Physical Activity**

Early physical activity (EPA) is defined as any body movement produced by skeletal muscles that require energy consumption (27), and is critical for many early mobilization strategies, focusing on encouraging movement and exercise within the first 24 to 48 hours after ICU admission, if patients’ clinical condition permits physical rehabilitation. Despite the initiation of early physical therapy in ICU-admitted patients, they could still require mechanical ventilation (28). This method mitigates the negative impacts of immobility and improves the recovery process for critically ill adults (29). Since physical function may only partially recover after ICU discharge, detailed evaluations during and after ICU stay can be crucial in identifying patients that face a substantial risk of functional deterioration. (27)

The first step towards early physical activity involves a detailed assessment of the patient's current health status. Several key factors are carefully reviewed to ensure safety of patients, such as hemodynamic stability, oxygenation levels, sedation depth, and overall health (2,30). Healthcare professionals develop a specific activity plan for ICU-admitted adult patients and the interventions can vary from basic in-bed exercises to more active movements, including several in-bed exercises; involve ankle pumps, leg lifts, and arm movements can provide enhanced circulation and maintain joint flexibility. This is typically done once the patient shows enough stability in their blood flow and breathing. The advancement of physical condition can be translated to different activities, such as sitting on the edge of the bed, moving to a chair, and standing with support (mechanical or nursing). These activities help build muscle strength and balance, setting the stage for out-of-bed exercises. (31,32)

The intensity and duration of physical activity is increased according to the patient's tolerance and recovery status. Sensors to detect motion can be used to objectively monitor active and sedentary physical activity over time (33). Each session is closely monitored, with vital signs like heart rate, blood pressure, oxygen saturation (34), and respiratory rate being continuously checked for any signs of distress. Adjustments are made to prioritize the patient's comfort and safety. EPA in critically ill patients can be lifesaving and can prevent complications such as ICU-acquired weakness, thromboembolism, and pulmonary issues, while also facilitating quick recovery of functional independence (Contributors, Early Mobilization in the ICU, 2024). By integrating physical activity early during the ICU stay, patients are better prepared to move on to the next stages of medical care, which can lead to shorter ICU and hospital stays (8,35) and enhanced long-term quality of life. (36)

1. **Neuromuscular Electrical Stimulation (NMES)**

Neuromuscular electrical stimulation uses a device that applies electrical impulses to nerves, causing muscle contractions that mimic the action that may originate from the nervous system when voluntary muscle contraction is difficult or impossible (37), without the need for neural stimuli for the recruitment of muscle fibers (38). This stimulation can improve strength and flexibility while helping to counteract the effects of inactivity. It is usually used to "re-train" or "re-educate" muscles, advocating the appropriate cardiovascular function through the activity of large muscle groups which aids in their recovery and strength building during large periods of immobility. This method is crucial for maintaining muscle strength and preventing atrophy in critically ill patients (39,40), even when they cannot engage in active movement. Additionally, several studies have reported that NMES has demonstrated substantial benefits in patients’ rehabilitation process, especially in the reduced duration of mechanical ventilation.

1. **ABCDEF Bundle**

The ABCDEF bundle is a detailed, evidence-based framework aimed at improving outcomes for critically ill patients during their stay in the ICU. It focuses on corresponding care strategies that tackle the complexities of ICU treatment, such as managing sedation, preventing delirium, and encouraging early mobilization (41,42). The primary goal of the bundle is to minimize ICU-related complications, improve recovery, and promote a patient-centered care approach. Components of the ABCDEF bundle have been linked with positive short-term benefits for ICU patients (43). The components include:

* + **A**: Assess, prevent, and manage pain.
  + **B**: Both spontaneous awakening trials (SAT) and spontaneous breathing trials (SBT)
  + **C**: Careful choice of sedation
  + **D**: Delirium assessment, prevention, and management.
  + **E**: Early mobilization and exercise.
  + **F**: Family engagement and empowerment.

1. **Cycling-Based Rehabilitation in the ICU**

In-bed cycling is an innovative early mobilization approach that is gaining widespread traction in ICU settings nowadays, while raising scientific interest (44). In-bed cycling is a form of early activity used by patients receiving MV in bed. In this activity, the patient’s lower limbs control the speed of the bicycle exercise in the ICU (45). The primary focus is enhancing physical recovery and reducing the negative impacts of immobility in critically ill patients (46–48). This method services specially designed cycle ergometers, enabling patients to engage in leg or arm cycling exercises, either actively or passively, based on their physical abilities. (49)

In practice, patients can cycle while lying in bed or sitting up, depending on their condition and the available equipment (49,50). The cycle ergometer is adjusted to fit the patient’s range of motion and ensure comfort and for those who cannot initiate movement, passive cycling is employed, where the ergometer involuntarily moves the patient’s legs or arms to mimic pedaling, and improves circulation, joint mobility, and sensory stimulation (51). Active-assisted cycling is another option, permitting patients to contribute to the pedaling motion as much as they can, with mechanical support compensating for any limitations. Fully conscious and stable patients can participate in active cycling, pedaling against adjustable resistance to enhance strength and endurance.

Cycling sessions usually last between 20 to 30 minutes, depending on how well the patient tolerates the activity for which resistance, speed, and frequency of sessions are gradually modified based on recovery progress and clinical feedback (52). This method promotes steady improvement in physical capabilities without placing excessive strain on the patient and helps them regain their functional stability. Specialized cycling therapy sessions have proven to be beneficial for the reduction of ICU stay for ICU admitted patients which assist with lower healthcare costs. (53)

1. **Transcutaneous Electrical Nerve Stimulation**

Transcutaneous Electrical Nerve Stimulation (TENS) is a non-invasive pain relief treatment commonly used in ICU settings to boost muscle activation, relieve nociceptive neuropathic, and musculoskeletal pain (54). TENS can be best described as the application of low-voltage electrical currents through electrodes that are placed on the patient’s skin close to the targeted nerve pathways, blocking or changing the perception of pain for critically ill patients admitted in the ICU. This electrical stimulation changes sensory nerve activity, which helps reduce pain by promoting the release of natural endorphins and blocking pain signals sent to the brain (55). Additionally, TENS is an effective treatment for compromised muscles thanks to its potential to preserve muscle protein synthesis and prevent muscle atrophy during extensive immobility (56). That way, TENS serves as a valuable treatment for persistent pain issues critically patients may face in the ICU.

In addition to pain relief, TENS can prevent ICU-AW and enhance overall quality of life after hospital discharge (57). Electrical stimulation can engage underlying muscle fibers, helping with the preservation of muscle mass and the prevention of muscle atrophy in critically ill patients who are either in bed for a substantial period or mechanically ventilated for an extensive time. Furthermore, TENS may help improve blood circulation, decrease swelling, and boost oxygen delivery to the stimulated tissues (58), while its low-risk profile and minimal side effects are valuable insights for further future application of TENS as a comprehensive rehabilitation and early mobilization plans for ICU patients. However, it is essential to define the health condition of every patient and monitor the whole treatment process to maximize its effectiveness and avoid side effects.

## Control - Comparator

The standard care (not early mobilization techniques) provided to critically ill adults admitted to the ICU. There are multiple variations for the usual care these patients receive, and this could be influenced by the experience of the doctors and the nursing staff of the hospital/clinic. Comparators include usual or standard ICU care, conventional physical therapy, and standard or late mobilization treatment, while we excluded the reviews which compared interventions to rehabilitate or mobilize patients outside the ICU. Although the usual or standard care could be different for each study, we considered the description for each case (if there is one) and grouped them according to their features. Our goal was a meticulous inquisition, and the comparator was crucial as a measurement method for the overall efficacy of early mobilization for the mechanically ventilated patients in the ICU sector.

## Outcomes

The outcomes of interest in this study were categorized into primary and secondary outcomes, reflecting the multifaceted benefits and potential challenges associated with early mobilization (EM) in ICU-admitted adult patients. These outcomes provide a comprehensive framework for evaluating the effectiveness and feasibility of EM interventions.

**Primary Outcomes**

1. **ICU-Acquired Weakness**

ICU-acquired weakness (ICU-AW) refers to a skeletal muscle disorder that causes significant muscle weakness and it is apparent in approximately 40% of the ICU-admitted patients (9), because of extended bed rest, immobility, systemic inflammation, and critical illness (59,60). The prevalence of ICU-AW may commence from either a neurogenic disorder, critical illness polyneuropathy (CIP), which is a myogenic disorder acknowledged as critical illness myopathy (CIM), or a combination of both cases (known as critical illness neuromyopathy) (1,5,61). Continuous progress of research surrounding ICU-AW indicates that molecular mechanisms, such as local immune activation triggered by both myogenic and neurogenic damages, are increasing the issue of identifying the primary pathogenesis (62).

The gold standard for a diagnosis is the Medical Research Council (MRC) (sum score of less than 48/60 or mean MRC score of 4 in all testable muscle groups) and the dominant-hand handgrip dynamometry scores (less than 11 kg (interquartile range (IQR) 10-40) in males and less than 7 kg (IQR 0-7.3) in females (63).

The severity of the ICU-AW symptoms and effects can vary, according to the patient’s profile and the timing of the intervention (64). There are patients who report physical symptoms that persist for years, while recovering from critical illness, suggesting they may have experienced an extreme issue of ICU-AW (65). It is a major focus of early mobilization strategies, due to its strong link with short-term and long-term functional problems such as functional impairment, prolonged reliance on mechanical ventilation, and extended rehabilitation needs. By initiating mobilization early, studies suggest a potential reduction in the prevalence and severity of ICU-AW, promoting faster physical recovery. (9,66)

1. **ICU Length of Stay**

The length of the ICU is a critical metric of both patient recovery and resource utilization from healthcare professionals. Early mobilization interventions have been linked with shorter ICU stays by facilitating earlier weaning from mechanical ventilation, reducing complications like delirium, and improving overall functional capacity (67,68). The reduction of ICU length of stay indicates an efficient recovery process and assists the working process of healthcare systems by lowering the initial costs. (69–71)

1. **Hospital Length of Stay**

Along with ICU-specific benefits, early mobilization may provide patients with shorter periods of hospitalization (72,73). By addressing ICU complications and overall adverse events, and enhancing mobility early in the care process, patients are usually recovering quicker, and they are discharged from the hospital sooner. This outcome reflects the broader implications of EM on the continuum of care.

**Secondary Outcomes**

1. **ICU Mortality**

Mortality rates in the ICU are a critical indicator of the effectiveness of interventions. While early mobilization alone is not a direct lifesaving measure, it may contribute to lower mortality rates by mitigating complications such as pneumonia (74), thromboembolism (75), and prolonged mechanical ventilation.

1. **Duration of Mechanical Ventilation (MV) & Weaning Duration**

Implementation of mechanical ventilation in critically ill patients improves gas exchange, lowers the work of breathing, and minimizes the risk of patients self-inflicted lung injury (76). When patients are mechanically ventilated for more than 3 weeks it is usually referred to as prolonged MV and represents a group of critically ill patients (77). Prolonged mechanical ventilation is coupled with numerous complications, such as ventilator-associated pneumonia (VAP) and diaphragm dysfunction. Early mobilization treatments can enhance the patient’s respiratory muscle strength and reduce sedation requirements, thus leading to faster weaning from mechanical ventilation. (78,79)

1. **Quality of Life**

Besides the immediate clinical outcomes, early mobilization treatments are effective for the chances of survival and overall health-related quality of life (HRQOL) for critically ill patients admitted in the ICU (80). The improvement of physical function (Activities of Daily Living), the reduction of psychological distress, plus the enhancement of cognitive outcomes are critical for the achievement of a meaningful recovery and introduction into normal daily life after the patient’s discharge from both the ICU setting and the hospital (81). However, despite many ICU patients recuperating from severe conditions, they might still face persistent issues after their hospitalization, such as dyspnea, exhaustion, anxiety, depression, sleep disruption, difficulty concentrating, stress, and pain. These issues can impair the ability to complete daily activities (ADL) (82). Quality of life metrics include tools within the short-form health survey family (SF-36, EQ5D), mental health assessments, and patient-reported outcomes, are essential in evaluating the broader impact of early mobilization. (83)

1. **Incidence and Duration of Delirium**

Delirium is a common organ and brain dysfunction presented as a collection of signs and symptoms that are classified by improper mental status supplemented by concentration issues, altered level of consciousness, and thinking puzzlement (84,85). Delirium is often met in critically ill adults, and it is also considered a substantial cause of morbidity and mortality, characterized by acute confusion and cognitive impairment, particularly those who are immobile and sedated. The rate of delirium incidents is around 29% for patients in the ICU while half of these cases become apparent within the first couple of days after admission to the ICU setting. (86)

There are three psychomotor subtypes that delirium can be classified into: hyperactive (characterized by restlessness, agitation, and aggression), hypoactive (characterized by drowsiness, motor hypoactivity, and lethargy), and mixed (fluctuation between hypoactive and hyperactive subtypes) (87). Since there are a few pharmaceutical alternates that have proven effective in treating delirium once it begins, managing ICU delirium has always been complicated. Incidence of delirium in critically ill patients is associated with adverse outcomes, including longer hospital stays, an increased risk of cognitive impairment, and ICU and hospital mortality (88). However, EM treatments have been associated with a reduced incidence and severity of delirium (43) by promoting wakefulness, engaging patients in purposeful activity, and minimizing sedative use.

1. **Adverse Events and ICU Complications**

Although early mobilization in the ICU provides substantial advantages for critically ill patients, it also carries certain risks (89). The adverse events and complications associated with early mobilization mainly decrease from the physiological weaknesses of these patients, their unstable clinical states, and the difficulties in safely implementing mobilization in settings that may present high risks. Sudden physiological responses during or after mobilization can cause safety concerns. These responses may occur from disturbances in either respiratory, cardiovascular or neurological stability. Vigorous assessments and monitoring, coupled with the appropriate intensity and timing of early treatment can ensure a safer recovery process for ICU patients. In that way, healthcare professionals can maximize the benefits of early mobilization while carefully monitoring the associated risks, highlighting the need to customize interventions based on each patient's unique condition and tolerance. (19)

# Methods

A protocol was developed apriori. Reporting of the present study is conducted according to the principles of Preferred Reporting Items for Overview of Systematic Reviews (PRIOR). A checklist of the PRIOR statement describing where each item is reported within the text of the present study (or when an item’s reporting was not applicable is provided in the Appendix Table 13. No funding was received for the design, conduction or writing of this study. The research process is outlined in the following steps:

## Search Strategy

A methodological and comprehensive search approach was devised to retrieve all relevant papers that met the study’s objectives. A meticulous database search involving the National Library of Medicine’s PubMed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), and Epistemonikos from their inception to January 2025 were conducted to detect relevant papers. Free-text and medical subject heading (MeSH) terms such as “early mobilization”, “intensive care unit”, “systematic review”, and “meta-analysis” were applied to the literature search strategy to identify articles relevant to the objectives of this review.

## Screening and Selection

Two reviewers independently screened the titles and abstracts of retrieved studies. Full texts of potentially relevant articles were assessed for eligibility. Disagreements were resolved through discussion or consultation with a third reviewer.

## Data Extraction

Data was collected using standardized extraction templates in Excel to maintain consistency in information and evaluation for each eligible study. The following data items were extracted: first author, journal, year of publication, funding, conflict of interest, number of included studies, number of participants, protocol availability, intervention group, control group, and outcomes.

## Quality Assessment

The methodological quality of included systematic reviews was appraised using the AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews 2) checklist (90). This tool evaluates the rigor and transparency of systematic review processes, including protocol registration, comprehensive search strategies, and risk of bias assessment, and the R package amstar2vis was used. (91)

## Risk of Bias Assessment

The risk of bias (RoB) assessment is a critical component for every systematic review, as it evaluates multiple aspects of the research by identifying limitations regarding the methodology that might influence the quality of the evidence. In this overview, the bias risk of the reviews included was derived from evaluations carried out in those reviews. This approach ensured that potential bias sources were systematically assessed, providing a foundation for understanding the evidence's quality. By critically examining these evaluations, this overview seeks to contextualize the strength of the findings and identify areas for enhancement in future research. The reviews utilized a variety of tools to assess bias risk, such as the PEDro scale/score (92), the Newcastle-Ottawa scale (93,94), and the Cochrane RoB Tools. The results highlighted common trends in bias risk among the included reviews. Frequent sources of bias included blinding procedures for participants, personnel, allocation concealment, blinding of outcomes, selective outcome reporting, and other inconsistencies in study inclusion criteria. Although most reviews issued a risk of bias assessment, plenty of them failed to address any potential publication bias, raising concerns about completeness.

## Data Synthesis & Analysis

A detailed table summarized the findings extracted from the eligible systematic reviews. The table included key characteristics of each eligible study, such as interventions, summarizing outcomes according to the different techniques that could be used for the early mobilization process of the ICU-admitted patients, quality assessments, and major conclusions. Additionally, we created a summary table for the effect estimates of every outcome and accompany it with a meta-analysis visualization to show the overall effect for each outcome in our study, alongside the appropriate metrics for the heterogeneity, the confidence interval and the p-value for the potential subgroup comparisons. Early mobilization for the patients’ health status was assessed at different time points; during and after both their ICU and hospital, while also examining the results several days (or months) after their hospitalization.

Additionally, we paid attention to the circumstances of the mobilization process and the correspondence from the patients, in terms of their physical and mental health, as we appreciated the mental issues a person could come across (delirium, etc.) if they remained stationary during their ICU admission. Additionally, we analyzed potential bundles (ABCDEF) that we came across and included in our paper, and their evaluation was at a different group, due to the nature of a multidimensional treatment procedure and its effect on the patients.

## Statistical Analysis

We performed our analysis and subgroup analysis using RStudio (2024.12.0+467), taking into consideration the corrected covered area (CCA) metric for the primary study overlaps while operating with the appropriate packages (ccaR) (95). Dichotomous variables were presented as relative risks (RR) or odds ratios (OR), whilst continuous variables were expressed as mean differences (MD), or similar metrics, between groups and associated 95% confidence intervals (CI).

Although there were multiple levels of early mobilization treatment, we focused on the total effectiveness of the procedure for the patients of our study. There was a distinction between the control and intervention groups, but there was also a distinction between the intervention groups, based on the treatment level the patients received on each occasion.

## Ethical Considerations

As an overview of systematic reviews, this study did not collect primary data and therefore does not require formal ethical approval. Nonetheless, ethical principles were maintained by accurately reporting findings and properly attributing sources. This section offers a structured approach for identifying and synthesizing evidence concerning early mobilization in ICU patients, thereby ensuring the rigor and reliability of the conclusions presented in this thesis.

# Results

## Study Selection

The process we followed for the selection of the reviews included in this overview is presented in Figure 1. First, we evaluated the 548 studies based on their title and abstract, removing 448 ineligible papers. Afterwards, we excluded 36 duplicate studies and the resulting number of papers eligible for full-text review was 64. Finally, we examined these studies based on full text, including supplementary material, leading to the final selection of 21 reviews which are presented in Table 1.

**Figure 1: Flow Diagram of Selected Studies**



**Screening**

Records removed based on *title/abstract*

(n=448)

Cochrane (n=99)

Epistemonikos (n=15)

PubMed (n=230)

CINAHL(n=104)

Duplicates excluded (n=36):

Records screened (n=100)

Records identified from:

Cochrane (n=101)

Epistemonikos (n=17)

PubMed (n=312)

CINAHL (n=118)

N=548

Reports excluded (n=43)

e.g. surgical interventions n=17

irrelevant outcomes n=3

mixed population n=5

old version n=1

no studies included n=1

no access n=9

wrong intervention n=6

safety concerns study n=1

Full-text review articles assessed for eligibility (n=64)

Total number of SRs with meta-analysis (n=21)

PubMed (n=14)

CINAHL (n=6)

Epistemonikos (n=1)

Cochrane (n=0)

**Included**

## Study Characteristics

We came across various treatments and control groups which are presented at Table 2, and the outcomes were vastly different with limited options for a meta-analysis. The diversity of interventions and control groups played a significant role in our evaluation while there were several systematic reviews that examined several parts of the early mobilization/rehabilitation procedure and combined the individual results into a unique group (80,96). Additionally, the timing of the intervention was different among the reviews and the primary studies, considering the admission of the patients (97,98), leading to plenty of subgroup analyses for the comparison of the ideal timing for the initiation of any treatment. Different groups or subgroups were a probable cause for high heterogeneity for the meta-analyses.

**Table 1: Basic Characteristics of the Included Studies**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Design**  **(RCT/no-RCT)** | **Patients** | **Mean Age** | **Intervention** | **Control** | **Outcomes** | **Risk of Bias Tool** |
| Tipping et al 2017 (99) | 14 (14/0) | 1753 | 58.2 | Early Mobilization & Active Exercise | Standard & Usual Care | ICU & Hospital Mortality, 6-Month Mortality | Cochrane Rob Tool |
| Taito et al 2018 (100) | 2 (2/0) | 75 | 62.5 | Cycling, Functional Electrical Stimulation, Early Mobilization  Usual Care | Usual Care | ICU Mortality | Cochrane Rob Tool |
| Fuke et al 2018 (101) | 6 (6/0) | 590 | NR | Early Rehabilitation | Standard & Usual Care, Physical Therapy, Patient-Controlled Self-Help Rehabilitation Program | ICU-Acquired Weakness, Delirium-Free Days, Quality of Life | Cochrane Rob Tool |
| Zhang et al 2019 (102) | 23 (23/0) | 2308 | 59.4 | Early Mobilization | Standard & Usual Care | ICU-AW, MV Duration, ICU & Hospital Mortality, 28-days Mortality, Ventilator-free Days | Cochrane Rob Tool |
| Higgins et al 2019 (93) | 9 (0/9) | 3372 | 45.8 | Early Mobilization | Usual Care | Hospital Mortality, Hospital Length of Stay, ICU Length of Stay, MV Duration | Newcastle-Ottawa Score |
| Ding et al 2019 (98) | 15 (15/0) | 1726 | NR | Early Mobilization | Usual Care | ICU-Acquired Weakness, MV Duration | Cochrane Rob Tool |
| Zang et al 2020 (103) | 15 (15/0) | 1941 | 57.6 | Early Mobilization, Early Physical Therapy | Standard & Usual Care, Routine ICU Care, Conventional Therapy | ICU-Acquired Weakness, ICU Mortality, ICU Length of Stay, Hospital Length of Stay, Ventilator-free Days | Cochrane Rob Tool |
| Wang et al 2020 (105) | 39 (39/0) | 3837 | 58.8 | Bundle[[1]](#footnote-1) & Usual Care | Standard & Usual Care, Routine Care, Conventional Therapy | ICU-Acquired Weakness, MV Duration, ICU & Hospital Length of Stay, ICU & Hospital Mortality, Delirium Rate | Cochrane Rob Tool |
| Zayed et al 2020 (104) | 6 (6/0) | 718 | 60 | Neuromuscular Electrical Stimulation | Usual Care | ICU Mortality, MV Duration, ICU Length of Stay | Cochrane Rob Tool |
| Takaoka et al 2020 (51) | 14 (13/1) | 926 | 61.9 | Cycling | Usual Care | MV Duration, ICU & Hospital Length of Stay, Quality of Life, ICU & Hospital Mortality | Cochrane Rob Tool |
| Nieto-Garcia et al 2021 (106) | 7 (0/7) | 7520 | NR | Early Mobilization | Usual Care | Hospital-Acquired Pressure Injuries | Cochrane Rob Tool |
| Lippi et al 2022 (92) | 12 (12/0) | 791 | 62.1 | Bundle [[2]](#footnote-2) | Standard & Usual Care, Nursing Inspection, Conventional Physiotherapy | Weaning Duration | PEDro Score |
| Sosnowski et al 2023 (43) | 18 (1/17) | 29576 | NR | ABCDEF Bundle | Standard Care | Delirium Incidence, Delirium Duration | Cochrane Rob Tool |
| Yu et al 2023 (97) | 43 (43/0) | 4147 | 55.6 | Early Mobilization | Usual Care | ICU-Acquired Weakness, Mortality, ICU Complications, MV Duration, ICU & Hospital Length of Stay | Cochrane Rob Tool |
| Paton et al 2023 (80) | 15 (15/0) | 2703 | 59.6 | Early Mobilization | Usual Care | Mortality, Adverse Events, Quality of Life | Cochrane Rob Tool |
| Nakanishi et al 2023 (107) | 18 (18/0) | 909 | NR | Neuromuscular Electrical Stimulation | No Neuromuscular Electrical Stimulation | ICU-Acquired Weakness, Adverse Events, Quality of Life, ICU Length of Stay, Mortality | Cochrane Rob Tool |
| Jarman et al 2023 (108) | 12 (10/2) | 1460 | NR | Physical Activity | Usual Care | Delirium Incidence | Cochrane Rob Tool |
| Jiroutkova et al 2024 (96) | 58 (58/0) | 5664 | NR | Bundle [[3]](#footnote-3) | Usual Care | MV Duration, ICU Length of Stay, ICU Mortality | Cochrane Rob Tool |
| Xu et al 2024 (109) | 23 (23/0) | 1312 | 54.4 | Neuromuscular Electrical Stimulation, Physical Therapy | Physical Therapy, Usual Care | ICU Length of Stay, MV Duration, ICU Mortality | Cochrane Rob Tool |
| Yang et al 2024 (94) | 19 (18/1) | 2181 | NR | Exercise Therapy, TENS, Air Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training | Conventional Care, Breathing Exercise, Pulmonary Function Training | Weaning Success, MV Duration, ICU Length of Stay, Delirium Incidence, ICU-Acquired Weakness, ICU Mortality | Newcastle-Ottawa Score |
| Zhao et al 2024 (110) | 4 (4/0) | 333 | NR | Occupational Therapy with Standard Non-Pharmacological Prevention, Standard Care Interventions | Standard Measures, Early Mobilization, Correction of Sensory Deficits, Environmental Management, Reduction of Medication | Delirium Duration, ICU & Hospital Length of Stay | Cochrane Rob Tool |

## AMSTAR2

The following table demonstrates the AMSTAR2 quality check that was conducted for the systematic reviews of the overview. We concluded that 18 reviews had critically low quality, 3 reviews issued a low quality, and none of the included studies was considered a high-quality review from the AMSTAR evaluation process.

**Table 2: AMSTAR2 Items**

| Reviews | 1. PICO components*A* | 2.\* Pre-established protocol*B* | 3. Explanation of included studies' design*A* | 4.\* Comprehensive search strategy*B* | 5. Duplicate study selection*A* | 6. Duplicate data extraction*A* | 7.\* List of excluded studies and justification*B* | 8. Description of included studies*B* | 9.\* Assessment of RoB in included studies*B,C* | 10. Funding sources*A* | 11.\* Use of appropriate statistical methods*C,D* | 12. RoB impact on synthesized results*D* | 13.\* Results interpretation with RoB reference*A* | 14. Heterogeneity explanation*A* | 15.\* Publication/ small study bias investigation*D* | 16. Conflict of interest declaration*A* | Overall confidence*E* |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tipping 2017 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | No | No | Yes | Yes | Yes | Critically Low |
| Fuke 2018 | Yes | Yes | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Critically Low |
| Taito 2018 | Yes | Yes | Yes | Partial Yes | Yes | Yes | Partial Yes | Partial Yes | Yes | No | Yes | No | No | Yes | No | Yes | Critically Low |
| Higgins 2019 | Yes | Partial Yes | No | Yes | Yes | Yes | No | Yes | No | No | No | No | No | Yes | No | Yes | Critically Low |
| Zhang 2019 | Yes | No | Yes | Partial Yes | Yes | No | No | Partial Yes | Yes | Yes | Yes | No | No | No | Yes | Yes | Critically Low |
| Ding 2019 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Partial Yes | Yes | No | No | No | Yes | No | Yes | Yes | Critically Low |
| Zang 2020 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Partial Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | No | Critically Low |
| Zayed 2020 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | No | No | Critically Low |
| Wang 2020 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Critically Low |
| Takaoka 2020 | Yes | Yes | Yes | Partial Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | No | No | Low |
| Nieto-Garcia 2021 | Yes | No | No | Partial Yes | Yes | Yes | No | Yes | Yes | No | No | No | No | Yes | Yes | Yes | Critically Low |
| Lippi 2022 | Yes | Partial Yes | Yes | Partial Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Low |
| Sosnowski 2023 | Yes | Partial Yes | Yes | Partial Yes | Yes | Yes | No | Partial Yes | Yes | No | No | No | Yes | Yes | No | Yes | Critically Low |
| Paton 2023 | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| Jarman 2023 | Yes | Partial Yes | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | No | Yes | Yes | Yes | No | Yes | Critically Low |
| Nakanishi 2023 | Yes | Yes | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Critically Low |
| Yu 2024 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Partial Yes | Yes | No | No | No | Yes | No | Yes | Yes | Critically Low |
| Xu 2024 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Critically Low |
| Jiroutkova 2024 | Yes | Partial Yes | Yes | Partial Yes | Yes | Yes | No | Partial Yes | No | No | Yes | No | No | No | No | Yes | Critically Low |
| Zhao 2024 | Yes | Yes | Yes | Partial Yes | Yes | Yes | No | Partial Yes | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Critically Low |
| Yang 2024 | Yes | No | Yes | Partial Yes | Yes | Yes | No | Partial Yes | No | No | No | No | No | Yes | No | Yes | Critically Low |
| AMSTAR 2, A MeaSurement Tool to Assess Systematic Reviews 2 (Shea et al. 2017; doi: 10.1136/bmj.j4008); PICO, participant, intervention, comparison, outcome; RoB, Risk of bias. | | | | | | | | | | | | | | | | | |
| \*Asterisk indicates a critical item (domain). | | | | | | | | | | | | | | | | | |
| *A*Possible responses: Yes/No. | | | | | | | | | | | | | | | | | |
| *B*Possible responses: Yes/Partial Yes/No. A 'Partial Yes' response is evaluated positively to the overall confidence rating. | | | | | | | | | | | | | | | | | |
| *C*Item response depends on separate assessment of randomized controlled trials (RCTs) and non-randomized studies of healthcare interventions (NRSI) in the review. | | | | | | | | | | | | | | | | | |

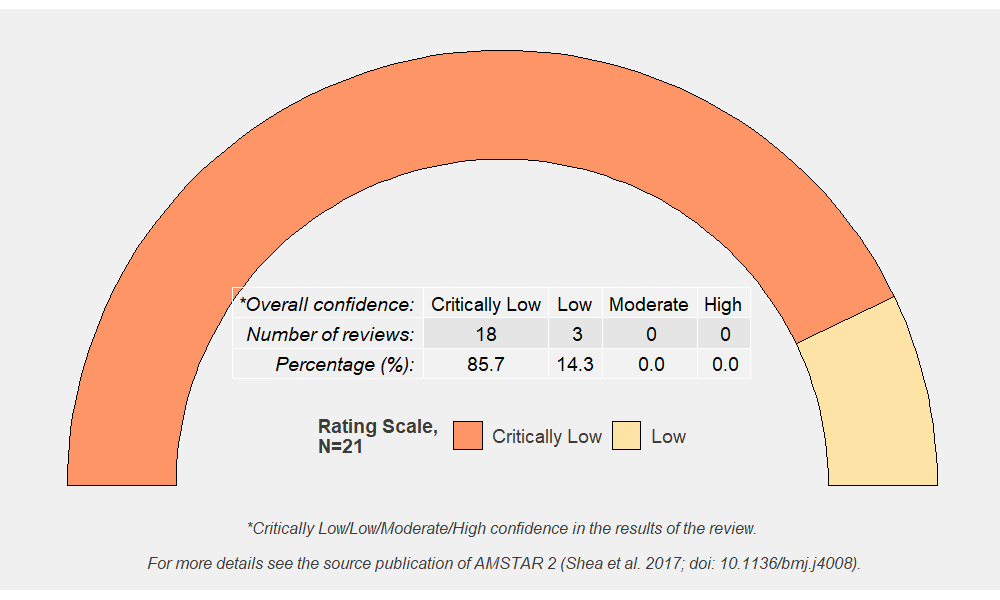
We also included the bar plot for a better understanding of the answers for each question of the AMSTAR2 evaluation process. The lack of pre-established protocols (47.6%), the lack of lists with excluded studies (85.7%), the lack of information about the funding source (91.7%), plus the lack of investigation for potential small study bias (61.9%) are some of the most critical issues for our reviews, leading to low confidence as seen below.

**Figure 2: AMSTAR2 Barplot**

A bar chart with different colored bars

AI-generated content may be incorrect.

**Figure 3: AMSTAR2 Overall Confidence**

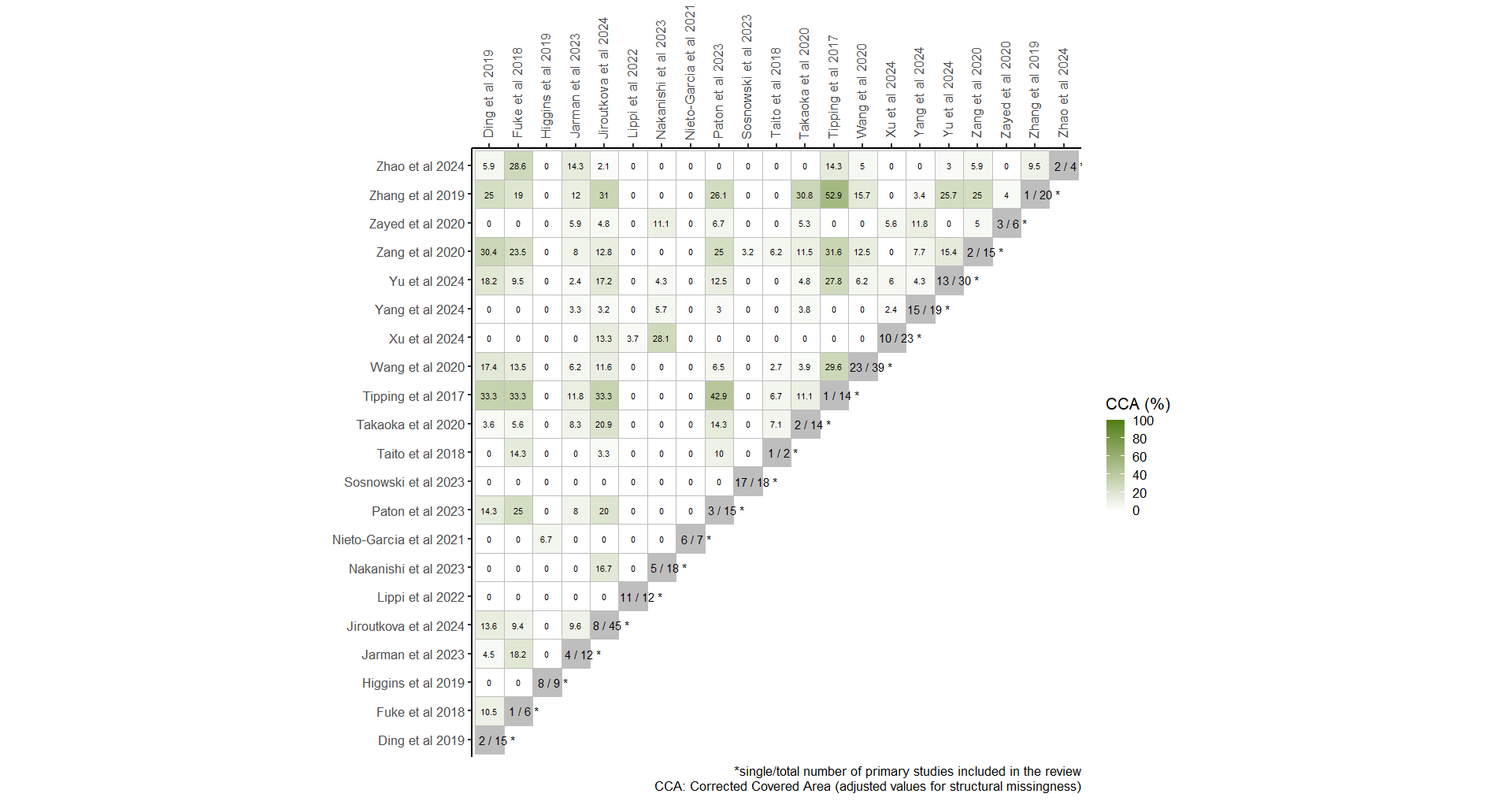


## Corrected Covered Area (CCA)

An important metric used for the evaluation of potential biases was the corrected covered area (CCA), and we gathered quantitative information regarding the similarity of primary studies for each systematic review included in our overview. The results were encouraging as the overlap was quite low. Therefore, we can describe the results that were produced by the reviews as independent (Table 3).

**Table 3: CCA Evaluation**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Reviews | N | r | c | Structural Missingness | CCA Proportion Adjusted | CCA Percentage Adjusted |
| 21 | 343 | 241 | 21 | 768 | 0.02517275 | 2.5 |

**Figure 4: CCA Heatmap**

## ICU-Acquired Weakness

Seven studies examined the potential of ICU-acquired weakness as an outcome for the ICU patients (Table 4) (97,98,101–103,105,107). Although the ICU-AW is usually reported at the ICU discharge time point, three reviews have monitored this outcome at hospital discharge (97,102,103). The results showed that early mobilization lowers significantly the chance of ICU-AW for critically ill patients, while NMES provided statistically significant results for every intervention timing (less than 24 hours – less than 72 hours) since patient’s admission apart from patients that were admitted in the ICU for more than 72 hours (97). In addition, Ding et al 2019 assessed the impact of early mobilization for ICU-AW through the SUCRA and mean rank metrics, according to the intervention timing after the initiation of MV. The results indicate that early mobilization produced the optimal recovery for patients who received treatment 72 to 96 hours after MV (80% significant likelihood), compared to the other groups (≤ 24 hours, 24-48 hours, 48-72 hours, > 96 hours, usual care). (98)

**Table 4: ICU-Acquired Weakness**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Fuke at al 2018 | Early Rehabilitation | 154 | 2 | OR | **0.42 (0.22, 0.82)** | 0% | NR | Mantel-Haenszel |
| Zhang et al 2019 | EM | 355 | 3 | RR | **0.6 (0.40, 0.90)** | 0% | NR | Mantel-Haenszel |
| Zang et al 2019 | EM, EPA | 892 | 7 | RR | **0.49 (0.26, 0.91)** | 89,8% | NR | NR |
| Wang et al 2020 | Bundle[[4]](#footnote-4) & Usual Care | 701 | 8 | RR | **0.49 (0.32, 0.74)** | 70% | NR | Mantel-Haenszel |
| Yu et al 2023 | EM (≤ 24h) | 498 | NR | RR | **0.44 (0.28, 0.68)** | NR | Moderate | NR |
| Yu et al 2023 | EM (< 24h) | 407 | NR | RR | **0.33 (0.16, 0.67)** | NR | Moderate | NR |
| Yu et al 2023 | EM (≤ 48h) | 656 | NR | RR | **0.33 (0.20, 0.52)** | NR | Moderate | NR |
| Yu et al 2023 | EM (≤ 72h) | 186 | NR | RR | 0.79 (0.29, 2.14) | NR | Very Low | NR |
| Nakanishi et al 2023 | NMES | 274 | 6 | RR | **0.48 (0.32, 0.72)** | 0% | Low | Mantel-Haenszel |
| Yang et al 2024 | TENS & Bundle[[5]](#footnote-5) | 272 | 4 | RR | 0.44 (0.18, 1.08) | 0% | NR | Mantel-Haenszel |

## ICU Length of Stay

Eleven studies evaluated the efficiency of early mobilization interventions for the patient’s length of stay in the ICU (Table 5) (51,93,94,96,97,103–105,107,109,110). The results were different for every intervention we came across for this outcome. Early mobilization and early physical therapy were positive, as the ICU length of stay was significantly lower for patients that received early mobilization or physical therapy treatment (93,97,103,105), but there was a single case where early mobilization was initiated more than 72 hours after the patients’ admission and the result showed no improvement (97). In addition, the NMES intervention was examined by four studies, but the results indicated no reduction in the amount of time patients spent in the ICU (96,104,107,109).

Zhao et al 2024 assessed the effectiveness of occupational therapy with standard non-pharmacological prevention or standard care intervention, but the ICU length of stay was not reduced significantly (110). Moreover, two studies weighed the impact of cycling as the primary intervention, and their results were not significant as well. Finally, Yang approached the subject in a different way, by examining the value of transcutaneous electrical nerve stimulation as a primary intervention, coupled with air pressure wave therapy, swallowing therapy, exercise therapy, and pulmonary function training. The outcome was a significantly lower time spent in the ICU for the patients. (94)

**Table 5: ICU Length of Stay**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Zang et al 2019 | EM, EPA | 1165 | 11 | MD | **-1.82 (-2.88, -0.76)** | 91,9% | NR | NR |
| Higgins et al 2019 | EM | 2674 | 5 | MD | -1.68 (-4.44, 1.08) | 77% | NR | Inverse Variance |
| Zayed et al 2020 | NMES | 214 | 3 | MD | -3.06 (-9.79, 3.68) | 44% | NR | Inverse Variance |
| Wang et al 2020 | Bundle[[6]](#footnote-6) & Usual Care | 3136 | 33 | MD | **-2.74 (-3.52, -1.97)** | 97% | NR | Inverse Variance |
| Takaoka et al 2020 | Cycling | 511 | 11 | MD | 0.23 (-1.44, 1.89) | 0% | Moderate | Inverse Variance |
| Yu et al 2023 | EM (≤ 24h) | NR | NR | MD | **-3 (-4.58, -1.42)** | NR | Low | NR |
| Yu et al 2023 | EM (> 24h) | NR | NR | MD | **-4.70 (-6.70, -2.71)** | NR | Low | NR |
| Yu et al 2023 | EM (≤ 48h) | NR | NR | MD | **-1.49 (-5.93, -2.95)** | NR | Very Low | NR |
| Yu et al 2023 | EM (≤ 72h) | NR | NR | MD | **-2.68 (-4.71, -0.65)** | NR | Moderate | NR |
| Yu et al 2023 | EM (> 72h) | NR | NR | MD | -2.46 (-5.30, 0.38) | NR | Very Low | NR |
| Nakanishi et al 2023 | NMES | 721 | 13 | MD | 1.24 (-1.43, 3.91) | 82% | Low | Inverse Variance |
| Jiroutkova et al 2024 | Cycling | 442 | 9 | MD | 1.27 (-1.68, 4.21) | 15% | NR | NR |
| Jiroutkova et al 2024 | NMES | 734 | 14 | MD | -1.47 (-3.62, 0.67) | 99% | NR | NR |
| Jiroutkova et al 2024 | PPR[[7]](#footnote-7) | 2688 | 20 | MD | **-1.86 (-3.52, -0.20)** | 74% | NR | NR |
| Jiroutkova et al 2024 | FES[[8]](#footnote-8) - Cycling | 322 | 2 | MD | -0.06 (-4.88, 4.72) | 0% | NR | NR |
| Jiroutkova et al 2024 | Overall | 4176 | 45 | MD | -1.16 (-2.32, 0) | 97% | NR | NR |
| Xu et al 2024 | NMES vs CG (Direct) | NR | 5 | MD | -2.78 (-11.02, 5.46) | 35% | Very Low | NR |
| Xu et al 2024 | NMES vs CG (Network) | NR | 5 | MD | -2.51 (-10.52, 5.49) | 35% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Direct) | NR | 2 | MD | -3.49 (-15.29, 8.31) | 0% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Network) | NR | 2 | MD | -5.23 (-14.29, 3.82) | 0% | Very Low | NR |
| Xu et al 2024 | PT vs CG (Direct) | NR | 2 | MD | -1.25 (-12.99, 10.49) | 45% | Very Low | NR |
| Xu et al 2024 | PT vs CG (Network) | NR | 2 | MD | -2.74 (-11.80, 6.31) | 45% | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Direct) | NR | 3 | MD | 3.65 (-5.93, 13.23) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Network) | NR | 3 | MD | 2.72 (-5.38, 10.82) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Direct) | NR | 3 | MD | 1.03 (-8.55, 10.61) | 23% | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Network) | NR | 3 | MD | 0.23 (-7.87, 8.32) | 23% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Direct) | NR | 14 | MD | -2.49 (-6.94, 1.95) | 98% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Network) | NR | 14 | MD | -2.49 (-6.94, 1.95) | 98% | Very Low | NR |
| Zhao et al 2024 | Bundle[[9]](#footnote-9) | 313 | 3 | SMD | -0.16 (-0.38, 0.07) | 0% | NR | Inverse Variance |
| Yang et al 2024 | TENS & Bundle[[10]](#footnote-10) | 1650 | 14 | SMD | **-1.41 (-1.94, -0.88)** | 96% | NR | Inverse Variance |

## Hospital Length of Stay

Six studies observed the amount of time spent in the hospital and tested the value of early treatment for their patients (Table 6) (51,93,97,103,105,110). Early mobilization, physical therapy and exercise provided both significant (93,97,103,105), and non-significant reduction for the hospital length of stay of their patients (51,110). Notably, there were no significant results for cases of early mobilization within 24 to 48 hours of ICU admission, plus early mobilization after 72 hours of admission. In addition, cycling and occupational therapy demonstrated no significant effects for the duration of hospitalization.

**Table 6: Hospital Length of Stay**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Zang et al 2019 | EM, EPA | NR | 11 | MD | **-3.9 (-5.94, -1.85)** | 95,9% | NR | NR |
| Higgins et al 2019 | EM | 2653 | 4 | MD | -6.61 (-13.49, 0.25) | 83% | NR | Inverse Variance |
| Wang et al 2020 | Bundle & Usual Care[[11]](#footnote-11) | 1259 | 17 | MD | **-3.71 (-5.70, -1.71)** | 85% | NR | Inverse Variance |
| Takaoka et al 2020 | Cycling | 393 | 8 | MD | -0.07 (-3.87, 3.73) | 0% | Moderate | Inverse Variance |
| Yu et al 2023 | EM (≤ 24h) | NR | NR | MD | **-3.28 (-4.61, -1.95)** | NR | Low | NR |
| Yu et al 2023 | EM (< 24h) | NR | NR | MD | **-3.61 (-5.53, -1.68)** | NR | Moderate | NR |
| Yu et al 2023 | EM (≤ 48h) | NR | NR | MD | -2.1 (-7.54, 3.34) | NR | Very Low | NR |
| Yu et al 2023 | EM (≤ 72h) | NR | NR | MD | **-2.79 (-5.06, -0.51)** | NR | Moderate | NR |
| Yu et al 2023 | EM (>72h) | NR | NR | MD | -3.47 (-7.16, 0.22) | NR | Very Low | NR |
| Zhao et al 2024 | Bundle[[12]](#footnote-12) | 313 | 3 | SMD | -0.01 (-0.23, 0.22) | 0% | NR | Inverse Variance |

## ICU Mortality

Ten reviews reported mortality data for ICU patients (Table 7) (51,94,96,99,100,102–105,109). Even though five reviews issued early mobilization as an intervention for their patients, results didn’t show any sizable differences for the incidents of ICU mortality. Additionally, the combination of NMES, cycling and the pulmonary therapy interventions didn’t result in significantly lowering ICU mortality cases, and the interventions issued by Jiroutkova et al 2024 were similarly not substantial for the subgroups and the overall meta-analysis (96). Although we came across several studies that examined reviews which used NMES, cycling, and pulmonary therapy as their intervention groups, there were no signs of significant lower mortality cases for the participants during their stay in the ICU. (51,94,104)

One review didn’t mention specifically the time point of the mortality rates for the patients, but the results of their analysis weren’t significant for both the combination NMES and physical therapy (97). While the timing of the EM intervention varied from less than 24 hours and after 72 hours, the (very) low GRADE score is concerning for the value of the evidence from Yu et al 2023. (97)

Notably, several reviews examined the mortality of the enrolled patients until the end of their hospitalization (51,93,99,102,105,110), or months after their discharge (80,99,107). Seven reviews investigated the hospital mortality rates, but there was no significant difference between the intervention and the control groups in any case. Furthermore, Paton et al 2023 examined the 6-month after discharge mortality rates for both the low-risk, high-risk and overall studies, but the analysis indicates that there is no significant difference between the two groups (80). In addition, Nakanishi et al 2023 reported the mortality rate for those who were monitored a month after their hospitalization, and the results were also non-significant (107).

**Table 7: ICU Mortality**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Tipping et al 2017 | EM & Active Exercise | 551 | 8 | RD | 0.02 (-0.01, 0.05) | 0% | NR | Mantel-Haenszel |
| Taito et al 2018 | Bundle[[13]](#footnote-13) | 75 | 2 | RR | 2.02 (0.46, 8.91) | 0% | Very Low | Mantel-Haenszel |
| Zhang et al 2019 | EM | 960 | 8 | RR | 1.12 (0.82, 1.52) | 0% | NR | Mantel-Haenszel |
| Zang et al 2019 | EM, EPA | 903 | 7 | RR | 1.31 (0.97, 1.76) | 0% | NR | NR |
| Zayed et al 2020 | NMES | 564 | 4 | RR | 1.3 (0.95, 1.78) | 0% | NR | Mantel-Haenszel |
| Wang et al 2020 | Bundle[[14]](#footnote-14) & Usual Care | 712 | 6 | RD | -0.03 (-0.08, 0.03) | 0% | NR | Mantel-Haenszel |
| Takaoka et al 2020 | Cycling | 670 | 7 | OR | 1.02 (0.79, 1.32) | 0% | NR | Mantel-Haenszel |
| Jiroutkova et al 2024 | Cycling | 807 | 10 | OR | 0.95 (0.67, 1.34) | 32% | Very Low | NR |
| Jiroutkova et al 2024 | NMES | 1245 | 19 | OR | 0.96 (0.72, 1.28) | 0% | NR | NR |
| Jiroutkova et al 2024 | PPR[[15]](#footnote-15) | 2932 | 22 | OR | 0.98 (0.81, 1.19) | 2% | NR | NR |
| Jiroutkova et al 2024 | FES[[16]](#footnote-16)-Cycling | 312 | 2 | OR | 1.31 (0.81, 2.10) | 0% | NR | NR |
| Jiroutkova et al 2024 | Overall | 5296 | 53 | OR | 1 (0.87, 1.14) | 0% | NR | NR |
| Xu et al 2024 | NMES vs CG (Direct) | NR | 4 | OR | 0.5 (0.24, 1.02) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs CG (Network) | NR | 4 | OR | 0.5 (0.24, 1.02) | 0% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Direct) | NR | 1 | OR | 0.29 (0.06, 1.53) | NA | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Network) | NR | 1 | OR | 0.35 (0.10, 1.21) | NA | Very Low | NR |
| Xu et al 2024 | PT vs CG (Direct) | NR | 1 | OR | 0.39 (0.08, 1.84) | NA | Very Low | NR |
| Xu et al 2024 | PT vs CG (Network) | NR | 1 | OR | 0.44 (0.13, 1.52) | NA | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Direct) | NR | 1 | OR | 1.13 (0.17, 7.24) | NA | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Network) | NR | 1 | OR | 1.42 (0.39, 5.18) | NA | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Direct) | NR | 1 | OR | 0.84 (0.14, 4.97) | NA | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Network) | NR | 1 | OR | 1.12 (0.31, 4.07) | NA | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Direct) | NR | 8 | OR | 0.79 (0.52, 1.21) | 0% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Network) | NR | 8 | OR | 0.79 (0.52, 1.21) | 0% | Very Low | NR |
| Yang et al 2024 | TENS & Bundle[[17]](#footnote-17) | 1034 | 6 | RR | 0.97 (0.50, 1.88) | 68% | NR | Mantel-Haenszel |

## Mechanical Ventilation & Weaning Duration

Ten reviews examined the difference in the duration of mechanical ventilation for patients that received early treatment (Table 8) (51,93,94,96–98,102,104,105,109). Specifically, Zhang et al 2019 examined the mechanically ventilated patients in detail by evaluating many subgroups, such as partial mechanical ventilation, ICU setting, random sequence generation methods, the various interventions, and timing of treatment. The effectiveness of the treatment wasn’t evident, and the results indicated no difference for any of the subgroup analysis. Early mobilization provided mixed results, as there was less time spent in MV for patients in three reviews (93,97,98,105), but Yu et al 2023 presented significant results just for patients who receive treatment within 24 hours after their ICU admission. Furthermore, Ding et al 2019 assessed the impact of the intervention timing with the SUCRA and mean rank metrics, and the results indicated that early mobilization within 48 to 72 hours after MV had the greatest significant likelihood (80%), compared to the other groups (≤ 24 hours, 24-48 hours, > 96 hours, > 5 days, > 7 days, usual care). (98)

Three reviews observed the effect of NMES on the duration of MV. Although Jiroutkova et al 2024 found significant results (96), the other reviews didn’t issue any notable results (104,109), and high heterogeneity may be an indication of the very low quality of evidence (GRADE) score for Xu et al 2024. Overall, these results should be considered with caution.

Two reviews evaluated the cycling treatment, and there was no significant difference in the duration of MV (51,97). In contrast, Yang et al 2024 performed a meta-analysis with TENS as the primary intervention, coupled with exercise therapy, air pressure wave therapy, swallowing therapy, and pulmonary function training, accumulating significant feedback for the MV duration. (94)

Lastly, weaning duration or success rate was another outcome, like MV duration, that was studied from three reviews, and Lippi et al 2022 was the only review with major difference in weaning duration for the ICU patients. (92,94)

**Table 8: Mechanical Ventilation & Weaning Duration**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Zhang et al 2019 | EM | 1536 | 17 | SMD | -0.33 (-0.66, 0) | NR | NR | NR |
| Higgins et al 2019 | EM | 2592 | 3 | MD | **-1.18 (-2.17, -0.19)** | 0% | NR | Inverse Variance |
| Zayed et al 2020 | NMES | 522 | 4 | MD | -2.07 (-5.06, 0.92) | 56% | NR | Inverse Variance |
| Wang et al 2020 | Bundle[[18]](#footnote-18) & Usual Care | 2248 | 26 | MD | **-2.1 (-2.47, -1.73)** | 97% | NR | Inverse Variance |
| Takaoka et al 2020 | Cycling | 676 | 11 | MD | 0.01 (-1.04, 1.07) | 0% | Moderate | Inverse Variance |
| Yu et al 2023 | EM (≤ 24h) | NR | NR | MD | **-2.46 (-4.35, -0.57)** | NR | Low | NR |
| Yu et al 2023 | EM (> 24h) | NR | NR | MD | -4.98 (-8.02, 1.94) | NR | Low | NR |
| Yu et al 2023 | EM (≤ 48h) | NR | NR | MD | -0.63 (-5.30, 4.04) | NR | Low | NR |
| Yu et al 2023 | EM (≤ 72h) | NR | NR | MD | -2.96 (-6.02, 0.10) | NR | Low | NR |
| Yu et al 2023 | EM (> 72h) | NR | NR | MD | -2.43 (-6.69, 1.83) | NR | Low | NR |
| Jiroutkova et al 2024 | Cycling | 723 | 9 | MD | -0.09 (-2.41, 2.22) | 0% | NR | NR |
| Jiroutkova et al 2024 | NMES | 888 | 17 | MD | **-3.06 (-4.70, -1.42)** | 98% | NR | NR |
| Jiroutkova et al 2024 | PPR[[19]](#footnote-19) | 2027 | 18 | MD | -1.68 (-3.16, -0.21) | 81% | NR | NR |
| Jiroutkova et al 2024 | FES[[20]](#footnote-20)-Cycling | 312 | 2 | MD | 0.44 (-3.68, 4.55) | 0% | NR | NR |
| Jiroutkova et al 2024 | Overall | 3950 | 46 | MD | **-1.76 (-2.76, -0.77)** | 97% | NR | NR |
| Xu et al 2024 | NMES vs CG (Direct) | NR | 2 | MD | -8.5 (-20.0, 3.01) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs CG (Network) | NR | 2 | MD | -6.47 (-15.26, 2.31) | 0% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Direct) | NR | 7 | MD | -2.84 (-9.48, 3.79) | 53% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs CG (Network) | NR | 7 | MD | -2.79 (-9.29, 3.72) | 53% | Very Low | NR |
| Xu et al 2024 | PT vs CG (Direct) | NR | 1 | MD | 1.1 (-15.13, 17.33) | NA | Very Low | NR |
| Xu et al 2024 | PT vs CG (Network) | NR | 1 | MD | -3.39 (-12.57, 5.79) | NA | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Direct) | NR | 3 | MD | -4.47 (-13.98, 5.05) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs NMES+PT (Network) | NR | 3 | MD | -3.69 (-11.83, 4.45) | 0% | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Direct) | NR | 12 | MD | -3.01 (-7.81, 1.79) | 100% | Very Low | NR |
| Xu et al 2024 | NMES vs PT (Network) | NR | 12 | MD | -3.08 (-7.83, 1.67) | 100% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Direct) | NR | 2 | MD | -0.95 (-12.61, 10.71) | 64% | Very Low | NR |
| Xu et al 2024 | NMES+PT vs PT (Network) | NR | 2 | MD | 0.6 (-7.92, 9.13) | 64% | Very Low | NR |
| Yang et al 2024 | TENS & Bundle[[21]](#footnote-21) | 1727 | 15 | SMD | **-1.08 (-1.58, -0.59)** | 95% | NR | Inverse Variance |

## Quality of Life

Four reviews assessed the effect of the intervention on the quality of life is considered both as a short-term and long-term outcome which was evaluated by several factors (Table 9) (51,80,101,107). Fuke et al 2018 accounted both the EQ5D and SF-36 scores for the health-related quality of life outcome at ICU discharge, but neither of the results showed any significant differences for the two patient groups (101). Moreover, two reviews examined the health-related quality of life, 6 months after hospitalization, with Paton et al 2023 using the EQ5D and SF-36 scores for the evaluation of the patient’s health. The results of their analyses weren’t statistically significant, and Takaoka et al 2020 has also included the GRADE score, which was very low. Lastly, Nakanishi et al 2023 evaluated the NMES intervention from a single RCT study, with no significant results, and great uncertainty in terms of the GRADE score. (107)

**Table 9: Quality of Life**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Fuke et al 2018 | Early Rehabilitation | 63 | 2 | SMD | 0.11 (-0.86, 1.09) | 72% | Very Low | Inverse Variance |
| Takaoka et al 2020 | Cycling | 103 | 2 | MD | 9.13 (-13.8, 32.05) | 75% | Very Low | Inverse Variance |
| Paton et al 2023 | EQSD Score | 651 | 3 | SMD | 0.03 (-0.12, 0.18) | 0% | NR | Inverse Variance |
| Paton et al 2023 | AQoL Score | 121 | 1 | SMD | -0.25 (-0.61, 0.11) | NA | NR | Inverse Variance |
| Paton et al 2023 | Overall | 772 | 4 | SMD | -0.01 (-0.16, 0.13) | 0% | NR | Inverse Variance |
| Nakanishi et al 2023 | NMES | 47 | 1 | MD | 0.2 (-0.03, 0.43) | NA | Very Low | Inverse Variance |

## Incidence & Duration of Delirium

Six reviews evaluated the risk of delirium (Table 10) (43,94,108), the duration of delirium (Table 11) (43,110), and the delirium-free days for ICU patients (101). The incidence of delirium was significantly lower for only Sosnowski et al 2023 (RR = 0.57, CI: 0.36; 0.90), providing a suggestion for the effectiveness of the ABCDEF bundle compared to standard care, which may be questionable due to high heterogeneity observed in the meta-analysis ( = 92%). The other three reviews found no sizable difference from their treatment groups.

**Table 10: Incidence of Delirium**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Sosnowski et al 2023 | ABCDEF Bundle | 2000 | 6 | RR | **0.57 (0.36, 0.9)** | 92% | NR | Mantel-Haenszel |
| Jarman et al 2023 | Physical Activity | 967 | 7 | RR | 0.85 (0.62, 1.17) | 51% | NR | Mantel-Haenszel |
| Yang et al 2024 | TENS & Bundle[[22]](#footnote-22) | 584 | 5 | RR | 0.79 (0.56, 1.11) | 4% | NR | Mantel-Haenszel |

Although Sosnowski et al 2023 ended up with significantly lower duration of delirium for patients who received the ABCDEF bundle (43), in favor of the standard care of the respective control groups, we came across worryingly high heterogeneity, leaving us doubtful about the value of the data. In addition, the implication of occupational therapy as an intervention with standard non-pharmacological prevention wasn’t enough for a substantial difference in the duration of delirium, as reported by Zhao et al 2024. (110)

Conspicuously, Wang et al 2020 reported the delirium rate at the end of hospitalization from the primary studies, and the result wasn’t significant (RR = 0.52, CI: 0.19; 1.44), with high heterogeneity ( = 97%) being an issue.

**Table 11: Delirium Duration**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Sosnowski et al 2023 | ABCDEF Bundle | 3418 | 5 | MD | **-1.37 (-2.61, -0.13)** | 96% | NR | Inverse Variance |
| Zhao et al 2024 | Bundle[[23]](#footnote-23) | 203 | 3 | SMD | -0.2 (-0.53, 0.14) | 26% | NR | Inverse Variance |

## Adverse Events & ICU Complications

Four reviews examined the possibility of adverse events and ICU complications for their group of patients, and the measurements included in the reviews were important for the evaluation of the evidence for the diversity of the reports (Table 12) (80,97,106,107). Firstly, many included studies of the review recorded minor adverse events only during the implementation of NMES and exercise intervention, for the detection of potential discomfort, musculoskeletal pain, muscle soreness, skin irritation and many more. The results indicated no significant difference between the groups, while the GRADE score was low for both intervention combinations.

Paton et al 2023 evaluated the risk of adverse effects with multiple subgroups, depending on ventilation status, dosage of early mobilization, and the risk status of the included studies. The risk was significantly bigger for the group of mechanically ventilated patients, and for the group of patients who received a high dose of early active mobilization opposed to usual care. However, the heterogeneity was also significant for the MV group, and the GRADE score was low for both cases, leading to considerations for the quality of evidence. (80)

Nakanishi et al 2023 performed a meta-analysis for the possibility of adverse effects, and the result was not significant, while also being very uncertain (RR = 6.87, CI: 0.84; 56.5, = 0%). Notably, there were no life-threatening events, but two studies reported a pricking sensation caused by NMES. Overall, the incomplete data, the lack of explanation for the evaluation of adverse events by the authors of the primary studies, and the questionable patient allocation on some occasions cast doubt on the quality of the evidence for this review. (107)

Moreover, Yu et al 2024 studied the ICU-associated complications as a primary outcome for the review based on the timing of the EM initiation. Every subgroup had significantly lower risk of adverse effects for their patients, with the SUCRA values illustrating that patients who received EM before 72 hours of ICU admission had the best response with a significant likelihood of 94.7%. Nonetheless, the GRADE score for three subgroups was low (≤ 24 hours, > 24 hours, ≤ 72 hours), and moderate for the last one (> 72 hours), raising an issue for the magnitude of the data. (97)

Lastly, Nieto-Garcia et al 2021 researched the effect of EM intervention for the prevention of hospital-acquired pressure injuries for critically ill patients. The results of the meta-analysis were not significant (OR = 0.97, CI: 0.49; 1.91, P = 0.93).

**Table 12: Adverse Events**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Review | Intervention | Patients | Studies | Effect Estimate | Effect (95% CI) | Heterogeneity | Quality of Evidence | Model |
| Paton et al 2023 | All Patients in MV | 11394 | 3 | RR | **2.29 (1.17, 4.48)** | 88% | Low | Mantel-Haenszel |
| Paton et al 2023 | Some Patients in MV | 6224 | 2 | RR | **0.33 (0.25, 0.43)** | 0% | Low | Mantel-Haenszel |
| Paton et al 2023 | Low Dose | 9798 | 2 | RR | 0.89 (0.17, 4.70) | 60% | Low | Mantel-Haenszel |
| Paton et al 2023 | High Dose | 2471 | 2 | RR | **3.01 (1.59, 5.68)** | 57% | NR | Mantel-Haenszel |
| Paton et al 2023 | Not Classified | 8318 | 1 | RR | **0.33 (0.25, 0.43)** | NA | NR | Mantel-Haenszel |
| Paton et al 2023 | Low-Risk Studies | 12269 | 4 | RR | 1.94 (0.98, 3.86) | 85% | NR | Mantel-Haenszel |
| Paton et al 2023 | Non-Low-Risk Studies | 5349 | 1 | RR | **0.33 (0.25, 0.43)** | NA | NR | Mantel-Haenszel |
| Paton et al 2023 | Overall | 17618 | 5 | RR | 1.13 (0.37, 3.43) | 97% | NR | Mantel-Haenszel |
| Nakanishi et al 2023 | NMES | 548 | 8 | RR | 6.87 (0.84, 56.5) | 0% | Very Low | Mantel-Haenszel |
| Yu et al 2023 | EM (≤ 24h) | 1083 | NR | RR | **0.74 (0.35, 0.63)** | NR | Low | NR |
| Yu et al 2023 | EM (> 24h) | 236 | NR | RR | **0.39 (0.19, 0.79)** | NR | Low | NR |
| Yu et al 2023 | EM (≤ 72h) | 496 | NR | RR | **0.17 (0.05, 0.55)** | NR | Low | NR |
| Yu et al 2023 | EM (> 72h) | 881 | NR | RR | **0.48 (0.35, 0.66)** | NR | Moderate | NR |

# Discussion

The significance of early mobilization (EM) in critically ill patients and its influence on various clinical outcomes are underscored by the results of this overview of systematic reviews. The results highlight how important EM is for the mitigation of ICU-AW incidents. Muscular dysfunction and muscle atrophy are well-established side effects of critical illness that are frequently made worse by prolonged bed rest. Some of the most precise interventions for this issue are inspiratory muscle therapy (IMT), neuromuscular electrical stimulation (NMES), functional electrical stimulation (FES), and transcutaneous electrical nerve stimulation (TENS) which were evident in nine of the included reviews. Moreover, physical therapy, including in-bed cycling, out-of-bed mobilization, active-assisted exercises, and passive range-of-motion exercises are great examples of early mobilization techniques that have shown a shielding effect against ICU-AW. Maintaining muscle mass and function, protecting neural integrity, and improving systemic circulation all help to achieve this protective effect and improve patient outcomes.

Additionally, EM is linked to a decrease in hospital and intensive care unit length of stay. According to the reviewed data, encouraging physical activity, passive and active mobilization, plus evading secondary complications like pressure injuries and pulmonary problems by providing an early intervention for adult patients early in their intensive care unit stay speeds up recovery and discharge. Besides lowering the burden on healthcare systems, shorter intensive care units and hospital stays also enhance resource use and lower the risk of infections, leading to efficient recovery during the ICU and hospital stay.

The benefits of EM are further supported by the secondary outcomes that were looked at in this review. Although it was a major factor in several reviews, ICU mortality didn’t show a downward trend in the included reviews, especially those with less severe illness at baseline. Another important factor to consider is functional status at discharge, since EM interventions have been associated with better post-ICU recovery trajectories and increased independence in daily living activities. EM treatment also has a positive impact on the length of mechanical ventilation because early physical activity helps maintain respiratory muscle strength, which makes it easier to wean from ventilatory support.

Quality of life following hospital discharge is a complex phenomenon that includes social, psychological, and physical aspects. Long-term impairments in mobility, cognitive function, and emotional well-being are common among ICU survivors. Despite the importance of these post-ICU results, none of the reviews have shown substantial differences in the health status of the patients after their hospitalization by the implementation of EM throughout their ICU stay. Early intervention further improves the prevention and treatment of delirium, a frequent and harmful condition among critically ill patients. Through mechanisms involving increased patient engagement, early mobilization interventions help preserve cognitive function and lower the length and intensity of delirium episodes.

Although the advantages of EM are numerous, worries about possible side effects and intensive care unit complications are still an important concern. Structured EM protocols, interdisciplinary coordination, and customized patient assessments are necessary to carefully manage the risk of pressure injuries and other complications. Most of the research shows that EM is useful for the rehabilitation of critically ill patients, but there are still some reviews in which the adverse events were more evident for the intervention groups. In summary, the implementation of safe and efficient interventions with few side effects when monitored appropriately and safety protocols were followed in every case. For a better understanding of the implications of these results, the difficulties in applying EM in intensive care units, and potential avenues for further study, the following paragraphs will examine these key points in detail.

## Suggestions for Clinical Practice

It has been repeatedly shown that early mobilization improves patient outcomes by lowering the incidence of ICU-acquired weakness (ICU-AW) (111). Integrating EM into routine ICU care protocols is crucial because extended bed rest and immobilization are major causes of muscle atrophy and functional decline in critically ill patients (112,113). Further demonstrating the importance of EM in improving recovery and maximizing resource use is the decrease in intensive care unit and hospital length of stay (LOS). Including lowering medical expenses, shorter stays also reduce the chance of hospital-acquired infections or injuries, plus other issues linked to extended intensive care unit stays.

Additionally, EM has been associated with improvements in secondary outcomes, including delirium prevention, functional status after discharge, mortality rate, health-related quality of life, and its physical benefits (32). These results lend confidence to a more comprehensive strategy for ICU patient care that prioritizes both long-term recovery and survival. To guarantee consistent application and optimize advantages, standardized guidelines are necessary, as evidenced by the differences in protocols among various healthcare settings.

## Challenges and Barriers to Implementation

Despite the established and evident-based benefits of various EM interventions, there are still considerable barriers that could prevent the initiation of EM treatments from being widely used in intensive care units. Specialized mobilization plans and treatments are necessary because of the wide range of patients admitted in the ICU health conditions, which is one of the main challenges for healthcare professionals who work closely with critically ill patients. Cautious clinical judgment is critical to weigh the advantages and disadvantages of EM, both active and passive, for patients with either clinical instability, numerous comorbidities, high levels of sedation, or prolonged duration of mechanical ventilation. (2)

The issue of resources, such as qualified staff and suitable equipment, which is concerning for many healthcare institutes, remains a significant obstacle for under-sized medical centers that frequently lack the appropriate equipment for these cases. The need for multidisciplinary healthcare teams that include doctors, nurses, physiotherapists, and occupational therapists is urgent for the safety and efficiency of the EM application, with several emergency medical programs. Implementing structured EM protocols in specific healthcare settings can be seriously hindered by stuff shortages and high patient-to-nurse ratios. (114)

Embracing resistance to EM is also influenced by safety concerns. Healthcare professionals have voiced their concerns about possible negative outcomes like hemodynamic instability, falls, or unintentional extubation (115). However, recent studies suggest that EM can be carried out without serious risks if appropriate training, supervision, and special attention to safety procedures are conducted accurately. The growing confidence and devotion to the implementation of EM strategies requires concentrating on these issues through education and protocol development. (24,116)

## Future Directions and Research Priorities

While current evidence supports the benefits of EM, further research is needed to refine its implementation and assess long-term outcomes. Several areas warrant further investigation:

1. **Standardization of Early Mobilization Protocols**: The timing, level of intensity, and kind of mobilization interventions employed in many studies vary widely. Standardized, evidence-based EM protocols can be shown to help guarantee efficacy and consistency in various intensive care unit settings.
2. **Patient Selection Criteria**: Optimizing customized treatment routines can be facilitated by determining which ICU patient subgroups benefit most from EM. Predictive models or biomarkers should be investigated in future research to help inform clinical judgment.
3. **Long-Term Functional Outcomes**: Even though EM has shown short-term advantages, its effects on functional recovery over the long term, return to work, and general health-related quality of life are still being studied. To evaluate these results, longitudinal studies with long follow-up times are required.
4. **Cost-Effectiveness Analyses**: Economic evaluations should be carried out to measure the cost savings linked to decreased ICU and hospital LOS, enhanced functional recovery, and fewer post-discharge rehabilitation requirements because EM programs are reliant to very specific resources.
5. **Technology Integration**: The utilization of cutting-edge technologies, such as wearable monitoring devices, virtual reality rehabilitation, and robotic-assisted mobilization systems could improve substantially the viability and efficacy of EM interventions. The function of these technologies in ICU mobilization tactics should be investigated in future studies.

# Conclusions

For adult ICU patients, early mobilization (EM) has emerged as a crucial tactic to mitigate the adverse consequences that may be caused from prolonged immobility. In order to evaluate the effects of EM on important clinical outcomes, including ICU-acquired weakness (ICU-AW), length of stay (LOS) in both ICU and hospital settings, and secondary indicators like ICU mortality, duration of mechanical ventilation or weaning duration, health-related quality of life after hospitalization, delirium occurrences and lengths, as well as potential adverse events or complications related to the ICU, this overview of systematic reviews and meta-analyses has compiled the available data.

Despite the strength of the evidence base for EM, there are still several gaps and restrictions. Inconsistencies in reported outcomes are caused by variations in EM protocols, patient population heterogeneity, and study methodology. Furthermore, high-quality randomized and non-randomized controlled trials, observational studies and longitudinal follow-up studies are necessary to further investigate the long-term effects of EM on post-ICU functional status and quality of life. There is evidence about the efficacy of early intervention for ICU-admitted adult patients, but we will need plenty of studies for the overall evaluation of these treatments.

The results of this review highlight the importance of incorporating EM into routine ICU care from a clinical and policy standpoint. EM programs can be implemented successfully if multidisciplinary cooperation between healthcare professionals, such as physiotherapists, nurses, doctors, and rehabilitation specialists. Effective mobilization strategies depend on standardized procedures, sufficient staff training, and institutional support. Future studies should concentrate on improving EM procedures, determining which patient subgroups gain the most, and investigating cutting-edge therapies that improve mobility results.

Overall, EM is a crucial intervention in the treatment of patients who are in critical condition, and it has been shown to improve a variety of clinical and functional outcomes. A more thorough and patient-centered approach to critical care is made possible through the mitigation of ICU-AW incidents, reduction of ICU and hospital length of stay, improvement of functional status, and improvement of post-discharge quality of life. Even though there are still implementation issues, ongoing efforts to improve EM techniques and incorporate them into standard practice will help ICU survivors recover and show greater long-term health status.

# Funding & Competing Interests

We, the authors of this overview, would like to address that there was no conflict of interest or financial support or funding of any kind for this study. Ethical approval was not considered necessary because authors retrieved and analyzed data from previously published studies, thus they had obtained consent from the authors of the primary studies.

# References

1. Jolley SE, Bunnell AE, Hough CL. ICU-Acquired Weakness. Vol. 150, Chest. Elsevier B.V.; 2016. p. 1129–40.

2. Hodgson CL, Capell E, Tipping CJ. Early Mobilization of Patients in Intensive Care: Organization, Communication and Safety Factors that Influence Translation into Clinical Practice. Vol. 22, Critical Care. BioMed Central Ltd.; 2018.

3. Did the review authors report on the sources of funding for the studies included in the review?

4. Reade MC, Finfer S. Sedation and Delirium in the Intensive Care Unit. New England Journal of Medicine. 2014 Jan 30;370(5):444–54.

5. Latronico N, Rasulo FA, Eikermann M, Piva S. Illness Weakness, Polyneuropathy and Myopathy: Diagnosis, treatment, and long-term outcomes. Vol. 27, Critical Care. BioMed Central Ltd; 2023.

6. for Healthcare Research A. AHRQ Safety Program for Mechanically Ventilated Patients Early Mobility Guide for Reducing Ventilator-Associated Events in Mechanically Ventilated Patients. 2017.

7. Morris PE, Goad A, Thompson C, Taylor K, Harry B, Passmore L, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med. 2008;36(8):2238–43.

8. Monsees J, Moore Z, Patton D, Watson C, Nugent L, Avsar P, et al. A systematic review of the effect of early mobilisation on length of stay for adults in the intensive care unit. Vol. 28, Nursing in Critical Care. John Wiley and Sons Inc; 2023. p. 499–509.

9. Early Active Mobilization during Mechanical Ventilation in the ICU. New England Journal of Medicine [Internet]. 2022 Nov 10;387(19):1747–58. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2209083

10. De Backer D, Norrenberg M. Let′s change our behaviors: From bed rest and heavy sedation to awake, spontaneously breathing and early mobilized Intensive Care Unit patients. Vol. 18, Indian Journal of Critical Care Medicine. Wolters Kluwer Medknow Publications; 2014. p. 558–9.

11. Pfluegler G, Kasper J, Luedtke K. The immediate effects of passive joint mobilisation on local muscle function. A systematic review of the literature. Musculoskelet Sci Pract. 2020 Feb 1;45.

12. Vollenweider R, Manettas AI, Häni N, de Bruin ED, Knols RH. Passive motion of the lower extremities in sedated and ventilated patients in the ICU – a systematic review of early effects and replicability of Interventions. Vol. 17, PLoS ONE. Public Library of Science; 2022.

13. Küçük AO, Hatınoğlu N, Apaydin U, Altunalan T, Küçük MP. The association of early passive mobilization with intracranial pressure in the adult intensive care unit: A prospective, cohort study. Nurs Crit Care. 2024;

14. Wiles L, Stiller K. Passive limb movements for patients in an intensive care unit: A survey of physiotherapy practice in Australia. J Crit Care. 2010 Sep;25(3):501–8.

15. Vollenweider R, Manettas AI, Häni N, de Bruin ED, Knols RH. Passive motion of the lower extremities in sedated and ventilated patients in the ICU – a systematic review of early effects and replicability of Interventions. Vol. 17, PLoS ONE. Public Library of Science; 2022.

16. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. In: Critical Care Medicine. 2003. p. 1250–6.

17. Pfluegler G, Borkovec M, Kasper J, McLean S. The immediate effects of passive hip joint mobilization on hip abductor/external rotator muscle strength in patients with anterior knee pain and impaired hip function. A randomized, placebo-controlled crossover trial. Journal of Manual and Manipulative Therapy. 2021;29(1):14–22.

18. da Silva Destro TR, de Campos Biazon TMP, Pott-Junior H, Rossi Caruso FC, Andaku DK, Garcia NM, et al. Early passive mobilization increases vascular reactivity response in critical patients with sepsis: a quasi-experimental study. Rev Bras Ter Intensiva. 2023;34(4):461–8.

19. Nydahl P, Sricharoenchai T, Chandra S, Kundt FS, Huang M, Fischill M, et al. Safety of patient mobilization and rehabilitation in the intensive care unit: Systematic review with meta-analysis. Vol. 14, Annals of the American Thoracic Society. American Thoracic Society; 2017. p. 766–77.

20. Green M, Marzano V, Leditschke IA, Mitchell I, Bissett B. Mobilization of intensive care patients: A multidisciplinary practical guide for clinicians. J Multidiscip Healthc. 2016 May 25;9:247–56.

21. Jang MH, Shin MJ, Shin YB. Pulmonary and physical rehabilitation in critically ill patients. Acute and Critical Care. 2019;34(1):1–13.

22. Jayachandran B, Venkatesan K, Tan SBC, Yeo LSH, Venkatacham J, Selvakumar MP, et al. Feasibility of Combining Functional Mobilisation with Resistance and Endurance Training for Mechanically Ventilated Patients in Intensive Care Unit Setting—A Pilot Study. J Clin Med. 2024 Apr 1;13(8).

23. Dubb R, Nydahl P, Hermes C, Schwabbauer N, Toonstra A, Parker AM, et al. Barriers and strategies for early mobilization of patients in intensive care units. Vol. 13, Annals of the American Thoracic Society. American Thoracic Society; 2016. p. 724–30.

24. Hodgson CL, Schaller SJ, Nydahl P, Timenetsky KT, Needham DM. Ten strategies to optimize early mobilization and rehabilitation in intensive care. Vol. 25, Critical Care. BioMed Central Ltd; 2021.

25. Schaller SJ, Scheffenbichler FT, Bein T, Blobner M, Grunow JJ, Hamsen U, et al. Guideline on positioning and early mobilisation in the critically ill by an expert panel. Intensive Care Med. 2024 Aug 1;50(8):1211–27.

26. Singam A. Mobilizing Progress: A Comprehensive Review of the Efficacy of Early Mobilization Therapy in the Intensive Care Unit. Cureus. 2024 Apr 4;

27. Surve S, Sinha MK, Shanbhag V, Maiya GA. Reporting of physical activity levels in intensive care unit survivors. Sci Rep [Internet]. 2025 Mar 5;15(1):7664. Available from: https://www.nature.com/articles/s41598-024-83262-1

28. Mendez-Tellez PA, Nusr R, Needham DM, Feldman D. Early Physical Rehabilitation in the ICU: A Review for the Neurohospitalist. Vol. 2, The Neurohospitalist. 2012. p. 96–105.

29. Hickmann CE, Castanares-Zapatero D, Bialais E, Dugernier J, Tordeur A, Colmant L, et al. Teamwork enables high level of early mobilization in critically ill patients. Ann Intensive Care. 2016 Dec 1;6(1).

30. Adler J, Malone D. Early Mobilization in the Intensive Care Unit: A Systematic Review [Internet]. Vol. 23, Cardiopulmonary Physical Therapy Journal. 2012. Available from: www.cebm.net.

31. Rawal H, Bakhru RN. Early Mobilization in the ICU. CHEST Critical Care. 2024 Mar;2(1):100038.

32. Schaller SJ, Scheffenbichler FT, Bein T, Blobner M, Grunow JJ, Hamsen U, et al. Guideline on positioning and early mobilisation in the critically ill by an expert panel. Intensive Care Med. 2024 Aug 1;50(8):1211–27.

33. Lehmkuhl L, Olsen HT, Brønd JC, Rothmann MJ, Dreyer P, Jespersen E. Daily variation in physical activity during mechanical ventilation and stay in the intensive care unit. Acta Anaesthesiol Scand. 2023 Apr 1;67(4):462–9.

34. Zomorodi M, Topley D, McAnaw M. Developing a mobility protocol for early mobilization of patients in a surgical/trauma ICU. Crit Care Res Pract. 2012;2012.

35. Zhang G, Zhang K, Cui W, Hong Y, Zhang Z. The effect of early mobilization for critical ill patients requiring mechanical ventilation: a systematic review and meta-analysis. Journal of Emergency and Critical Care Medicine. 2018 Jan 26;2:9–9.

36. Zhang C, Wang X, Mi J, Zhang Z, Luo X, Gan R, et al. Effects of the High-Intensity Early Mobilization on Long-Term Functional Status of Patients with Mechanical Ventilation in the Intensive Care Unit. Crit Care Res Pract. 2024;2024.

37. García-Pérez-de-Sevilla G, Sánchez-Pinto Pinto B. Effectiveness of physical exercise and neuromuscular electrical stimulation interventions for preventing and treating intensive care unit-acquired weakness: A systematic review of randomized controlled trials. Vol. 74, Intensive and Critical Care Nursing. Churchill Livingstone; 2023.

38. Wageck B, Nunes GS, Silva FL, Damasceno MCP, de Noronha M. Application and effects of neuromuscular electrical stimulation in critically ill patients: Systematic review. Vol. 38, Medicina Intensiva. Ediciones Doyma, S.L.; 2014. p. 444–54.

39. Nussbaum EL, Houghton P, Anthony J, Rennie S, Shay BL, Hoens AM. Neuromuscular electrical stimulation for treatment of muscle impairment: Critical review and recommendations for clinical practice. Vol. 69, Physiotherapy Canada. University of Toronto Press Inc.; 2017. p. 1–76.

40. Flodin J. NEUROMUSCULAR ELECTRICAL STIMULATION IN PHYSICAL INACTIVITY.

41. Barr J, Downs B, Ferrell K, Talebian M, Robinson S, Kolodisner L, et al. Improving Outcomes in Mechanically Ventilated Adult ICU Patients Following Implementation of the ICU Liberation (ABCDEF) Bundle Across a Large Healthcare System. Crit Care Explor. 2024 Jan 19;6(1):E1001.

42. Marra A, Ely EW, Pandharipande PP, Patel MB. The ABCDEF Bundle in Critical Care. Vol. 33, Critical Care Clinics. W.B. Saunders; 2017. p. 225–43.

43. Sosnowski K, Lin F, Chaboyer W, Ranse K, Heffernan A, Mitchell M. The effect of the ABCDE/ABCDEF bundle on delirium, functional outcomes, and quality of life in critically ill patients: A systematic review and meta-analysis. Vol. 138, International Journal of Nursing Studies. Elsevier Ltd; 2023.

44. Ringdal M, Warren Stomberg M, Egnell K, Wennberg E, Zätterman R, Rylander C. In-bed cycling in the ICU; patient safety and recollections with motivational effects. Acta Anaesthesiol Scand. 2018 May 1;62(5):658–65.

45. Yu L, Jiang JX, Zhang Y, Chen YZ, Shi Y. Use of in-bed cycling combined with passive joint activity in acute respiratory failure patients receiving mechanical ventilation. Ann Cardiothorac Surg. 2020 Mar 1;9(2):175–81.

46. Zink EK, Kumble S, Beier M, George P, Stevens RD, Bahouth MN. Physiological Responses to In-Bed Cycle Ergometry Treatment in Intensive Care Unit Patients with External Ventricular Drainage. Neurocrit Care. 2021 Dec 1;35(3):707–13.

47. Wi S, Shin HI, Hyun SE, Sung KS, Lee WH. Feasibility and safety of in-bed cycling/stepping in critically ill patients: A study protocol for a pilot randomized controlled clinical trial. PLoS One. 2024 May 1;19(5 May).

48. Kho ME, Martin RA, Toonstra AL, Zanni JM, Mantheiy EC, Nelliot A, et al. Feasibility and safety of in-bed cycling for physical rehabilitation in the intensive care unit. J Crit Care. 2015 Dec 1;30(6):1419.e1-1419.e5.

49. Kimawi I, Lamberjack B, Nelliot A, Toonstra AL, Zanni J, Huang M, et al. Safety and Feasibility of a Protocolized Approach to In-Bed Cycling Exercise in the Intensive Care Unit: Quality Improvement Project [Internet]. Vol. 97, Physical Therapy . 2017. Available from: https://academic.oup.com/ptj

50. Kho ME, Martin RA, Toonstra AL, Zanni JM, Mantheiy EC, Nelliot A, et al. Feasibility and safety of in-bed cycling for physical rehabilitation in the intensive care unit. J Crit Care. 2015 Dec 1;30(6):1419.e1-1419.e5.

51. Takaoka A, Utgikar R, Rochwerg B, Cook DJ, Kho ME. The Efficacy and Safety of In-Intensive Care Unit Leg-Cycle Ergometry in Critically Ill Adults A Systematic Review and Meta-analysis. Vol. 17, Annals of the American Thoracic Society. American Thoracic Society; 2020. p. 1289–307.

52. Hodgson C, Needham D, Haines K, Bailey M, Ward A, Harrold M, et al. Feasibility and inter-rater reliability of the ICU Mobility Scale. Heart and Lung: Journal of Acute and Critical Care. 2014 Jan;43(1):19–24.

53. O’Grady HK, Hasan H, Rochwerg B, Cook DJ, Takaoka A, Utgikar R, et al. Leg Cycle Ergometry in Critically Ill Patients — An Updated Systematic Review and Meta-Analysis. NEJM Evidence [Internet]. 2024 Nov 26;3(12). Available from: https://evidence.nejm.org/doi/10.1056/EVIDoa2400194

54. Jones I, Johnson MI. Transcutaneous electrical nerve stimulation. Continuing Education in Anaesthesia, Critical Care and Pain. 2009;9(4):130–5.

55. Viderman D, Nabidollayeva F, Aubakirova M, Sadir N, Tapinova K, Tankacheyev R, et al. The Impact of Transcutaneous Electrical Nerve Stimulation (TENS) on Acute Pain and Other Postoperative Outcomes: A Systematic Review with Meta-Analysis. Vol. 13, Journal of Clinical Medicine. Multidisciplinary Digital Publishing Institute (MDPI); 2024.

56. de Moraes AV, Costa JDS, Do Nascimento JMR. The effects of transcutaneous electrostimulation in patients in the intensive care unit. Vol. 9, Revista Pesquisa em Fisioterapia. BAHIANA - School of Medicine and Public Health; 2019. p. 572–80.

57. Balke M, Teschler M, Schäfer H, Pape P, Mooren FC, Schmitz B. Therapeutic Potential of Electromyostimulation (EMS) in Critically Ill Patients—A Systematic Review. Vol. 13, Frontiers in Physiology. Frontiers Media S.A.; 2022.

58. Li L, Li F, Zhang X, Song Y, Li S, Yao H. The effect of electrical stimulation in critical patients: a meta-analysis of randomized controlled trials. Vol. 15, Frontiers in Neurology. Frontiers Media SA; 2024.

59. Callahan LA, Supinski GS. Prevention and treatment of ICU-acquired weakness: Is there a stimulating answer? Vol. 41, Critical Care Medicine. 2013. p. 2457–8.

60. Watanabe S, Hirasawa J, Naito Y, Mizutani M, Uemura A, Nishimura S, et al. Association between the early mobilization of mechanically ventilated patients and independence in activities of daily living at hospital discharge. Sci Rep. 2023 Dec 1;13(1).

61. Chen J, Huang M. Intensive care unit-acquired weakness: Recent insights. Vol. 4, Journal of Intensive Medicine. Chinese Medical Association; 2024. p. 73–80.

62. Wang W, Xu C, Ma X, Zhang X, Xie P. Intensive Care Unit-Acquired Weakness: A Review of Recent Progress With a Look Toward the Future. Vol. 7, Frontiers in Medicine. Frontiers Media S.A.; 2020.

63. Piva S, Fagoni N, Latronico N. Intensive care unit–acquired weakness: unanswered questions and targets for future research: . Vol. 8, F1000Research. F1000 Research Ltd; 2019.

64. Fuentes-Aspe R, Gutierrez-Arias R, González-Seguel F, Marzuca-Nassr GN, Torres-Castro R, Najum-Flores J, et al. Which factors are associated with acquired weakness in the ICU? An overview of systematic reviews and meta-analyses. Vol. 12, Journal of Intensive Care. BioMed Central Ltd; 2024.

65. Fan E, Cheek F, Chlan L, Gosselink R, Hart N, Herridge MS, et al. An official american thoracic society clinical practice guideline: The diagnosis of intensive care unit-acquired weakness in adults. Am J Respir Crit Care Med. 2014 Dec 15;190(12):1437–46.

66. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. www.thelancet.com [Internet]. 2009;373. Available from: www.thelancet.com

67. Campbell MR, Campbell MR(. CORE Scholar CORE Scholar The Effect of an Early Mobility Protocol in Critically Ill The Effect of an Early Mobility Protocol in Critically Ill Mechanically Ventilated Patients on Incidence and Duration of Mechanically Ventilated Patients on Incidence and Duration of Delirium and Length of Stay Delirium and Length of Stay Repository Citation Repository Citation [Internet]. Available from: https://corescholar.libraries.wright.edu/nursing\_dnp

68. Taito S, Shime N, Ota K, Yasuda H. Early mobilization of mechanically ventilated patients in the intensive care unit. Vol. 4, Journal of Intensive Care. BioMed Central Ltd.; 2016.

69. Kansal A, Latour JM, See KC, Rai S, Cecconi M, Britto C, et al. Interventions to promote cost-effectiveness in adult intensive care units: consensus statement and considerations for best practice from a multidisciplinary and multinational eDelphi study. Crit Care. 2023 Dec 1;27(1).

70. Wunsch H, Gershengorn H, Scales DC. Economics of ICU Organization and Management. Vol. 28, Critical Care Clinics. 2012. p. 25–37.

71. Reardon PM, Fernando SM, Van Katwyk S, Thavorn K, Kobewka D, Tanuseputro P, et al. Characteristics, Outcomes, and Cost Patterns of High-Cost Patients in the Intensive Care Unit. Crit Care Res Pract. 2018;2018.

72. Hodgson C, Bellomo R, Berney S, Bailey M, Buhr H, Denehy L, et al. Early mobilization and recovery in mechanically ventilated patients in the ICU: A bi-national, multi-centre, prospective cohort study. Crit Care. 2015 Feb 26;19(1).

73. Zang K, Chen B, Wang M, Chen D, Hui L, Guo S, et al. The effect of early mobilization in critically ill patients: A meta-analysis. Nurs Crit Care. 2020 Nov 1;25(6):360–7.

74. Clark DE, Lowman JD, Griffin RL, Matthews HM, Reiff DA. Effectiveness of an early mobilization protocol in a trauma and burns intensive care unit: A retrospective cohort study. Phys Ther. 2013 Feb;93(2):186–96.

75. Al-Dorzi HM, AlQahtani S, Al-Dawood A, Al-Hameed FM, Burns KEA, Mehta S, et al. Association of early mobility with the incidence of deep-vein thrombosis and mortality among critically ill patients: a post hoc analysis of PREVENT trial. Crit Care. 2023 Dec 1;27(1).

76. Kim G, Oh DK, Lee SY, Park MH, Lim CM. Impact of the timing of invasive mechanical ventilation in patients with sepsis: a multicenter cohort study. Crit Care. 2024 Dec 1;28(1).

77. Dolinay T, Hsu L, Maller A, Walsh BC, Szűcs A, Jerng JS, et al. Ventilator Weaning in Prolonged Mechanical Ventilation—A Narrative Review. Vol. 13, Journal of Clinical Medicine. Multidisciplinary Digital Publishing Institute (MDPI); 2024.

78. Huang HY, Huang CY, Li LF. Prolonged Mechanical Ventilation: Outcomes and Management. Vol. 11, Journal of Clinical Medicine. MDPI; 2022.

79. Bissett B, Gosselink R, Van Haren FMP. Respiratory Muscle Rehabilitation in Patients with Prolonged Mechanical Ventilation: A Targeted Approach. Vol. 24, Critical Care. BioMed Central Ltd.; 2020.

80. Paton M, Chan S, Tipping CJ, Stratton A, Serpa Neto A, Lane R, et al. The Effect of Mobilization at 6 Months after Critical Illness — Meta-Analysis. NEJM Evidence. 2023 Jan 24;2(2).

81. Patel BK, Wolfe KS, Patel SB, Dugan KC, Esbrook CL, Pawlik AJ, et al. Effect of early mobilisation on long-term cognitive impairment in critical illness in the USA: a randomised controlled trial. Lancet Respir Med. 2023 Jun 1;11(6):563–72.

82. Papageorgiou D, Triantafyllou C, Stavropoulou A, Kelesi M, Kaba E, Evgenikos K, et al. The evaluation of the quality of life in survivors of critical illness after discharge from Intensive Care Unit (ICU): A prospective cohort study [Internet]. 2023. Available from: http://medrxiv.org/lookup/doi/10.1101/2023.04.24.23289053

83. Li Y, Fang D, Wu Q. Health-related quality of life among critically ill patients after discharge from the ICU—A systematic review protocol. PLoS One. 2023 Aug 1;18(8 August).

84. Mart MF, Williams Roberson S, Salas B, Pandharipande PP, Ely EW. Prevention and Management of Delirium in the Intensive Care Unit. Semin Respir Crit Care Med. 2021 Feb 1;42(1):112–26.

85. Johnson GU, Towell-Barnard A, Mclean C, Ewens B. Delirium prevention and management in an adult intensive care unit through evidence-based nonpharmacological interventions: A scoping review. 2024; Available from: http://creativecommons.org/licenses/by/4.0/

86. van den Boogaard M, Slooter AJC. Delirium in critically ill patients: current knowledge and future perspectives. Vol. 19, BJA Education. Elsevier Ltd; 2019. p. 398–404.

87. Renzi S, Gitti N, Piva S. Delirium in the intensive care unit: a narrative review. Vol. 71, Journal of Gerontology and Geriatrics. Pacini Editore S.p.A./AU-CNS; 2023. p. 22–9.

88. Fiest KM, Soo A, Lee CH, Niven DJ, Ely EW, Doig CJ, et al. Long-term outcomes in ICU patients with delirium a population-based cohort study. Am J Respir Crit Care Med. 2021 Aug 15;204(4):412–20.

89. Da Conceição TMA, Gonzáles AI, De Figueiredo FCXS, Rocha Vieira DS, Bündchen DC. Safety criteria to start early mobilization in intensive care units. Systematic review. Vol. 29, Revista Brasileira de Terapia Intensiva. Associacao de Medicina Intensiva Brasileira - AMIB; 2017. p. 509–19.

90. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ (Online). 2017;358.

91. Bougioukas KI, Karakasis P, Pamporis K, Bouras E, Haidich AB. amstar2Vis: An R package for presenting the critical appraisal of systematic reviews based on the items of AMSTAR 2. Res Synth Methods. 2024 May 1;15(3):512–22.

92. Lippi L, de Sire A, D’Abrosca F, Polla B, Marotta N, Castello LM, et al. Efficacy of Physiotherapy Interventions on Weaning in Mechanically Ventilated Critically Ill Patients: A Systematic Review and Meta-Analysis. Vol. 9, Frontiers in Medicine. Frontiers Media S.A.; 2022.

93. Higgins SD, Erdogan M, Coles SJ, Green RS. Early mobilization of trauma patients admitted to intensive care units: A systematic review and meta-analyses. Injury. 2019 Nov 1;50(11):1809–15.

94. Yang Y, Zhang RJ, Yuan XN, Gu YQ, Li YN, Wu SP, et al. Clinical effect of pulmonary rehabilitation in patients with mechanical ventilation: A meta-analysis. International Journal of Artificial Organs. 2024 Feb 1;47(2):96–106.

95. Bougioukas KI, Diakonidis T, Mavromanoli AC, Haidich AB. ccaR: A package for assessing primary study overlap across systematic reviews in overviews. Res Synth Methods. 2023 May 1;14(3):443–54.

96. Jiroutková K, Duska F, Waldauf P. Should New Data on Rehabilitation Interventions in Critically Ill Patients Change Clinical Practice? Updated Meta-Analysis of Randomized Controlled Trials. Crit Care Med. 2024 Jun 1;52(6):E299–303.

97. Ruo Yu L, Jia Jia W, Meng Tian W, Tian Cha H, Ji Yong J. Optimal timing for early mobilization initiatives in intensive care unit patients: A systematic review and network meta-analysis. Vol. 82, Intensive and Critical Care Nursing. Churchill Livingstone; 2024.

98. Ding N, Zhang Z, Zhang C, Yao L, Yang L, Jiang B, et al. What is the optimum time for initiation of early mobilization in mechanically ventilated patients? A network meta-analysis. PLoS One. 2019 Oct 1;14(10).

99. Tipping CJ, Harrold M, Holland A, Romero L, Nisbet T, Hodgson CL. The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review. Vol. 43, Intensive Care Medicine. Springer Verlag; 2017. p. 171–83.

100. Taito S, Taito M, Banno M, Tsujimoto H, Kataoka Y, Tsujimoto Y. Rehabilitation for patients with sepsis: A systematic review and meta-analysis. Vol. 13, PLoS ONE. Public Library of Science; 2018.

101. Fuke R, Hifumi T, Kondo Y, Hatakeyama J, Takei T, Yamakawa K, et al. Early rehabilitation to prevent postintensive care syndrome in patients with critical illness: A systematic review and meta-analysis. Vol. 8, BMJ Open. BMJ Publishing Group; 2018.

102. Zhang L, Hu W, Cai Z, Liu J, Wu J, Deng Y, et al. Early mobilization of critically ill patients in the intensive care unit: A systematic review and meta-analysis. PLoS One. 2019 Oct 1;14(10).

103. Zang K, Chen B, Wang M, Chen D, Hui L, Guo S, et al. The effect of early mobilization in critically ill patients: A meta-analysis. Nurs Crit Care. 2020 Nov 1;25(6):360–7.

104. Zayed Y, Kheiri B, Barbarawi M, Chahine A, Rashdan L, Chintalapati S, et al. Effects of neuromuscular electrical stimulation in critically ill patients: A systematic review and meta-analysis of randomised controlled trials. Vol. 33, Australian Critical Care. Elsevier Ireland Ltd; 2020. p. 203–10.

105. Wang J, Ren D, Liu Y, Wang Y, Zhang B, Xiao Q. Effects of early mobilization on the prognosis of critically ill patients: A systematic review and meta-analysis. Vol. 110, International Journal of Nursing Studies. Elsevier Ltd; 2020.

106. Nieto-García L, Carpio-Pérez A, Moreiro-Barroso MT, Alonso-Sardón M. Can an early mobilisation programme prevent hospital-acquired pressure injures in an intensive care unit?: A systematic review and meta-analysis. Int Wound J. 2021 Apr 1;18(2):209–20.

107. Nakanishi N, Yoshihiro S, Kawamura Y, Aikawa G, Shida H, Shimizu M, et al. Effect of Neuromuscular Electrical Stimulation in Patients with Critical Illness: An Updated Systematic Review and Meta-Analysis of Randomized Controlled Trials. Vol. 51, Critical Care Medicine. Lippincott Williams and Wilkins; 2023. p. 1386–96.

108. Jarman A, Chapman K, Vollam S, Stiger R, Williams M, Gustafson O. Investigating the impact of physical activity interventions on delirium outcomes in intensive care unit patients: A systematic review and meta-analysis. Vol. 24, Journal of the Intensive Care Society. SAGE Publications Inc.; 2023. p. 85–95.

109. Xu C, Yang F, Wang Q, Gao W. Effect of neuromuscular electrical stimulation in critically ill adults with mechanical ventilation: a systematic review and network meta-analysis. BMC Pulm Med. 2024 Dec 1;24(1).

110. Zhao J, Fan K, Zheng S, Xie G, Niu X, Pang J, et al. Effect of occupational therapy on the occurrence of delirium in critically ill patients: a systematic review and meta-analysis. Vol. 15, Frontiers in Neurology. Frontiers Media SA; 2024.

111. Denehy L, Lanphere J, Needham DM. Ten reasons why ICU patients should be mobilized early. Intensive Care Med. 2017 Jan 1;43(1):86–90.

112. Rawal H, Bakhru RN. Early Mobilization in the ICU. CHEST Critical Care. 2024 Mar;2(1):100038.

113. Truong AD, Fan E, Brower RG, Needham DM. Bench-to-bedside review: mobilizing patients in the intensive care unit--from pathophysiology to clinical trials. Vol. 13, Critical care (London, England). 2009. p. 216.

114. Kim C, Kim S, Yang J, Choi M. Nurses’ perceived barriers and educational needs for early mobilisation of critical ill patients. Australian Critical Care. 2019 Nov 1;32(6):451–7.

115. Jones Baro R, Martínez Camacho M, Go A, Gonza mez, Delgado Camacho J, Melo Villalobos A, et al. INTENSIVE CARE I EMERGENCY MEDICINE I ANAESTHESIOLOGY I CARDIOLOGY I MANAGEMENT I LEADERSHIP VOLUME 24 ISSUE 4 2 0 2 4 Mobilisation The ABCs of Physical Therapy for Solid Organ Transplant Patients. ICU Management & Practice.

116. Jones Baro R, Martínez Camacho M, Go A, Gonza mez, Delgado Camacho J, Melo Villalobos A, et al. INTENSIVE CARE I EMERGENCY MEDICINE I ANAESTHESIOLOGY I CARDIOLOGY I MANAGEMENT I LEADERSHIP VOLUME 24 ISSUE 4 2 0 2 4 Mobilisation The ABCs of Physical Therapy for Solid Organ Transplant Patients. ICU Management & Practice.

# Appendix

Search Strategy

A comprehensive search of electronic databases was conducted to identify relevant systematic reviews and meta-analyses. The databases included PubMed, Cochrane Library, and Epistemonikos.

Medical subject heading (MeSH) terms and the appropriate free-text keywords for the database searching included the following search algorithms:

*("Early Ambulation"[MeSH] OR "early mobilization" OR "early ambulation") AND ("Intensive Care Units"[MeSH] OR "intensive care unit" OR ICU) AND ("Meta-Analysis as Topic"[MeSH] OR "meta-analysis" OR "systematic review")*

and

*("meta-analysis as topic"[MESH:NOEXP] OR Meta-Analysis[PT] OR "network meta-analysis"[mesh:noexp] OR "indirect comparison"[TIAB:~1] OR meta analyses[TIAB] OR meta analysis[TIAB] OR meta analytic[TIAB] OR meta analytical[TIAB] OR meta analytics[TIAB] OR meta analyze[TIAB] OR meta analyzed[TIAB] OR metaanalyses[TIAB] OR metaanalysis[TIAB] OR metaanalytic[TIAB] OR metaanalyze[TIAB] OR metaanalyzed[TIAB] OR "network comparison"[TIAB:~1] OR "network meta analyses"[TIAB] OR "network meta analysis"[TIAB] OR "network metaanalyses"[TIAB] OR "network metaanalysis"[TIAB] OR (systematic[tiab] AND (meta regression[TIAB] OR metaregression[TIAB])))*

We worked accordingly on the Epistemonikos database for studies that meet our criteria from the inclusion and exclusion criteria with the following query:

*(title:((title:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness) OR abstract:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness)) AND (title:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy) OR abstract:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy)) AND (title:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic) OR abstract:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic))) OR abstract:((title:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness) OR abstract:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness)) AND (title:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy) OR abstract:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy)) AND (title:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic) OR abstract:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic)))) 1) (title:((title:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness) OR abstract:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness)) AND (title:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy) OR abstract:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy)) AND (title:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic) OR abstract:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic))) OR abstract:((title:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness) OR abstract:(critical care OR intensive care OR critical\* ill\* OR mechanical ventilation OR delirium OR acquired weakness)) AND (title:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy) OR abstract:(mobilisation OR mobilization OR mobility OR rehabilitation OR physiotherapy OR physical therapy)) AND (title:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic) OR abstract:(meta-analysis OR metaanalysis OR systematic OR network meta-analysis OR comparison OR systematic))))*

Additionally, the research algorithm for CINAHL was the following:

*Search: (TI/AB (mobilisation OR mobilization OR mobility OR functional mobility OR physiotherapy OR rehabilitation) ) AND TI/AB (critical care OR intensive care OR critical\* ill\* OR invasive mechanical ventilation OR non invasive mechanical ventilation OR intensive care unit acquired weakness OR ICUAW OR delirium ))*

*and*

*MW meta-analysis OR PT Meta-Analysis OR MW network meta-analysis OR ( TI/AB (indirect comparison OR meta analyses OR meta analysis OR meta analytic OR meta analytical OR meta analytics OR meta analyze OR meta analyzed OR metaanalyses OR metaanalysis OR metaanalytic OR metaanalyze OR metaanalyzed OR network comparison OR network meta analyses OR network meta analysis OR network metaanalyses OR network metaanalysis ) OR ( TI/AB (systematic AND (meta regression OR metaregression))) )*

The search was limited to articles published in English, but there was no limitation for the publication timing of the reviews which were selected for this thesis.

List of excluded studies

|  |  |
| --- | --- |
| Study | Exclusion Criteria |
| Low-Medium and High-Intensity Inspiratory Muscle Training in Critically Ill Patients: A Systematic Review and Meta-Analysis | Neurological ICU |
| Should We Use the Functional Electrical Stimulation-Cycling Exercise in Clinical Practice? Physiological and Clinical Effects Systematic Review With Meta-analysis | Irrelevant Outcomes |
| Effects of exercise interventions on functioning and health-related quality of life following hospital discharge for recovery from critical illness: A systematic review and meta-analysis of randomized  trials | No Access |
| Association of active mobilization variables with adverse events and mortality in patients requiring mechanical ventilation in the intensive care unit: a systematic review and meta-analysis | Mixed Population |
| Clinical Impact of the Implementation Strategies Used to Apply the 2013 Pain, Agitation/Sedation, Delirium or 2018 Pain, Agitation/Sedation, Delirium, Immobility, Sleep Disruption Guideline  Recommendations: A Systematic Review and Meta-Analysis | Wrong Intervention |
| Effect of early systemic rehabilitation on muscle strength and prognosis of patients undergoing mechanical ventilation in intensive care unit: a Meta-analysis | No Access |
| Early mobilization within 72 hours after admission of critically ill patients in the intensive care unit: A systematic review with network meta-analysis | Cardiac Surgery |
| Effects of Mobilization within 72 h of ICU Admission in Critically Ill Patients: An Updated Systematic Review and Meta-Analysis of Randomized Controlled Trials | CABG |
| The effects of early mobilization in mechanically ventilated adult ICU patients: systematic review  and meta-analysis | CABG |
| Early mobilization for prevention and treatment of delirium in critically ill patients: Systematic review and meta-analysis | Cardiac Surgery |
| Responsiveness of Critically Ill Adults With Multimorbidity to Rehabilitation Interventions: A Patient-Level Meta-Analysis Using Individual Pooled Data From Four Randomized Trials | No Access |
| Effects of different types and frequencies of early rehabilitation on ventilator weaning among patients in intensive care units: A systematic review and meta-analysis | Cardiac Surgery |
| A Step Forward for Intensive Care Unit Patients: Early Mobility Interventions and Associated Outcome Measures | No Access |
| Effect of neuromuscular electrical stimulation on muscle strength in patients with mechanical ventilation in intensive care unit: cumulative Meta-analysis and trial sequential analysis | No Access |
| Effects of non-pharmacologic prevention on delirium in critically ill patients: A network meta-analysis | Neurological & Stroke ICU |
| Comparative effectiveness of non-pharmacological interventions for preventing delirium in critically ill adults: A systematic review and network meta-analysis | Light Therapy |
| Efficacy of Respiratory Physiotherapy Interventions for Intubated and Mechanically Ventilated Adults  with Pneumonia: A Systematic Review and Meta-Analysis | Wrong Intervention |
| Meta-analysis of effects of neuromuscular electrical stimulation of lower limbs on patients  with mechanical ventilation in intensive care unit | No Access |
| Effect of mechanical ventilation and pulmonary rehabilitation in patients with ICU-acquired weakness: a systematic review and meta-analysis | Pulmonary Rehabilitation |
| Early activity in mechanically ventilated patients – a meta-analysis | CABG |
| Early mobilization on mortality of patients with mechanical ventilation in intensive care unit after discharge: a Meta-analysis | No Access |
| Systematic early versus late mobilization or standard early mobilization in mechanically ventilated adult ICU patients: systematic review and meta-analysis | Cardiothoracic Surgery |
| Effects of nonpharmacological delirium-prevention interventions on critically ill patients' clinical,  psychological, and family outcomes: A systematic review and meta-analysis | Abdominal, Cardiac & Liver Surgery |
| Effects of Inspiratory Muscle Training and Early Mobilization on Weaning of Mechanical Ventilation: A Systematic Review and Network Meta-analysis | Surgery |
| Effects of Rehabilitation Interventions on Clinical Outcomes in Critically Ill Patients: Systematic Review and Meta-Analysis of Randomized Controlled Trials | Updated Version Included |
| Early rehabilitation reduces the likelihood of developing intensive care unit-acquired weakness: a systematic review and meta-analysis | Cardiothoracic Surgery |
| Early versus delayed mobilization for in-hospital mortality and health-related quality of life among critically ill patients: a systematic review and meta-analysis | CABG & Cardiac Surgery |
| Early rehabilitation to prevent post-intensive care syndrome in critical illness patients: a Meta-analysis | No Access |
| Effect of early mobilization on the physical function of patients in intensive care unit: a Meta-analysis | No Access |
| Inspiratory Muscle Rehabilitation in Critically Ill Adults. A Systematic Review and Meta-Analysis | Wrong Intervention |
| Early intervention (mobilization or active exercise) for critically ill adults in the intensive care unit | Cardiac Surgery |
| Outcomes of safe patient handling and mobilization programs: A meta-analysis | Irrelevant Outcomes |
| Safety of Patient Mobilization and Rehabilitation in the Intensive Care Unit. Systematic Review with Meta-Analysis | Safety Concerns Study |
| Effect of Early Rehabilitation during Intensive Care Unit Stay on Functional Status: Systematic Review and Meta-Analysis | Surgery |
| Physical rehabilitation for critical illness myopathy and neuropathy | No Studies Included |
| An evaluation of neuromuscular electrical stimulation in critical care using the ICF framework: a systematic review and meta-analysis | Stroke |
| Interventions for preventing critical illness polyneuropathy and critical illness myopathy | Mixed Interventions |
| Physical therapy for the critically ill in the ICU: a systematic review and meta-analysis | Surgery |
| ABCDE and ABCDEF care bundles: A systematic review of the implementation process in intensive care units | Pediatric ICU |
| A systematic review of the effect of early mobilization on length of stay for adults in the intensive care unit | Liver Transplant & Surgery |
| Passive motion of the lower extremities in sedated and ventilated patients in the ICU - a  systematic review of early effects and replicability of Interventions | Abdominal Surgery |
| Rehabilitation and early mobilization in the critical patient: systematic review | Coronary ICU |
| Early Mobilization Dose Reporting in Randomized Clinical Trials With Patients Who Were Mechanically Ventilated: A Scoping Review | Irrelevant Outcomes |

**Table 13: PRIOR Checklist (preferred reporting items for overview of systematic reviews)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section Topic** | **Item No** | **Item** | **Location where item is reported** |
| **Title** | | | |
| Title | 1 | Identify the report as an overview of systematic reviews. | Page 1 |
| **Abstract** | | | |
| Abstract | 2 | Provide a comprehensive and accurate summary of the purpose, methods, and results of the overview of systematic reviews. | Page 7 |
| **Introduction** | | | |
| Rationale | 3 | Describe the rationale for conducting the overview of reviews in the context of existing knowledge. | Page 8 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) addressed by the overview of reviews. | Page 8 (last paragraph) |
| **Methods** | | | |
| Eligibility Criteria | 5a | Specify the inclusion and exclusion criteria for the overview of reviews. If supplemental primary studies were included, this should be stated, with a rationale. | Page 9 (Inclusion & Exclusion Criteria) |
| 5b | Specify the definition of “systematic review” as used in the inclusion criteria for the overview of reviews. | Page 9 (1st paragraph) |
| Information sources | 6 | Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify systematic reviews and supplemental primary studies (if included). Specify the date when each source was last searched or consulted. | Page 7 (Methods),  Page 19 (Search Strategy) |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, such that they could be reproduced. Describe any search filters and limits applied | 55-56 (Appendix – Search Algorithms) |
| Selection process | 8a | Describe the methods used to decide whether a systematic review or supplemental primary study (if included) met the inclusion criteria of the overview of reviews. | Page 19 (Screening) |
| 8b | Describe how overlap in the populations, interventions, comparators, and/or outcomes of systematic reviews was identified and managed during study selection. | Page 27 (CCA Evaluation) |
| Data collection process | 9a | Describe the methods used to collect data from reports. | Page 19 (Data Collection) |
| 9b | If applicable, describe the methods used to identify and manage primary study overlap at the level of the comparison and outcome during data collection. For each outcome, specify the method used to illustrate and/or quantify the degree of primary study overlap across systematic reviews. | Page 27 (CCA Evaluation) |
| 9c | If applicable, specify the methods used to manage discrepant data across systematic reviews during data collection. | Not applicable |
| Data items | 10 | List and define all variables and outcomes for which data were sought. Describe any assumptions made and/or measures taken to identify and clarify missing or unclear information. | Page 21, Page 23-24 (Table) |
| Risk of bias assessment | 11a | Describe the methods used to assess risk of bias or methodological quality of the included systematic reviews. | Page 20 (Risk of Bias Assessment) |
| 11b | Describe the methods used to collect data on (from the systematic reviews) and/or assess the risk of bias of the primary studies included in the systematic reviews. Provide a justification for instances where flawed, incomplete, or missing assessments are identified but not reassessed. | Page 19 (Methods), Page 20 (Risk of Bias Assessment) |
| 11c | Describe the methods used to assess the risk of bias of supplemental primary studies (if included). | Not applicable |
| Synthesis methods | 12a | Describe the methods used to summarize or synthesize results and provide a rationale for the choice(s). | Page 20 (Data Synthesis & Analysis) |
| 12b | Describe any methods used to explore possible causes of heterogeneity among results. | Page 21 (last paragraph) |
| 12c | Describe any sensitivity analyses conducted to assess the robustness of the synthesized results | Page 21 (last paragraph) |
| Reporting bias assessment | 13 | Describe the methods used to collect data on (from the systematic reviews) and/or assess the risk of bias due to missing results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included). | Page 19 (Data Collection), Page 25-26 (AMSTAR2) |
| Certainty assessment | 14 | Describe the methods used to collect data on (from the systematic reviews) and/or assess certainty (or confidence) in the body of evidence for an outcome. | Page 19-20 (Methods) |
| **Results** | | | |
| Systematic review and supplemental primary study selection | 15a | Describe the results of the search and selection process, including the number of records screened, assessed for eligibility, and included in the overview of reviews, ideally with a flow diagram. | Page 22 (Flow Diagram) |
| 15b | Provide a list of studies that might appear to meet the inclusion criteria, but were excluded, with the main reason for exclusion. | Page 57-58 (List of excluded studies) |
| Characteristics of systematic reviews and supplemental primary studies | 16 | Cite each included systematic review and supplemental primary study (if included) and present its characteristics. | Page 23-24 (Table) |
| Primary study overlap | 17 | Describe the extent of primary study overlap across the included systematic reviews. | Page 27 (CCA Evaluation) |
| Risk of bias in systematic reviews, primary studies, and supplemental primary studies | 18a | Present assessments of risk of bias or methodological quality for each included systematic review. | Page 25-26 (AMSTAR2) |
| 18b | Present assessments (collected from systematic reviews or assessed anew) of the risk of bias of the primary studies included in the systematic reviews. | Page 20 (Risk of Bias Assessment) |
| 18c | Present assessments of the risk of bias of supplemental primary studies (if included). | Not applicable |
| Summary of synthesis of results | 19a | For all outcomes, summarize the evidence from the systematic reviews and supplemental primary studies (if included). If meta-analyses were done, present for each the summary estimate and its precision and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page 28-36 (Results) |
| 19b | If meta-analyses were done, present results of all investigations of possible causes of heterogeneity. | Not applicable |
| 19c | If meta-analyses were done, present results of all sensitivity analyses conducted to assess the robustness of synthesized results. | Not applicable |
| Reporting biases | 20 | Present assessments (collected from systematic reviews and/or assessed anew) of the risk of bias due to missing primary studies, analyses, or results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included) for each summary or synthesis assessed. |  |
| Certainty of evidence | 21 | Present assessments (collected or assessed anew) of certainty (or confidence) in the body of evidence for each outcome. | Page 28-36 (Results) |
| **Discussion** | | | |
| Discussion | 22a | Summarize the main findings, including any discrepancies in findings across the included systematic reviews and supplemental primary studies (if included). | Page 39-41 (Conclusions) |
| 22b | Provide a general interpretation of the results in the context of other evidence. | Page 39-41 (Conclusions) |
| 22c | Discuss any limitations of the evidence from systematic reviews, their primary studies, and supplemental primary studies (if included) included in the overview of reviews. Discuss any limitations of the overview of reviews methods used. | Page 37-38 (Discussion) |
| 22d | Discuss implications for practice, policy, and future research (both systematic reviews and primary research). Consider the relevance of the findings to the end users of the overview of reviews, e.g., healthcare providers, policymakers, patients, among others. | Page 37-38 (Challenges and Barriers to Implementation) |
| **Other information** | | | |
| Registration and protocol | 23a | Provide registration information for the overview of reviews, including register name and registration number, or state that the overview of reviews was not registered. | Page 18 (Methods) |
| 23b | Indicate where the overview of reviews protocol can be accessed, or state that a protocol was not prepared. | Page 18 (Methods) |
| 23c | Describe and explain any amendments to information provided at registration or in the protocol. Indicate the stage of the overview of reviews at which amendments were made. | Page 18 (Methods) |
| Support | 24 | Describe sources of financial or non-financial support for the overview of reviews, and the role of the funders or sponsors in the overview of reviews. | Page 41 (Funding & Competing Interests) |
| Competing interests | 25 | Declare any competing interests of the overview of reviews’ authors. | Page 41 (Funding & Competing Interests) |
| Author information | 26a | Provide contact information for the corresponding author. | Page 2 |
| 26b | Describe the contributions of individual authors and identify the guarantor of the overview of reviews. | Page 6 |
| Availability of data and other materials | 27 | Report which of the following are available, where they can be found, and under which conditions they may be accessed: template data collection forms; data collected from included systematic reviews and supplemental primary studies; analytic code; any other materials used in the overview of reviews. | Page 42-54 (References) |

1. Standardized Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-1)
2. Early Mobilization, Inspiratory Muscle Training, Conventional Physiotherapy, Early Rehabilitation, Artificial Airway Humidification [↑](#footnote-ref-2)
3. Cycling, Neuromuscular Electrical Stimulation, Protocolized Physical Rehabilitation, Functional Electrical Stimulation-Assisted Cycle Ergometry [↑](#footnote-ref-3)
4. Standardized Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-4)
5. Exercise Therapy, Air Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training [↑](#footnote-ref-5)
6. Standard Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-6)
7. Protocolized Physical Rehabilitation [↑](#footnote-ref-7)
8. Functional Electrical Stimulation [↑](#footnote-ref-8)
9. Occupational Therapy with Standard Non-Pharmacological Prevention, Standard Care Interventions [↑](#footnote-ref-9)
10. Exercise Therapy, Aire Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training [↑](#footnote-ref-10)
11. Standardized Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-11)
12. Occupational Therapy with Standard Non-Pharmacological Prevention, Standard Care Interventions [↑](#footnote-ref-12)
13. Cycling, Functional Electrical Stimulation, Early Mobilization, Usual Care [↑](#footnote-ref-13)
14. Standardized Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-14)
15. Protocolized Physical Rehabilitation [↑](#footnote-ref-15)
16. Functional Electrical Stimulation [↑](#footnote-ref-16)
17. Exercise Therapy, Air Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training [↑](#footnote-ref-17)
18. Standardized Early Mobilization, Enhanced Mobilization, Intensive Physical Therapy Program, Physiotherapy [↑](#footnote-ref-18)
19. Protocolized Physical Rehabilitation [↑](#footnote-ref-19)
20. Functional Electrical Stimulation [↑](#footnote-ref-20)
21. Exercise Therapy, Air Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training [↑](#footnote-ref-21)
22. Exercise Therapy, Air Pressure Wave Therapy, Swallowing Training, Pulmonary Function Training [↑](#footnote-ref-22)
23. Occupational Therapy with Standard Non-Pharmacological Prevention, Standard Care Interventions [↑](#footnote-ref-23)