



CONFERENCE REPORTS AND EXPERT PANEL



# Guideline on positioning and early mobilisation in the critically ill by an expert panel

Stefan J. Schaller<sup>1\*</sup> , Flora T. Scheffenbichler<sup>2</sup>, Thomas Bein<sup>3</sup>, Manfred Blobner<sup>2,4</sup>, Julius J. Grunow<sup>1</sup>, Uwe Hamsen<sup>5,6</sup>, Carsten Hermes<sup>7,8</sup>, Arnold Kaltwasser<sup>9</sup>, Heidrun Lewald<sup>4</sup>, Peter Nydahl<sup>10,11</sup>, Anett Reißhauer<sup>12</sup>, Leonie Renzewitz<sup>13,14</sup>, Karsten Siemon<sup>15</sup>, Thomas Staudinger<sup>16</sup>, Roman Ullrich<sup>17,18</sup>, Steffen Weber-Carstens<sup>1</sup>, Hermann Wrigge<sup>19,20</sup>, Dominik Zergiebel<sup>21</sup> and Sina M. Coldewey<sup>22,23\*</sup> 

© 2024 The Author(s)

## Abstract

A scientific panel was created consisting of 23 interdisciplinary and interprofessional experts in intensive care medicine, physiotherapy, nursing care, surgery, rehabilitative medicine, and pneumology delegated from scientific societies together with a patient representative and a delegate from the Association of the Scientific Medical Societies who advised methodological implementation. The guideline was created according to the German Association of the Scientific Medical Societies (AWMF), based on The Appraisal of Guidelines for Research and Evaluation (AGREE) II. The topics of (early) mobilisation, neuromuscular electrical stimulation, assist devices for mobilisation, and positioning, including prone positioning, were identified as areas to be addressed and assigned to specialist expert groups, taking conflicts of interest into account. The panel formulated PICO questions (addressing the population, intervention, comparison or control group as well as the resulting outcomes), conducted a systematic literature review with abstract screening and full-text analysis and created summary tables. This was followed by grading the evidence according to the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence and a risk of bias assessment. The recommendations were finalized according to GRADE and voted using an online Delphi process followed by a final hybrid consensus conference. The German long version of the guideline was approved by the professional associations. For this English version an update of the systematic review was conducted until April 2024 and recommendation adapted based on new evidence in systematic reviews and randomized controlled trials. In total, 46 recommendations were developed and research gaps addressed.

**Keywords:** Guideline, Patient positioning, Early mobilisation, Physical therapy modalities, Critical illness, Critical care

## Introduction

In adult critically ill patients in intensive care units (ICU), prolonged immobility is associated with several short- and long-term sequelae such as intensive care unit-acquired weakness (ICUAW) [1], loss of muscle mass [2, 3] and functionality [4], delirium [5–8], cognitive decline [9, 10], and reduced quality of life [10] which may be minimised by early mobilisation. There is increasing evidence that electrophysiological changes in the neuromuscular system occur as early as 48 h after admission

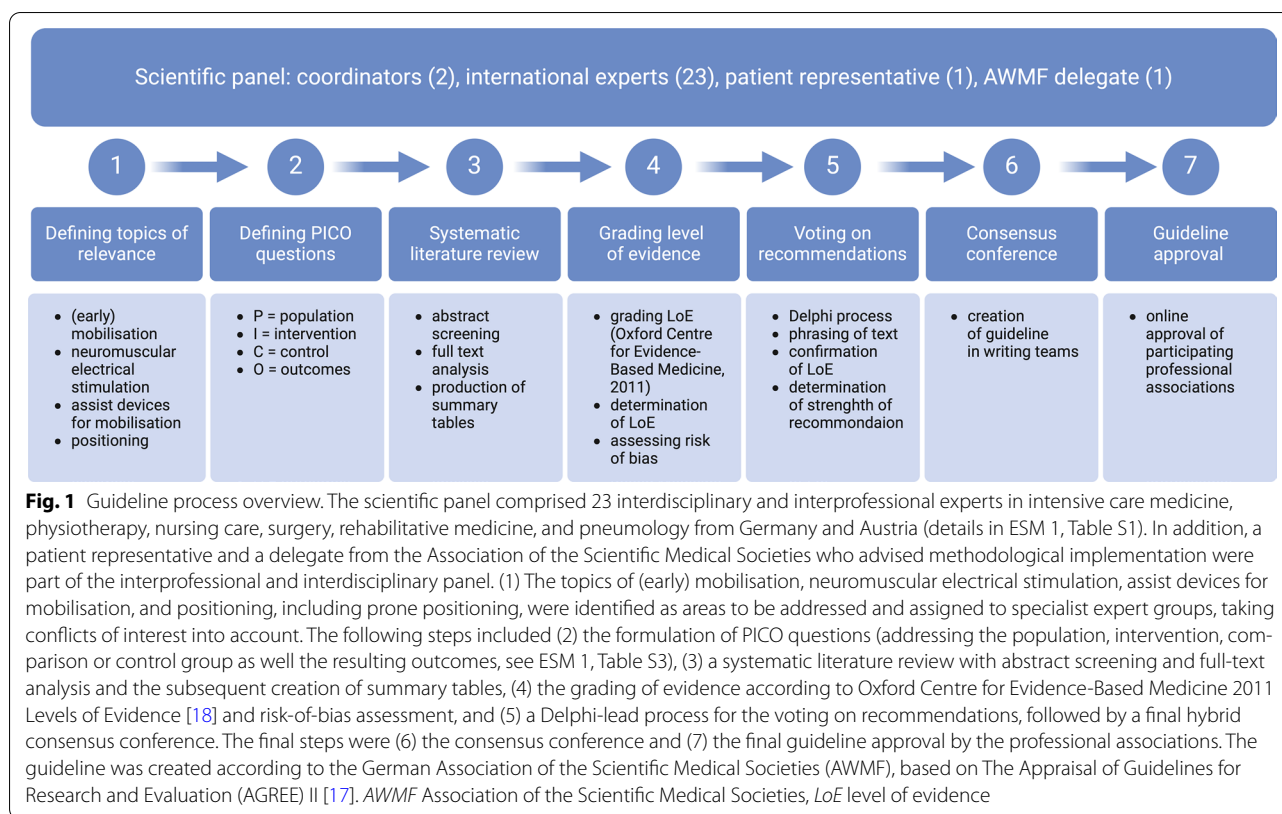
\*Correspondence: stefan.schaller@charite.de; sina.coldewey@med.uni-jena.de

<sup>1</sup> Department of Anaesthesiology and Intensive Care Medicine (CCM/CVK), Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Germany

<sup>22</sup> Department of Anaesthesiology and Intensive Care Medicine, Jena University Hospital, Jena, Germany

Full author information is available at the end of the article

Stefan J. Schaller and Sina M. Coldewey are the joined senior authors and contributed equally.



[11]. The complex pathophysiological changes within neuromuscular pathways promote the upregulation of muscle-wasting systems, leading to ICUAW [11]. This results in a loss of muscle mass and, importantly, in a loss of functionality and insulin resistance [12]. Inflammation, a common coexisting condition in critically ill patients, amplifies these effects [13–15].

An interdisciplinary and interprofessional panel of experts from Germany and Austria formulated clinical key questions, conducted a systematic literature review, and developed a guideline to support healthcare providers in implementing positioning and early mobilisation for critically ill adult patients in the ICU. Early mobilisation was defined as mobilisation commencing within 72 h of ICU admission.

## Methods

### Panel composition

This interdisciplinary and interprofessional guideline, an update from [16], was formulated by experts representing scientific societies in Austria and Germany [electronic supplementary material (ESM) 1, Table S1], following a more rigorous methodology than the previous version, which adhered to the Manual for Guidelines of the Association of the Scientific Medical Societies in Germany (AWMF) [17].

### Literature review and evidence preparation

A systematic literature search on Pubmed, Cochrane Library, PEDro (Physiotherapy Evidence Database) and Cinahl (Cumulative Index to Nursing and Allied Health Literature) was conducted in April 2021, with another update in June 2022. Search terms are provided in ESM 1, Table S2. Two reviewers independently screened titles and abstracts for each chapter and graded full texts based on the Oxford Centre of Evidence-Based Medicine Level of Evidence (version 2011) [18]. The risk of bias was assessed using the Cochrane Risk of Bias Tool (RoB2) [19], the Robis tool [20] or the Agree-2 tool [21], depending on the study type. This was followed by level of evidence (LoE) modification of the studies (see ESM 2). Discrepancies between reviewers were resolved through independent third-party expert review at each step and subsequently assessed by the guideline members.

### Clinical recommendations and structured consensus

In three online Delphi rounds, the phrasing, referenced studies in the recommendation, including their LoE, and strength of recommendation using GRADE (strong (recommend) and weak (suggest) recommendations) [22] were voted (and commented) on (Fig. 1). In the final hybrid structured consensus meeting, the recommendations that had not yet achieved 100% agreement in the previous Delphi rounds

were finally discussed and voted on. Only recommendations with more than 75% agreement were included in the guideline; firm agreement was defined as >95%. Details on the regulation of conflicts can be found in ESM 1, Methods.

**Table 1 Recommendations on positioning**

#	Recommendation	LoE
1.1	We recommend elevation of the upper body $\geq 40^\circ$ in intubated patients, considering possible haemodynamic side effects and an increased risk of pressure ulcers	1
1.2	We suggest performing upper body elevation in patients with increased ICP to achieve the most favourable effect on cerebral perfusion pressure	4 and guideline adaptation
1.3	We suggest avoiding upper body elevation with flexion of the knees and hips in patients with elevated intraabdominal pressure or at its risk and suggest favouring the anti-Trendelenburg position for upper body elevation	3 and guideline adaptation
1.4	We are unable to make a recommendation for or against lateral positioning for the prevention of pulmonary complications without lung injury	3
1.5	We suggest performing a lateral position of about $90^\circ$ with the healthy side down (good lung down) when ventilating patients with unilateral lung damage to improve gas exchange	3
1.6	We recommend regular modification of positioning to avoid the flat supine position as an inappropriate form of positioning	5, expert consensus
1.7	We suggest not to use continuous lateral rotation therapy	2
2.1	We recommend prone positioning in invasively ventilated patients with ARDS and impaired arterial oxygenation ( $\text{PaO}_2/\text{FiO}_2 < 150$ mmHg)	1
2.2	We recommend considering prone positioning at an early stage and implementing it as soon as it is indicated	1
2.3	We recommend prone positioning for at least 12, preferably 16 h	1
2.4	We recommend applying the generally recommended principles of optimised ventilation for ventilation in the prone position, including the limitation of tidal volumes, prevention of derecruitment and integration of spontaneous breathing components	1
2.5	We suggest stabilising the patient haemodynamically and optimising volume status prior to prone positioning. The use of catecholamines is not a contraindication for prone positioning	5, expert consensus
2.6	We suggest considering prone positioning in patients following abdominal surgery, patients with abdominal pathologies, or patients with abdominal obesity after individual consideration of benefits (improvement in oxygenation) and risks (increase in intraabdominal pressure with risk of surgical complication, acute renal failure, or hypoxic hepatitis)	4
2.7	We recommend that patients at risk of increased ICP are monitored continuously or closely during prone positioning. The head should be positioned in a centred position and lateral rotation should be avoided	5, expert consensus
2.8	We suggest that prone positioning should only be carried out in individual cases after considering risks and benefits in an interdisciplinary fashion involved when the following contraindications exist: - open abdomen - spinal instability - increased ICP - cardiac arrhythmias with haemodynamic consequences - shock [23]	5, expert consensus
2.9	We suggest terminating prone positioning if improvement in supine oxygenation persists (4 h after repositioning: $\text{PaO}_2/\text{FiO}_2 \geq 150$ with a $\text{PEEP} \leq 10$ cm $\text{H}_2\text{O}$ and a $\text{FiO}_2 \leq 0.6$ )	2
2.10	We suggest that prone positioning therapy should be discontinued if at least two positioning attempts have been unsuccessful	5, expert consensus
2.11	We recommend complete ( $180^\circ$ ) rather than incomplete prone positioning as there is no evidence to improve clinical outcomes for incomplete prone positioning and complete prone positioning has a stronger effect on oxygenation	2
2.12	We recommend to carefully examine the areas at risk for pressure ulcers during prone positioning to minimise the risk of development	1
2.13	We recommend awake proning in non-invasively ventilated patients with COVID-19 and acute hypoxic respiratory failure	1
2.14	We are unable to make a recommendation for or against awake proning in non-invasively ventilated patients without COVID-19	5, expert consensus
2.15	We are unable to make a recommendation for the duration of awake proning	5, expert consensus
2.16	We suggest performing prone positioning in ARDS patients with veno-venous ECMO therapy	2

COVID-19 coronavirus disease 2019, ECMO extracorporeal membrane oxygenation,  $\text{FiO}_2$  fraction of inspired oxygen, ICP intracranial pressure,  $\text{PaO}_2$  partial pressure of oxygen, PEEP positive end-expiratory pressure

### Additional literature update and adaptations of recommendations

An additional literature update from 1 June 2022 until 4 April 2024 was conducted during the review process. Methodological details and results are presented in ESM 1, Literature search update and modification. Changed recommendations based on the update are marked with an asterisk (\*) in the manuscript.

### Recommendations for clinical questions

After reviewing 14,258 titles and abstracts since 2014, 446 studies were included (details in ESM 1, Fig. S1). A translation of the German full-text version, including links to evidence tables, is provided in ESM 3.

We developed 46 recommendations: 23 for positioning, 17 for mobilisation, 4 for devices and robotics, and 2 for neuromuscular electrical stimulations (NMES).

### Positioning of critically ill patients

For recommendations on positioning of critically ill patients see then Table 1.

#### *Should ICU patients receive upper body elevation?*

Upper body elevation reduces the incidence of ventilator-associated pneumonia (VAP) and duration of ventilation compared with the supine position but does not influence ICU or hospital length of stay (LOS) and mortality [24]. An elevation of 30–60° versus 0–10° had significant benefits concerning clinically suspected VAP but no difference for microbiologically confirmed VAP, LOS and duration of ventilation. In another meta-analysis comparing 45° with 30° upper body elevation, the 45° group had a lower incidence of VAP and gastric reflux compared with 30° elevation with an increased risk of developing decubitus ulcers (Recommendation 1.1) [25].

Furthermore, upper body elevation in patients with brain injury should be individualised, including regular cerebral perfusion pressure (CPP) and intracranial pressure (ICP) monitoring at 0°, 15°, and 30° to capture gravity-dependent effects. In all positions, the head should be positioned straight to ensure venous return (Recommendation 1.2) [26].

Notably, observational studies consistently show an association between higher degrees of upper body elevation and increased intraabdominal pressure (Recommendation 1.3) [27–29].

Most studies on upper body elevation were performed in ventilated patients. Therefore, generalisability may be limited for non-ventilated patients, where the positive effects of upper body elevation due to a higher level

of consciousness and lower aspiration risk may be less pronounced.

#### *Should ICU patients be placed in the lateral position to prevent VAP?*

A randomised controlled trial (RCT) investigating lateral 5–10° head-down position (lateral Trendelenburg positioning with side changes every 6 h) versus upper body elevation to prevent VAP was terminated early due to a low VAP incidence, lack of benefits in secondary outcomes, and six serious adverse events intervention group. Although patients with lateral positioning had a lower incidence of VAP, no significant difference in 28-day mortality occurred (Recommendation 1.4) [30].

In a Cochrane Review on the effect of lateral positioning, only two studies with a very low sample size investigated the effect in ICU patients with unilateral lung injury [31]. The mean difference in oxygenation between good lung down versus bad lung down was approximately 50 mmHg (Recommendation 1.5). Immobilisation in the same position poses many risks, and the flat supine position should be strictly limited to interventions that require it (Recommendation 1.6) [32].

#### *Should ICU patients receive continuous lateral rotation therapy?*

In an RCT of ventilated ICU patients comparing continuous lateral rotation therapy (CLRT), a continuous rotation of the patient along the longitudinal axis, with usual care, there was no difference in microbiologically confirmed VAP between groups. Importantly, 39% of patients showed intolerance to CLRT during the weaning phase [33, 34], reflected by a deeper sedation level in the intervention group [35]. A meta-analysis in trauma patients showed a reduction in nosocomial pneumonia for prophylactic CLRT versus usual care but no effect on existing pneumonia or mortality (Recommendation 1.7) [36].

#### *How should prone positioning be conducted?*

Prone positioning of 16 h daily for patients affected with acute respiratory distress syndrome (ARDS) with a duration of ventilation < 36 h and a PaO<sub>2</sub>/FiO<sub>2</sub> < 150 mmHg showed a significant survival benefit for 28-day mortality (Recommendation 2.1) [37]. Meta-regressions of continuous predictors indicated threshold values for a significant position effect at ≥ 12 prone h/day, ≤ 8.5 mL/kg tidal volume, and PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 130 [38].

*Duration of prone positioning* Most subgroup analyses within meta-analyses [38–40] have found a significant sur-

vival benefit using a cutoff value of 12 h of prone positioning. In contrast, Sud et al. [41] and Lee et al. [42] defined 16 and 10 h as the minimum duration, respectively, and found a survival advantage with a more extended period of prone positioning aligning with the frequently used 12 h cutoff. According to available evidence, a minimum duration of 12 h seems necessary for a positive effect of prone positioning, with each additional hour improving it (Recommendation 2.3). However, a period longer than 16 h has yet to be studied [37].

*Start of prone positioning* In a Cochrane review, a subgroup analysis revealed a positive effect on mortality if patients were placed in prone position  $\leq 48$  h of the start of mechanical ventilation [43]. These are congruent with the time frames in another meta-analysis and the PROSEVA trial [37, 40].

No studies explicitly analyse the optimal time to start the prone positioning. However, all available studies and the positive physiological effects indicate that it is optimal to start immediately after its indication (Recommendation 2.2).

*End of prone positioning* It has not yet been investigated when therapy in the prone position can be terminated. Based on the survival benefit in the PROSEVA trial, prone positioning should be performed until there is an improvement in oxygenation ( $\text{PaO}_2/\text{FiO}_2 \geq 150$ ) under de-escalated ventilation (positive end-expiratory pressure (PEEP)  $\leq 10$  cmH<sub>2</sub>O and  $\text{FiO}_2 \leq 0.6$ ) 4 h after supine positioning [37] (Recommendation 2.9).

Due to the lack of evidence as to whether and for how long prone positioning should be performed in non-responders, the pragmatic expert recommendation is that prone positioning therapy should be terminated after two unsuccessful attempts (lack of improvement in oxygenation) (Recommendation 2.10).

*Ventilator parameters be set during prone positioning* Subgroup analyses of meta-analyses suggest that the limitation of tidal volume is necessary for the mortality benefit from prone positioning [44]. While most of the meta-analyses have used a cutoff of 8 ml/kg predicted body weight, evidence suggests that lowering this cutoff has a beneficial effect [44].

Gainnier et al. showed that prone positioning and PEEP have an additive effect on improving oxygenation [45]. Specific evidence on the optimal PEEP setting in the prone position is lacking.

Although deep sedation and analgesia are commonly used in the prone position to avoid discomfort, spontaneous breathing is also possible during prone positioning (Recommendation 2.4) [44].

*Preparation of prone positioning* The studies on the haemodynamic effects of prone positioning in patients with ARDS showed that the intervention was haemodynamically well tolerated and may also positively affect right ventricular load [46–49]. The volume status of patients should be optimised prior to positioning. Studies on the relevance of vasopressor therapy in the context of prone positioning are lacking. Due to the lack of negative haemodynamic effects of prone positioning, ongoing vasopressor therapy is not a contraindication (Recommendation 2.5).

*Prone positioning and intraabdominal pressure* During prone position, the intraabdominal pressure increased from  $12 \pm 4$  mmHg to  $14 \pm 5$  mmHg [49]. In obese patients undergoing prone positioning, an increased rate of hypoxic hepatitis and renal failure was present, without a mortality difference [50]. According to a case–control study, obese patients did not experience more complications, and the oxygenation improved more compared with non-obese patients [51]. Due to lacking evidence, the possible positive effects of prone positioning in obese patients or patients who underwent abdominal surgery should be critically evaluated (Recommendation 2.6).

*Prone positioning and intracerebral lesions* In an RCT, six patients (24%) with continuous ICP monitoring had a significant ICP increase from 11 to 24 mmHg during prone positioning [52]. Two studies confirmed these findings, which found a higher frequency of ICP  $> 20$  mmHg and decreased CPP in neuro-ICU ARDS patients receiving prone positioning [53, 54]. However, patients benefited from prone positioning regarding oxygenation [53–55]. In contrast, others did not report ICP changes in prone position [56].

Based on the available evidence, a recommendation concerning patients with acute cerebral lesions and prone positioning in ARDS is currently not possible [57], and it is required to weigh the potential harms and benefits individually (Recommendation 2.7).

*Prone positioning and extracorporeal membrane oxygenation* In a systematic review including 13 trials, prone positioning additive to veno-venous (VV-) extracorporeal membrane oxygenation (ECMO) showed a significant survival benefit [58], which was not confirmed in a similar review [59].

Based on the available literature, including current evidence in patients affected with coronavirus disease 2019 (COVID-19) and the safe applicability, we recommend prone positioning of ARDS patients with VV-ECMO in experienced centres (Recommendation 2.16) [58, 60–64].

*Further considerations for prone positioning* Prone positioning is recommended for moderate to severe ARDS, but individual assessment is crucial due to potential comorbidities. A multi-professional and interdisciplinary consensus should balance potential benefits and risks in cases of an open abdomen, unstable spine, increased intracranial pressure, haemodynamically effective cardiac arrhythmias, or shock (Recommendation 2.8).

*Incomplete prone position* Scientific studies on incomplete prone positioning are scarce [65, 66]. Based on the magnified effect on oxygenation of complete vs. incomplete prone position [66] and evidence for a reduction in mortality for prone vs. supine position [37], the complete prone position seems superior (Recommendation 2.11).

*Risks and side effects* Prone positioning causes a weight redistribution to body parts not typically exposed in healthy individuals. Meta-analysis and RCTs have repeatedly shown that prone positioning significantly increases the risk of pressure ulcers [41, 43, 66–73]. Therefore, it is recommended to regularly conduct thorough inspection of the vulnerable locations (Recommendation 2.12).

#### **Should ICU patients receive awake proning during non-invasive ventilation?**

In multiple meta-analyses and a meta-analysis of meta-analyses, there was a significant reduction in the need for intubation [74, 75] and a reduced mortality [75–77] when awake prone positioning was used in critically ill COVID-19 patients.

Accordingly, it is recommended that this measure be performed in this patient population (Recommendation 2.13). A recommendation concerning other causes of hypoxic lung failure is currently not possible (Recommendation 2.14).

*Duration of awake prone positioning* Very heterogeneous protocols were applied in the published trials with conflicting results regarding dose–response relationships [77–84]. Due to the heterogeneity of results, no recommendation can be made regarding the duration and frequency of prone positioning while awake (Recommendation 2.15).

#### **Mobilisation**

For recommendations on mobilisation see then Table 2.

#### **When should (early) mobilisation be started in the ICU?**

In RCTs, an early start of mobilisation within 72 h of mechanical ventilation had a beneficial effect on functional independence, mobility, ICU LOS, hospital LOS, delirium-free days, ventilation-free days, discharge home and long-term cognitive and functional benefits [4, 10, 85]. On the contrary, other studies with delayed start of mobilisation after five and seven days, respectively, found no effect on outcomes [86, 87]. In addition, a network meta-analysis demonstrated a decreased risk of ICUAW and shortened ventilation duration when mobilisation was started within 72–96 h or 48–72 h of ventilation, respectively [88]. Given the available evidence from meta-analyses [89–93], early mobilisation should be started within 72 h of ICU admission (Recommendation 3.1).

#### **How should (early) mobilisation be performed?**

*Mobilisation protocol* Protocols are known to increase the feasibility, safety, duration, and level of mobilisation [94, 95]. Most mobilisation protocols include passive and active mobilisation elements, ranging from passive mobilisation to walking independently [96–101]. The various mobilisation protocols differ in terms of initiation criteria, patient cohort, and levels of mobilisation [99, 100, 102–107].

The ICU mobility scale (IMS), which is commonly used, includes only active mobilisation, and its protocol aims to mobilise the patient to the highest possible level at the beginning of the mobilisation session [108]. This leads to higher mobilisation levels and longer mobilisation duration than the control group [109–111]. However, this early active mobilisation concept was not superior to standard of care with early mobilisation [112].

Similarly, by applying the surgical optimisation mobilisation score (SOMS) protocol, patients achieved the highest level of mobilisation at ICU discharge compared to the control group [4]. However, the SOMS algorithm consists of passive and active components, ranging from no mobilisation to ambulation. Passive mobilisation represents the lowest level in most mobilisation protocols. It is applied when the patient's consciousness, cognition or haemodynamics are impaired so that active mobilisation cannot be performed [102–104, 113]. Passive mobilisation benefits patients with impaired consciousness and stroke patients [105, 113–115] but has not yet been compared with active mobilisation.

The benefits of mobilisation protocols that combine passive and active mobilisation have been shown [4, 95, 115] (Recommendations 3.11, 3.14). Due to the robust

**Table 2 Recommendations on mobilisation**

#	Recommendations	LoE
3.1	We recommend starting early mobilisation of ICU patients within 72 h of ICU admission	1
3.2	We recommend that the hospital management provides the personnel and material conditions to enable (early) mobilisation in line with these recommendations	5
3.3	We recommend the implementation of early mobilisation in all critically ill patients who were previously functionally independent and for whom there are no contraindications	1
3.4	We suggest performing early mobilisation in critically ill patients who were functionally dependent prior to ICU admission and for whom there are no contraindications	3
3.5* 3.7*	We recommend mobilising patients on CRRT or ECMO therapy after consultation with the interprofessional team and if there are no contraindications	CRRT: 2; ECMO: 3
3.6	We suggest mobilising patients with subarachnoid haemorrhage or external ventricular drainage after interdisciplinary consultation, considering potential risks and benefits	3
3.8	We recommend an explicit prescription of medically required immobilisation	5, expert consensus
3.9	We recommend mobilisation in patients with adequate respiratory and cardiovascular reserve. However, we are currently unable to make an evidence-based recommendation on absolute values that are considered a contraindication to mobilisation	5, expert consensus
3.10*	We suggest discontinuing a mobilisation session if according to clinical judgement, it poses a risk to the patient. These criteria may be: - desaturation < 86% - heart rate increase > 30% from baseline - systolic blood pressure rise $\geq$ 40 mmHg from baseline - diastolic blood pressure rise $\geq$ 20 mmHg from baseline - mean arterial pressure < 60 mmHg - new onset or worsened cardiac arrhythmia requiring treatment - deterioration of the level of consciousness compared to the start - pain that cannot be treated with adequate pain therapy	5, expert consensus
3.11 3.14	We recommend a protocol-based approach for implementing mobilisation with active and passive components	Protocol: 1 Components: 2
3.12	We suggest integrating safety criteria (e.g. pulmonary or cardiovascular conditions) into the mobilisation protocol	2
3.13	For preparing a mobilisation session, we suggest - informing the patient, - providing sufficient staff, and - securing/extending artificial airways, intravenous lines, or other drains	5, expert consensus
3.15*	We are unable to make a recommendation on the daily mobilisation duration	5, expert consensus
3.16*	We recommend stepwise mobilisation to the highest possible level	1
3.17*	We recommend the integration of (early) mobilisation into a treatment bundle covering the management of pain, anxiety, agitation, delirium, and conduction of spontaneous breathing trials in ventilated patients (e.g. ABCDEF bundle)	2
3.18	We are unable to make a recommendation for or against the combination of mobilisation with increased protein intake	5, expert consensus
3.19	We are unable to make a recommendation for or against the involvement of relatives in (early) mobilisation	5, expert consensus

ABCDEF, Assess, prevent, and manage pain, Both Spontaneous Awakening Trials (SAT) and Spontaneous Breathing Trials (SBT), Choice of analgesia and sedation, Delirium: assess, prevent, and manage, Early mobility and exercise, and Family engagement and empowerment

CRRT continuous renal replacement therapy, ECMO extracorporeal membrane oxygenation, ICU intensive care unit, IMS ICU Mobility Scale, LoE level of evidence, SOMS Surgical ICU Optimal Mobilisation Score

\*Recommendation changed after the consensus conference due to literature search update. Original consented wording and explanation of the change is presented in ESM 1, Literature search update and modification

data available on the superiority of mobilisation, immobilisation should be the exception (Recommendation 3.8).

**Level and duration of mobilisation** The effect of the level of mobilisation on patient outcomes was investigated in an observational study, whereby a higher level of mobilisation was associated with a better state of health [109]. Active mobilisation, measured by  $IMS \geq 4$  (standing), reduced the risk of developing ICUAW [110]. Similarly, a retrospective analysis indicated that achieving an  $IMS \geq 4$

within 5 days of ICU admission increased the likelihood of being discharged home [111]. The TEAM trial, however, which initiated active mobilisation at the highest possible level and aimed to achieve the maximum level of activity, demonstrated no benefit [112]. A recent meta-analysis demonstrated positive effects on duration of ventilation, especially by progressive mobilisation programmes [116]. Consequently, a stepwise approach without overburdening the patients is recommended (Recommendation 3.16\*).

There is evidence that the duration of mobilisation influences the effectiveness of mobilisation on patient outcomes. A higher dose reduced the risk of unfavourable discharge disposition and mortality and led to shorter ICU and hospital LOS [117, 118]. In a meta-analysis, a pre-defined subgroup analysis of three studies indicated that a higher dose of mobilisation ( $\geq 30$  min/day) led to improved quality of life at 6 months [2]. A recent observational study further confirmed this, demonstrating that a mobilisation duration of more than 40 min positively impacts functional outcomes at ICU discharge [119]. The individual mobilisation dose for each patient may depend on the baseline physical criteria and the underlying disease (Recommendation 3.15\*). Further studies in this area are required.

#### **Which patients should receive early mobilisation?**

**Functional status** The evidence for the effects of early mobilisation differs between specific patient groups based on the inclusion and exclusion criteria used; most studies enrolled critically ill patients who had been functionally independent prior to ICU admission. In these patients, the beneficial effect of early mobilisation is pronounced in outcomes such as duration of ventilation, ICU LOS, muscle strength, and ICUAW (see ESM 1, Table S4) [120–122] (Recommendation 3.3).

Currently, no studies specifically investigate the effect of (early) mobilisation in patients with functional dependence prior to ICU admission. However, some studies do not explicitly exclude these patients. Two RCTs, including patients  $\geq 60$  years after cardiac surgery or septic shock, demonstrated that mobilisation reduces the hospital LOS and improves health-related quality of life [123, 124]. Another non-randomised controlled study showed that mobilisation increased the level of mobilisation on the last day of rehabilitation, even in previously functionally dependent patients [125]. In a multivariate analysis within a matched cohort, frail patients did not exhibit functional deterioration more frequently than non-frail patients, suggesting that efforts should be made to at least maintain the functional status in this patient group (Recommendation 3.4) [126].

**Renal replacement therapy and ECMO** Concerns about catheter and tube dislocation are a common barrier to mobilisation. In patients who were mobilised during continuous renal replacement therapy (CRRT), only 1.8% of 436 patients experienced an adverse event [127] (Recommendation 3.5). In a prospective observational study including patients receiving ECMO, mobilisation was conducted on 24.9% of 1242 ECMO days. Low blood flow alarms occurred in 3.4% of mobilisations. All adverse events were self-limiting or resolved by the treatment

team [128]. Another observational study had a similar rate of 3.6% of adverse events [129]. One accidental femoral cannula displacement during one mobilisation episode, with immediate and effective recannulation, is reported [128]. Therefore, only centres with the necessary expertise in ECMO therapy should perform mobilisation in this high-risk cohort, following consultation with the inter-professional team and thorough evaluation of contraindications (Recommendation 3.7).

**Neurocritical ICU patients** Neurocritical care patients commonly have bed rest due to concerns about alterations in intracranial pressure and vasospasm [130]. In a pre-post-study in neurocritical ICU patients diagnosed with subarachnoid haemorrhage, cerebral malignancy, or stroke, (early) mobilisation following a progressive protocol was safe, increased mobility, and reduced VAP rates and ICU and hospital LOS [131]. These effects were confirmed in patients with severe brain injury [132]. In contrast, data derived from stroke patients in stroke units (i.e. not in an ICU) indicate that very early mobilisation (<24 h) may be harmful [133] (Recommendation 3.6).

#### **When should a mobilisation session be discontinued, and what are the contraindications for mobilisation?**

Adverse events occur in 2.6–3.9% of cases, which makes close monitoring a critical tool for recognising a deterioration in vital signs at an early stage [134, 135]. To date, there have been no studies comparing different discontinuation criteria. Thus, the clinical symptoms used in the literature were adopted [101, 136, 137], which are considered reference values without general validity (Recommendation 3.10\*).

Assessing respiratory and cardiovascular reserves before mobilisation to adjust intensity appropriately is necessary (Recommendation 3.9). No evidence supports absolute parameters as safety criteria for mobilisation initiation, emphasising the importance of the patient's overall clinical presentation. Values in ESM 1, Table S8, are expert-based, aiding individual risk–benefit assessment. We recommend integrating ICU-specific safety criteria into mobilisation protocols (Recommendation 3.12). If mobilisation is not possible during the assessment, implementing therapeutic measures for improvement, followed by a re-evaluation, is warranted [136].

#### **What are the requirements to perform (early) mobilisation?**

Early mobilisation therapy must overcome structural barriers to mobilisation such as insufficient personnel and financial support and a lack of equipment [138, 139]. The hospital management is responsible for creating the conditions for implementing this guideline's recommendations (Recommendation 3.2).



**Table 3 Recommendations for mobilisation assist devices and robotics**

#	Recommendation	LoE
4.1	We are unable to make a recommendation for or against the use of supine cycling in combination with (early) mobilisation	2
4.2	We suggest considering supine cycling as part of (early) mobilisation only when functional training is not sufficiently possible	1
4.3	We recommend monitoring intracranial pressure in patients at risk of intracranial pressure elevations when using a supine cycling	2
4.4	We are unable to make a recommendation for or against the use of assist devices (e.g. tilt tables, treadmills with body weight support) or robotics	5, expert consensus

***How should mobilisation be implemented in intensive care?***

Implementing bundles that include (early) mobilisation consistently improve patient outcomes [6, 7, 140, 141]. In a multicentre cohort study, ABCDEF bundle implementation correlated with a reduced likelihood of severe outcomes [142]. Recommendations from other guidelines and the implied synergistic effect of accompanying elements support a coordinated bundle approach (Recommendation 3.17\*).

***How should a mobilisation session be prepared?***

Before mobilisation, the treatment team and the patient should be informed. Therapeutic measures, such as line or tube extensions, should be adjusted for safe continuation during mobilisation. Alarm limits should be modified for safety and additional staff support should be considered. These aspects should be planned individually within the interprofessional team based on the patient's clinical background. The patient's status, consciousness, and vital signs should be closely monitored during mobilisation. In ventilated patients, essential ventilation parameters should be continuously monitored (Recommendation 3.13).

***How can nutrition supplement (early) mobilisation?***

The interaction between exercise, energy consumption, and diet in critically ill patients remains unclear. Active transfer to the chair for 20 minutes required less than five additional kilocalories in ventilated patients [143]. A meta-analysis of 19 studies comparing high versus low protein intake showed no impact on mortality, ventilation duration, or ICU/hospital length of stay but significantly reduced muscle atrophy [144], while the EFFORT trial showed no benefit and a signal of harm in patients with acute kidney injury and high organ failure scores [145]. Increased protein intake with NMES [146] or supine cycling [147] has been associated with reduced muscle atrophy. However, current evidence is insufficient for a recommendation (Recommendation 3.18).

***How should relatives be involved in critically ill patients' (early) mobilisation?***

The burden on ICU patients' relatives has garnered recent scientific attention. Involvement in care, including mobilisation therapy, has been well-received by the treatment team, patients, and their families [148]. The ABCDE bundle has expanded to ABCDEF (F for family) to acknowledge this aspect. Limited evidence prevents a recommendation on caregiver involvement in mobilisation currently (Recommendation 3.19).

**Mobilisation assist devices and robotics**

For recommendations on assist devices and robotics see then Table 3.

***Background***

Assist devices include equipment-assisted (e.g. supine cycling, treadmill, and tilt table) and robotic-assisted measures (e.g. automated stepping device) for passive, assisted-active or active mobilisation. Assist devices represent an opportunity to overcome barriers to (early) mobilisation, such as staff shortages while adapting to the patient's individual rehabilitation needs.

***Do mobilisation assist devices or robotics have a beneficial effect?***

Supine cycling is the most studied assist device; however, it is often evaluated as part of heterogeneous study protocols concerning intervention, control group, and outcomes. The combination of bed cycling with mobilisation showed no improvement in functionality or quality of life [149–151].

In eight of nine RCTs and meta-analyses [149, 152–159], the duration of ventilation was not influenced by the additional use of cycling in the supine position. Similarly, in seven of nine RCTs and meta-analyses [73, 75–80, 82, 83], cycling in bed did not reduce ICU or hospital LOS. In patients with acute respiratory failure, cycling in the supine position led to improved functionality, a shorter duration of mechanical ventilation and a shorter ICU LOS [154] (Recommendations 4.1, 4.2).

**Table 4 Recommendations on NMES**

#	Recommendation	LoE
5.1	We suggest considering neuromuscular electrical stimulation for (early) mobilisation of critically ill patients	1
5.2	We recommend continuously monitoring intracranial pressure in patients with already established intracranial pressure monitoring when using neuromuscular electrical stimulation	2

Cycling in the supine position is safe [151, 152, 154, 160]. Only one RCT showed increased intracranial pressure elevations in the intervention group who received a progressive mobility programme, including functional electrical stimulation and bed cycling. In the subgroup of patients with intracranial pressure monitoring, the combination of early mobilisation, NMES and supine cycling led to an increase in intracranial pressure compared to early mobilisation alone (Recommendation 4.3) [149].

There are only a few studies that investigate assistive devices. Kwakman et al. trained patients on a treadmill using their body weight until they could walk with walking aids. The authors found a significantly shorter hospital LOS compared to supervised physiotherapy sessions [161]. In a pilot RCT, stepping verticalization was evaluated in addition to physiotherapy sessions. In patients with impaired consciousness, the intervention led to a longer ICU LOS but improved Disability Rating Scale and the Coma Recovery Scale (Recommendation 4.4) [162].

### Neuromuscular electrical stimulation

For recommendations on NMES see then Table 4.

#### Background

NMES is the non-invasive, transcutaneous application of electrical stimuli that leads to active muscle contraction independent of the patient's cooperation. This therapeutic option can be particularly beneficial in the early phase of a critical illness when patients are often sedated but pathophysiological catabolic processes are already taking place at the muscular level [11].

#### Should NMES be used in the early mobilisation of intensive care patients?

Several systematic reviews and meta-analyses reported beneficial effects of NMES on physical function [137, 163], muscle strength [163, 164], duration of mechanical ventilation [164, 165], extubation success rate [166], and ICU and hospital LOS [164]. In contrast, others showed no differences in these outcomes (Recommendation 5.1) [153, 167].

NMES is generally a safe intervention [165, 168]. However, in a monocentric RCT, the intervention group that

received protocol-based physiotherapy with functional electrical stimulation (combination of NMES and in-bed cycling) showed significantly more ICP elevations and poorer health-related quality of life in the cognitive domain [149]. Therefore, assessing ICP information is recommended for patients with already established ICP monitoring (Recommendation 5.2).

### Conclusion and outlook

The beneficial effect of mobilisation in critically ill patients is evident. Still, it is necessary to determine which dose of mobilisation (frequency, duration, level, exertion) is appropriate for which group of patients to achieve the best possible outcome.

The same applies to positioning, where the optimal dosage (frequency and duration), especially for prone positioning, needs to be clarified.

Further evidence will most likely lead us down the path of individualised positioning and mobilisation therapy, similar to other areas of medicine. Despite technological progress, (early) mobilisation and positioning remain a (physical) effort that should be a collective responsibility of the whole intensive care team. This guideline should make a useful contribution to this effort.

#### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1007/s00134-024-07532-2>.

#### Author details

<sup>1</sup> Department of Anaesthesiology and Intensive Care Medicine (CCM/CVK), Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Germany. <sup>2</sup> Department of Anaesthesiology and Intensive Care Medicine, Ulm University, Ulm, Germany. <sup>3</sup> Universität Regensburg, Regensburg, Germany. <sup>4</sup> Department of Anaesthesiology and Intensive Care Medicine, School of Medicine and Health, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany. <sup>5</sup> Ruhr University Bochum, Bochum, Germany. <sup>6</sup> Department of General and Trauma Surgery, BG University Hospital Bergmannsheil, Ruhr University Bochum, Bochum, Germany. <sup>7</sup> Hochschule für Angewandte Wissenschaften Hamburg (HAW Hamburg), Hamburg, Germany. <sup>8</sup> Akkon-Hochschule für Humanwissenschaften, Berlin, Germany. <sup>9</sup> Academy of the District Hospitals Reutlingen, Kreiskliniken Reutlingen, Reutlingen, Germany. <sup>10</sup> University Hospital of Schleswig-Holstein, Kiel, Germany. <sup>11</sup> Institute of Nursing Science and Development, Paracelsus Medical University, Salzburg, Austria. <sup>12</sup> Department of Rehabilitation Medicine, Charité-Universitätsmedizin Berlin, Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany. <sup>13</sup> Department of Physiotherapy, University Hospital Essen, University of Duisburg-Essen, Essen, Germany. <sup>14</sup> Department of Hematology and Stem Cell Transplantation, University Hospital Essen, University of Duisburg-Essen,

Essen, Germany. <sup>15</sup> Department of Pneumology, Fachkrankenhaus Kloster Grafschaft, Schmallingenberg, Germany. <sup>16</sup> Department of Medicine I, Medical University of Vienna, Vienna, Austria. <sup>17</sup> Department of Anaesthesia, General Intensive Care and Pain Medicine, Medical University of Vienna, Vienna, Austria. <sup>18</sup> Department of Anaesthesiology and Intensive Care Medicine, AUVVA Trauma Center Vienna, Vienna, Austria. <sup>19</sup> Department of Anaesthesiology, Intensive Care and Emergency Medicine, Pain Therapy, Bergmannstrost Hospital, Halle, Germany. <sup>20</sup> Medical Faculty, Martin-Luther University Halle-Wittenberg, Halle, Germany. <sup>21</sup> Münster University Hospital (UKM), Münster, Germany. <sup>22</sup> Department of Anaesthesiology and Intensive Care Medicine, Jena University Hospital, Jena, Germany. <sup>23</sup> Septomics Research Center, Jena University Hospital, Jena, Germany.

### Acknowledgements

We would like to thank the following project collaborators supporting the work: Charité–Universitätsmedizin Berlin, Department of Anaesthesiology, and Intensive Care Medicine (CCM/CKV), Berlin Germany: Buyukli, Alyona; Daum, Nils; Meyer, Josephin; Schellenberg, Clara; Warner, Linus Oliver; Grimm, Aline; Bald, Annika; Baum, Felix; Verfuß, Michael; Arsene, Vanessa; Hollstein, Wiebke; Carbon, Niklas Martin; Lindholz, Maximilian; Berg, Nicolas. Jena University Hospital, Department of Anaesthesiology and Intensive Care Medicine, Jena, Germany: Engelmann, Markus; Götze, Juliane; Neu, Charles; Pfohl, Silke. Association of the Scientific Medical Societies in Germany (AWMF): Nothacker, Monika. Patient representative from the Global Sepsis Alliance: Kredler, Dennis.

### Funding

Open Access funding enabled and organized by Projekt DEAL. This project was partly supported by the German Society of Anaesthesiology and Intensive Care Medicine (DGAI).

### Data availability

The authors confirm that all information supporting the recommendations is available within the article and its supplemental information.

### Declarations

### Conflicts of interest

SJS received grants and non-financial support from Reactive Robotics GmbH (Munich, Germany), ASP GmbH (Attendorn, Germany), STIMIT AG (Biel, Switzerland), ESICM (Geneva, Switzerland), grants, personal fees, and non-financial support from Fresenius Kabi Deutschland GmbH (Bad Homburg, Germany), grants from the Innovationsfond of The Federal Joint Committee (G-BA), personal fees from Springer Verlag GmbH (Vienna, Austria) for educational purposes and Advanz Pharma GmbH (Bielefeld, Germany), non-financial support from national and international societies (and their congress organisers) in the field of anaesthesiology and intensive care medicine, outside the submitted work. Dr. Schaller holds stocks in small amounts from Alphabet Inc., Bayer AG, and Siemens AG; these holdings have not affected any decisions regarding his research or this guideline. MB received research support from MIPM (Mammendorf, Germany) and GE Healthcare (Helsinki, Finland), reports consulting fees from Senzime, (Uppsala, Sweden), received honoraria for giving lectures from GE Healthcare (Helsinki, Finland) and Grünenthal (Aachen, Germany), all outside the submitted work. MB participated in a DSMB sponsored by GE Healthcare (Helsinki, Finland). UH reports personal fees for lectures from Pfizer, outside the submitted work. CH reports personal fees for lectures from Baxter, Arjo, and TapMed, non-financial support from national and international societies (and their congress organisers) in the field of anaesthesiology, intensive care medicine and nursing, outside the submitted work. AK reports personal fees for lectures and non-financial support from B Braun and Avanos, non-financial support from national societies (and their congress organisers) in the field of anaesthesiology, intensive care medicine and nursing, outside the submitted work. HL reports personal fees for lectures from Xavant Technology (Pty) Ltd, outside the submitted work. TS reports personal fees for lectures from Mitsubishi Pharma, Getinge and Xenios, outside the submitted work. RU reports grants from APEPTICO GmbH, Bayer AG, Philips, and Biotest, personal fees for lectures from Biotest and medical societies, reports a patent WO2017064285 A—Membrankatheter, participation in a DSMB of F4 Pharma GmbH and CCORE Technologies GmbH, as well as a leadership role in CCORE Technologies GmbH, all outside the submitted work. SW reports grants from Dräger GmbH, outside the submitted work. HW reports grants and consulting

fees from Liberate Medical, personal fees from lectures from Arjo. All the other authors report no conflict of interest.

### Open Access

This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 28 February 2024 Accepted: 15 June 2024

Published: 29 July 2024

### References

- Zhang L, Hu W, Cai Z, Liu J, Wu J, Deng Y, Yu K, Chen X, Zhu L, Ma J, Qin Y (2019) Early mobilization of critically ill patients in the intensive care unit: a systematic review and meta-analysis. *PLoS ONE* 14:e0223185. <https://doi.org/10.1371/journal.pone.0223185>
- Tipping CJ, Harrold M, Holland A, Romero L, Nisbet T, Hodgson CL (2017) The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review. *Intensive Care Med* 43:171–183. <https://doi.org/10.1007/s00134-016-4612-0>
- Fazzini B, Markl T, Costas C, Blobner M, Schaller SJ, Prowle J, Puthuchery Z, Wackerhage H (2023) The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. *Crit Care* 27:2. <https://doi.org/10.1186/s13054-022-04253-0>
- Schaller SJ, Anstey M, Blobner M, Edrich T, Grabitz SD, Gradwohl-Matis I, Heim M, Houle T, Kurth T, Latronico N, Lee J, Meyer MJ, Peponis T, Talmor D, Velmahos GC, Waak K, Walz JM, Zafonte R, Eikermann M (2016) Early, goal-directed mobilisation in the surgical intensive care unit: a randomised controlled trial. *Lancet* 388:1377–1388. [https://doi.org/10.1016/S0140-6736\(16\)31637-3](https://doi.org/10.1016/S0140-6736(16)31637-3)
- Nydahl P, Jeitziner MM, Vater V, Sivarajah S, Howroyd F, McWilliams D, Osterbrink J (2023) Early mobilisation for prevention and treatment of delirium in critically ill patients: systematic review and meta-analysis. *Intensive Crit Care Nurs* 74:103334. <https://doi.org/10.1016/j.iccn.2022.103334>
- Kang J, Cho YS, Lee M, Yun S, Jeong YJ, Won YH, Hong J, Kim S (2023) Effects of nonpharmacological interventions on sleep improvement and delirium prevention in critically ill patients: a systematic review and meta-analysis. *Aust Crit Care* 36:640–649. <https://doi.org/10.1016/j.jaacc.2022.04.006>
- Sosnowski K, Lin F, Chaboyer W, Ranse K, Heffernan A, Mitchell M (2023) 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. *Int J Nurs Stud* 138:104410. <https://doi.org/10.1016/j.ijnurstu.2022.104410>
- Matsuura Y, Ohno Y, Toyoshima M, Ueno T (2023) Effects of non-pharmacologic prevention on delirium in critically ill patients: a network meta-analysis. *Nurs Crit Care* 28:727–737. <https://doi.org/10.1111/nicc.12780>
- Allahbakhshian A, Khalili AF, Gholizadeh L, Esmaily L (2023) Comparison of early mobilization protocols on postoperative cognitive dysfunction, pain, and length of hospital stay in patients undergoing coronary artery bypass graft surgery: a randomized controlled trial. *Appl Nurs Res* 73:151731. <https://doi.org/10.1016/j.apnr.2023.151731>

10. Patel BK, Wolfe KS, Patel SB, Dugan KC, Esbrook CL, Pawlik AJ, Stulberg M, Kemple C, Teele M, Zeleny E, Hedeker D, Pohlman AS, Arora VM, Hall JB, Kress JP (2023) Effect of early mobilisation on long-term cognitive impairment in critical illness in the USA: a randomised controlled trial. *Lancet Respir Med* 11:563–572. [https://doi.org/10.1016/S2213-2600\(22\)00489-1](https://doi.org/10.1016/S2213-2600(22)00489-1)
11. Friedrich O, Reid MB, Van den Berghe G, Vanhorebeek I, Hermans G, Rich MM, Larsson L (2015) The sick and the weak: neuropathies/myopathies in the critically ill. *Physiol Rev* 95:1025–1109. <https://doi.org/10.1152/physrev.00028.2014>
12. Dirks ML, Miotto PM, Goossens GH, Senden JM, Petrick HL, van Kranenburg J, van Loon LJC, Holloway GP (2020) Short-term bed rest-induced insulin resistance cannot be explained by increased mitochondrial H<sub>2</sub>O<sub>2</sub> emission. *J Physiol* 598:123–137. <https://doi.org/10.1113/JP278920>
13. Wollersheim T, Woehlecke J, Krebs M, Hamati J, Lodka D, Luther-Schroeder A, Langhans C, Haas K, Radtke T, Kleber C, Spies C, Labeit S, Schuelke M, Spuler S, Spranger J, Weber-Carstens S, Fielitz J (2014) Dynamics of myosin degradation in intensive care unit-acquired weakness during severe critical illness. *Intensive Care Med* 40:528–538. <https://doi.org/10.1007/s00134-014-3224-9>
14. Weber-Carstens S, Schneider J, Wollersheim T, Assmann A, Bierbrauer J, Marg A, Al Hasani H, Chadt A, Wenzel K, Koch S, Fielitz J, Kleber C, Faust K, Mai K, Spies CD, Luft FC, Boschmann M, Spranger J, Spuler S (2013) Critical illness myopathy and GLUT4: significance of insulin and muscle contraction. *Am J Respir Crit Care Med* 187:387–396. <https://doi.org/10.1164/rccm.201209-1649OC>
15. Dos Santos C, Hussain SN, Mathur S, Picard M, Herridge M, Correa J, Bain A, Guo Y, Advani A, Advani SL, Tomlinson G, Katzberg H, Streutker CJ, Cameron JJ, Schols A, Gosker HR, Batt J, Group MI, Investigators RP, Canadian Critical Care Translational Biology G (2016) Mechanisms of chronic muscle wasting and dysfunction after an intensive care unit stay: a pilot study. *Am J Respir Crit Care Med* 194:821–830. <https://doi.org/10.1164/rccm.201512-2344OC>
16. Bein T, Bischoff M, Bruckner U, Gebhardt K, Henzler D, Hermes C, Lewandowski K, Max M, Nothacker M, Staudinger T, Tryba M, Weber-Carstens S, Wrigge H (2015) S2e guideline: positioning and early mobilisation in prophylaxis or therapy of pulmonary disorders: Revision 2015: S2e guideline of the German Society of Anaesthesiology and Intensive Care Medicine (DGAI). *Anaesthesist* 64(Suppl 1):1–26. <https://doi.org/10.1007/s00101-015-0071-1>
17. AWMF (2012) AWMF guidance manual and rules for guideline development. [https://www.awmf.org/fileadmin/user\\_upload/dateien/download\\_regelwerk/AWMF-Guidance\\_2013.pdf](https://www.awmf.org/fileadmin/user_upload/dateien/download_regelwerk/AWMF-Guidance_2013.pdf). Accessed 12 May 2024
18. Centre for Evidence-Based Medicine. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocbcm-levels-of-evidence>. Accessed 13 May 2024
19. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT (2019) RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 366:l4898. <https://doi.org/10.1136/bmj.l4898>
20. Whiting P, Savović J, Higgins JPT, Caldwell DM, Reeves BC, Shea B, Davies P, Kleijnen J, Churchill R (2016) ROBIS: a new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* 69:225–234. <https://doi.org/10.1016/j.jclinepi.2015.06.005>
21. Brouwers MC, Kerkvliet K, Spithoff K (2016) The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 352:i1152. <https://doi.org/10.1136/bmj.i1152>
22. Balslem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH (2011) GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 64:401–406. <https://doi.org/10.1016/j.jclinepi.2010.07.015>
23. Standl T, Annecke T, Cascorbi I, Heller AR, Sabashnikov A, Teske W (2018) The nomenclature, definition and distinction of types of shock. *Dtsch Arztebl Int* 115:757–768. <https://doi.org/10.3238/arztebl.2018.0757>
24. Pozuelo-Carrascosa DP, Cobo-Cuenca AI, Carmona-Torres JM, Laredo-Aguilera JA, Santacruz-Salas E, Fernandez-Rodriguez R (2022) Body position for preventing ventilator-associated pneumonia for critically ill patients: a systematic review and network meta-analysis. *J Intensive Care* 10:9. <https://doi.org/10.1186/s40560-022-00600-z>
25. Zhuo X, Pan L, Zeng X (2021) The effects of the 45 degrees semi-recumbent position on the clinical outcomes of mechanically ventilated patients: a systematic review and meta-analysis study. *Ann Palliat Med* 10:10643–10651. <https://doi.org/10.21037/apm-21-2359>
26. Huttner H (2023) Intrakranieller Druck (ICP), S1-Leitlinie. <https://register.awmf.org/de/leitlinien/detail/030-105>. Accessed 12 May 2024
27. McBeth PB, Zygun DA, Widder S, Cheatham M, Zengerink I, Glowka J, Kirkpatrick AW (2007) Effect of patient positioning on intra-abdominal pressure monitoring. *Am J Surg* 193:644–647. <https://doi.org/10.1016/j.amjsurg.2007.01.013>
28. Cheatham ML, De Waele JJ, De Laet I, De Keulenaer B, Widder S, Kirkpatrick AW, Cresswell AB, Malbrain M, Bodnar Z, Mejia-Mantilla JH, Reis R, Parr M, Schulze R, Puig S, World Society of the Abdominal Compartment Syndrome Clinical Trials Working G (2009) The impact of body position on intra-abdominal pressure measurement: a multicenter analysis. *Crit Care Med* 37:2187–2190. <https://doi.org/10.1097/CCM.0b013e3181a021fa>
29. Samimian S, Ashrafi S, Khaleghdoost Mohammadi T, Yeganeh MR, Ashraf A, Hakimi H, Dehghani M (2021) The correlation between head of bed angle and intra-abdominal pressure of intubated patients: a pre-study clinical trial. *Arch Acad Emerg Med* 9:e23
30. Li Bassi G, Panigada M, Ranzani OT, Zanella A, Berra L, Cressoni M, Parrini V, Kandil H, Salati G, Selvaggi P, Amatu A, Sanz-Moncosi M, Biagioni E, Tagliaferri F, Furla M, Mercurio G, Costa A, Manca T, Lindau S, Babel J, Cavana M, Chiurazzi C, Marti JD, Consonni D, Gattinoni L, Pesenti A, Wiener-Kronish J, Bruschi C, Ballotta A, Salsi P, Livigni S, Iotti G, Fernandez J, Girardis M, Barbagallo M, Moise G, Antonelli M, Caspani ML, Vezzani A, Meybohm P, Gasparovic V, Geat E, Amato M, Niederman M, Kolobow T, Torres A, Gravity VAPN (2017) Randomized, multicenter trial of lateral trendelenburg versus semirecumbent body position for the prevention of ventilator-associated pneumonia. *Intensive Care Med* 43:1572–1584. <https://doi.org/10.1007/s00134-017-4858-1>
31. Hewitt N, Bucknall T, Faraone NM (2016) Lateral positioning for critically ill adult patients. *Cochrane Database Syst Rev*. <https://doi.org/10.1002/14651858.CD007205.pub2>
32. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, Zawistowski C, Bemis-Dougherty A, Berney SC, Bienvenu OJ, Brady SL, Brodsky MB, Denehy L, Elliott D, Flatley C, Harabin AL, Jones C, Louis D, Meltzer W, Muldoon SR, Palmer JB, Perme C, Robinson M, Schmidt DM, Scruth E, Spill GR, Storey CP, Render M, Votto J, Harvey MA (2012) Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. *Crit Care Med* 40:502–509. <https://doi.org/10.1097/CCM.0b013e318232da75>
33. Staudinger T, Bojic A, Holzinger U, Meyer B, Rohwer M, Mallner F, Schellongowski P, Robak O, Laczika K, Frass M, Locker GJ (2010) Continuous lateral rotation therapy to prevent ventilator-associated pneumonia. *Crit Care Med* 38:486–490. <https://doi.org/10.1097/CCM.0b013e3181bc8218>
34. Hanneman SK, Gusick GM, Hamlin SK, Wachtel SJ, Cron SG, Jones DJ, Oldham SA (2015) Manual vs automated lateral rotation to reduce preventable pulmonary complications in ventilator patients. *Am J Crit Care* 24:24–32. <https://doi.org/10.4037/ajcc2015171>
35. Schieren M, Wappler F, Klodt D, Sakka SG, Lefering R, Jacker V, Defosse J (2020) Continuous lateral rotational therapy in thoracic trauma—a matched pair analysis. *Injury* 51:51–58. <https://doi.org/10.1016/j.injury.2019.11.009>
36. Schieren M, Piekarski F, Dusse F, Marcus H, Poels M, Wappler F, Defosse J (2017) Continuous lateral rotational therapy in trauma—a systematic review and meta-analysis. *J Trauma Acute Care Surg* 83:926–933. <https://doi.org/10.1097/TA.0000000000001572>
37. Guerin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, Mercier E, Badet M, Mercat A, Baudin O, Clavel M, Chatellier D, Jaber S, Rosselli S, Mancebo J, Sirodot M, Hilbert G, Bengler C, Richecoeur J, Gainnier M, Bayle F, Bourdin G, Leray V, Girard R, Baboi L, Ayzac L, Group PS (2013) Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 368:2159–2168. <https://doi.org/10.1056/NEJMoa1214103>
38. Moran JL, Graham PL (2021) Multivariate meta-analysis of the mortality effect of prone positioning in the acute respiratory distress syndrome. *J*

- Intensive Care Med 36:1323–1330. <https://doi.org/10.1177/08850666211014479>
39. Munshi L, Del Sorbo L, Adhikari NKJ, Hodgson CL, Wunsch H, Meade MO, Uleryk E, Mancebo J, Pesenti A, Ranieri VM, Fan E (2017) Prone position for acute respiratory distress syndrome: a systematic review and meta-analysis. *Ann Am Thorac Soc* 14:S280–S288. <https://doi.org/10.1513/AnnalsATS.201704-343OT>
  40. Mora-Arteaga JA, Bernal-Ramirez OJ, Rodriguez SJ (2015) The effects of prone position ventilation in patients with acute respiratory distress syndrome: A systematic review and metaanalysis. *Med Intensiva* 39:359–372. <https://doi.org/10.1016/j.medin.2014.11.003>
  41. Sud S, Friedrich JO, Adhikari NK, Taccone P, Mancebo J, Polli F, Latini R, Pesenti A, Curley MA, Fernandez R, Chan MC, Beuret P, Voggenreiter G, Sud M, Tognoni G, Gattinoni L, Guerin C (2014) Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome: a systematic review and meta-analysis. *CMAJ* 186:E381–390. <https://doi.org/10.1503/cmaj.140081>
  42. Lee JM, Bae W, Lee YJ, Cho YJ (2014) The efficacy and safety of prone positional ventilation in acute respiratory distress syndrome: updated study-level meta-analysis of 11 randomized controlled trials. *Crit Care Med*. 42(5):1252–62. <https://doi.org/10.1097/CCM.000000000000122>
  43. Bloomfield R, Noble DW, Sudlow A (2015) Prone position for acute respiratory failure in adults. *Cochrane Database Syst Rev*. <https://doi.org/10.1002/14651858.CD008095.pub2>
  44. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, Adhikari NKJ, Amato MBP, Branson R, Brower RG, Ferguson ND, Gajic O, Gattinoni L, Hess D, Mancebo J, Meade MO, McAuley DF, Pesenti A, Ranieri VM, Rubenfeld GD, Rubin E, Seckel M, Slutsky AS, Talmor D, Thompson BT, Wunsch H, Uleryk E, Brozek J, Brochard LJ, American Thoracic Society ESoICM, Society of Critical Care M (2017) An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 195:1253–1263. <https://doi.org/10.1164/rccm.201703-0548ST>
  45. Gainnier M, Michelet P, Thirion X, Arnal JM, Sainty JM, Papazian L (2003) Prone position and positive end-expiratory pressure in acute respiratory distress syndrome. *Crit Care Med* 31:2719–2726. <https://doi.org/10.1097/01.CCM.0000094216.49129.4B>
  46. Jozwiak M, Teboul JL, Anguel N, Persichini R, Silva S, Chemla D, Richard C, Monnet X (2013) Beneficial hemodynamic effects of prone positioning in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 188:1428–1433. <https://doi.org/10.1164/rccm.201303-0593OC>
  47. Ruste M, Bitker L, Yonis H, Riad Z, Louf-Durier A, Lissonde F, Perinel-Ragey S, Guerin C, Richard JC (2018) Hemodynamic effects of extended prone position sessions in ARDS. *Ann Intensive Care* 8:120. <https://doi.org/10.1186/s13613-018-0464-9>
  48. Hering R, Vorwerk R, Wrigge H, Zinserling J, Schroder S, von Spiegel T, Hoeft A, Putensen C (2002) Prone positioning, systemic hemodynamics, hepatic indocyanine green kinetics, and gastric intramucosal energy balance in patients with acute lung injury. *Intensive Care Med* 28:53–58. <https://doi.org/10.1007/s00134-001-1166-5>
  49. Hering R, Wrigge H, Vorwerk R, Brensing KA, Schroder S, Zinserling J, Hoeft A, Spiegel TV, Putensen C (2001) The effects of prone positioning on intraabdominal pressure and cardiovascular and renal function in patients with acute lung injury. *Anesth Analg* 92:1226–1231. <https://doi.org/10.1097/0000539-200105000-00027>
  50. Weig T, Janitza S, Zoller M, Dolch ME, Miller J, Frey L, Kneidinger N, Johnson T, Schubert M, Irlbeck M (2014) Influence of abdominal obesity on multiorgan dysfunction and mortality in acute respiratory distress syndrome patients treated with prone positioning. *J Crit Care* 29:557–561. <https://doi.org/10.1016/j.jccr.2014.02.010>
  51. De Jong A, Molinari N, Sebbane M, Prades A, Futier E, Jung B, Chanques G, Jaber S (2013) Feasibility and effectiveness of prone position in morbidly obese patients with ARDS: a case-control clinical study. *Chest* 143:1554–1561. <https://doi.org/10.1378/chest.12-2115>
  52. Beuret P, Carton MJ, Nourdine K, Kaaki M, Tramoni G, Ducreux JC (2002) Prone position as prevention of lung injury in comatose patients: a prospective, randomized, controlled study. *Intensive Care Med* 28:564–569. <https://doi.org/10.1007/s00134-002-1266-x>
  53. Roth C, Ferbert A, Deinsberger W, Kleffmann J, Kastner S, Godau J, Schuler M, Tryba M, Gehling M (2014) Does prone positioning increase intracranial pressure? A retrospective analysis of patients with acute brain injury and acute respiratory failure. *Neurocrit Care* 21:186–191. <https://doi.org/10.1007/s12028-014-0004-x>
  54. Reinprecht A, Greher M, Wolfsberger S, Dietrich W, Illievich UM, Gruber A (2003) Prone position in subarachnoid hemorrhage patients with acute respiratory distress syndrome: effects on cerebral tissue oxygenation and intracranial pressure. *Crit Care Med* 31:1831–1838. <https://doi.org/10.1097/01.CCM.0000063453.93855.0A>
  55. Nekludov M, Bellander BM, Mure M (2006) Oxygenation and cerebral perfusion pressure improved in the prone position. *Acta Anaesthesiol Scand* 50:932–936. <https://doi.org/10.1111/j.1399-6576.2006.01099.x>
  56. Thelander A, Cider A, Nellgard B (2006) Prone position in mechanically ventilated patients with reduced intracranial compliance. *Acta Anaesthesiol Scand* 50:937–941. <https://doi.org/10.1111/j.1399-6576.2006.01037.x>
  57. Wright JM, Gerges C, Shammassian B, Labak CM, Herring EZ, Miller B, Alkhachroum A, Kottapally M, Huang Wright C, Rodgers RB, Sedney C, Ngwenya LB, Stippler M, Sieg E, Babu MA, Hoffer A, Hejal R (2021) Prone position ventilation in neurologically ill patients: a systematic review and proposed protocol. *Crit Care Med* 49:e269–e278. <https://doi.org/10.1097/CCM.0000000000004820>
  58. Papazian L, Schmidt M, Hajage D, Combes A, Petit M, Lebreton G, Rillinger J, Giani M, Le Breton C, Duburcq T, Jozwiak M, Wengenmayer T, Roux D, Parke R, Loundou A, Guerville C, Boyer L (2022) Effect of prone positioning on survival in adult patients receiving venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. *Intensive Care Med* 48:270–280. <https://doi.org/10.1007/s00134-021-06604-x>
  59. Poon WH, Ramanathan K, Ling RR, Yang IX, Tan CS, Schmidt M, Shekar K (2021) Prone positioning during venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. *Crit Care* 25:292. <https://doi.org/10.1186/s13054-021-03723-1>
  60. Giani M, Martucci G, Madotto F, Belliato M, Fanelli V, Garofalo E, Forlini C, Lucchini A, Panarello G, Bottino N, Zanella A, Fossi F, Lissoni A, Peroni N, Brazzi L, Bellani G, Navalesi P, Arcadipane A, Pesenti A, Foti G, Grasselli G (2021) Prone positioning during venovenous extracorporeal membrane oxygenation in acute respiratory distress syndrome: A multicenter cohort study and propensity-matched analysis. *Ann Am Thorac Soc* 18:495–501. <https://doi.org/10.1513/AnnalsATS.202006-625OC>
  61. Liu C, Chen Y, Chen Y, Chen B, Xie G, Chen Y (2021) Effects of prone positioning during extracorporeal membrane oxygenation for refractory respiratory failure: a systematic review. *SN Compr Clin Med* 3:2109–2115. <https://doi.org/10.1007/s42399-021-01008-w>
  62. Petit M, Fetita C, Gaudemer A, Treluyer L, Lebreton G, Francheau G, Hekimian G, Chommeloux J, Pineton de Chambrun M, Brechot N, Luyt CE, Combes A, Schmidt M (2022) Prone-positioning for severe acute respiratory distress syndrome requiring extracorporeal membrane oxygenation. *Crit Care Med* 50:264–274. <https://doi.org/10.1097/CCM.00000000000005145>
  63. Rillinger J, Zotzmann V, Bemtgen X, Schumacher C, Biever PM, Duereschmied D, Kaier K, Stachon P, von Zur MC, Zehender M, Bode C, Staudacher DL, Wengenmayer T (2020) Prone positioning in severe ARDS requiring extracorporeal membrane oxygenation. *Crit Care* 24:397. <https://doi.org/10.1186/s13054-020-03110-2>
  64. Zaaqoq AM, Barnett AG, Griffiee MJ, MacLaren G, Jacobs JP, Heinsar S, Suen JY, Bassi GL, Fraser JF, Dalton HJ, Peek GJ, Consortium C-CC (2022) Beneficial effect of prone positioning during venovenous extracorporeal membrane oxygenation for coronavirus disease 2019. *Crit Care Med* 50:275–285. <https://doi.org/10.1097/CCM.00000000000005296>
  65. Bein T, Sabel K, Scherer A, Papp-Jambor C, Hekler M, Dubb R, Schlitt HJ, Taeger K (2004) Comparison of incomplete (135 degrees) and complete prone position (180 degrees) in patients with acute respiratory distress syndrome. Results of a prospective, randomised trial. *Anaesthetist* 53:1054–1060. <https://doi.org/10.1007/s00101-004-0754-5>
  66. Cao Z, Yang Z, Liang Z, Cen Q, Zhang Z, Liang H, Liu R, Zeng L, Xie Y, Wang Y (2020) Prone versus supine position ventilation in adult patients with acute respiratory distress syndrome: a meta-analysis of

- randomized controlled trials. *Emerg Med Int* 2020:4973878. <https://doi.org/10.1155/2020/4973878>
67. Girard R, Baboi L, Ayzac L, Richard JC, Guerin C, Proseva Trial G (2014) The impact of patient positioning on pressure ulcers in patients with severe ARDS: results from a multicentre randomised controlled trial on prone positioning. *Intensive Care Med* 40:397–403. <https://doi.org/10.1007/s00134-013-3188-1>
  68. Gonzalez-Seguel F, Pinto-Concha JJ, Aranis N, Leppe J (2021) Adverse events of prone positioning in mechanically ventilated adults with ARDS. *Respir Care* 66:1898–1911. <https://doi.org/10.4187/respcare.09194>
  69. Patton D, Latimer S, Avsar P, Walker RM, Moore Z, Gillespie BM, O'Connor T, Nugent L, Budri A, Brien NO, Chaboyer W (2021) The effect of prone positioning on pressure injury incidence in adult intensive care unit patients: a meta-review of systematic reviews. *Aust Crit Care*. <https://doi.org/10.1016/j.aucc.2021.10.003>
  70. Binda F, Galazzi A, Marelli F, Gambazza S, Villa L, Vinci E, Adamini I, Laquintana D (2021) Complications of prone positioning in patients with COVID-19: a cross-sectional study. *Intensive Crit Care Nurs* 67:103088. <https://doi.org/10.1016/j.iccn.2021.103088>
  71. Elmer N, Liebl ME, Brehm K, Schwedtke C, Drebingler D, Pille C, Reißhauer A (2022) Folgeschäden durch Beatmung in Bauchlage bei COVID-19 und ihre Relevanz für die Frührehabilitation—eine retrospektive Kohortenstudie. *Physikalische Medizin, Rehabilitationsmedizin, Kurortmedizin*. <https://doi.org/10.1055/a-1888-0020>
  72. Elmer N, Reissshauer A, Brehm K, Vockeroth C, Liebl ME (2022) Long-term complications of prone position ventilation with relevance for acute and postacute rehabilitation: a systematic review of the literature. *Eur J Phys Rehabil Med*. <https://doi.org/10.23736/S1973-9087.22.07529-3>
  73. Sud S, Friedrich JO, Taccone P, Polli F, Adhikari NK, Latini R, Pesenti A, Guerin C, Mancebo J, Curley MA, Fernandez R, Chan MC, Beuret P, Voggenreiter G, Sud M, Tognoni G, Gattinoni L (2010) Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Intensive Care Med* 36:585–599. <https://doi.org/10.1007/s00134-009-1748-1>
  74. Schmid B, Griesel M, Fischer AL, Romero CS, Metzendorf MI, Weibel S, Fichtner F (2022) Awake prone positioning, high-flow nasal oxygen and non-invasive ventilation as non-invasive respiratory strategies in COVID-19 acute respiratory failure: a systematic review and meta-analysis. *J Clin Med*. <https://doi.org/10.3390/jcm11020391>
  75. Tekantapeh ST, Nader ND, Ghojzadeh M, Fereidouni F, Soleimanpour H (2024) Prone positioning effect on tracheal intubation rate, mortality and oxygenation parameters in awake non-intubated severe COVID-19-induced respiratory failure: a review of reviews. *Eur J Med Res* 29:63. <https://doi.org/10.1186/s40001-024-01661-6>
  76. Beran A, Mhanna M, Srour O, Ayes H, Sajdeya O, Ghazaleh S, Mhanna A, Ghazaleh D, Khokher W, Maqsood A, Assaly R (2022) Effect of prone positioning on clinical outcomes of non-intubated subjects with COVID-19. *Respir Care* 67:471–479. <https://doi.org/10.4187/respcare.09362>
  77. Fazzini B, Page A, Pearse R, Puthuchery Z (2022) Prone positioning for non-intubated spontaneously breathing patients with acute hypoxaemic respiratory failure: a systematic review and meta-analysis. *Br J Anaesth* 128:352–362. <https://doi.org/10.1016/j.bja.2021.09.031>
  78. Li J, Luo J, Pavlov I, Perez Y, Tan W, Roca O, Tavernier E, Kharat A, McNicholas B, Ibarra-Estrada M, Vines DL, Bosch NA, Rampon G, Simpson SQ, Walkey AJ, Fralick M, Verma A, Razak F, Harris T, Laffey JG, Guerin C, Ehrmann S, Awake Prone Positioning Meta-Analysis G (2022) Awake prone positioning for non-intubated patients with COVID-19-related acute hypoxaemic respiratory failure: a systematic review and meta-analysis. *Lancet Respir Med* 10:573–583. [https://doi.org/10.1016/S2213-2600\(22\)00043-1](https://doi.org/10.1016/S2213-2600(22)00043-1)
  79. Ponna Reddy M, Subramaniam A, Afroz A, Billah B, Lim ZJ, Zubarev A, Blecher G, Tiruvoipati R, Ramanathan K, Wong SN, Brodie D, Fan E, Shekar K (2021) Prone positioning of nonintubated patients with coronavirus disease 2019—a systematic review and meta-analysis. *Crit Care Med* 49:e1001–e1014. <https://doi.org/10.1097/CCM.00000000000005086>
  80. Tan W, Xu DY, Xu MJ, Wang ZF, Dai B, Li LL, Zhao HW, Wang W, Kang J (2021) The efficacy and tolerance of prone positioning in non-intubated patients with acute hypoxemic respiratory failure and ARDS: a meta-analysis. *Ther Adv Respir Dis* 15:17534666211009408. <https://doi.org/10.1177/17534666211009407>
  81. Ehrmann S, Li J, Ibarra-Estrada M, Perez Y, Pavlov I, McNicholas B, Roca O, Mirza S, Vines D, Garcia-Salcedo R, Aguirre-Avalos G, Trump MW, Nay MA, Dellamonica J, Nseir S, Mogri I, Cosgrave D, Jayaraman D, Masclans JR, Laffey JG, Tavernier E, Awake Prone Positioning Meta-Trial G (2021) Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. *Lancet Respir Med* 9:1387–1395. [https://doi.org/10.1016/S2213-2600\(21\)00356-8](https://doi.org/10.1016/S2213-2600(21)00356-8)
  82. Esperatti M, Busico M, Fuentes NA, Gallardo A, Osatnik J, Vitali A, Wasinger EG, Olmos M, Quintana J, Saavedra SN, Lagazio AI, Andrada FJ, Kakisu H, Romano NE, Matarrese A, Mogadouro MA, Mast G, Moreno CN, Niquin GDR, Barbaresi V, Bruhn Cruz A, Ferreyro BL, Torres A, Argentine Collaborative Group on High F, Prone P (2022) Impact of exposure time in awake prone positioning on clinical outcomes of patients with COVID-19-related acute respiratory failure treated with high-flow nasal oxygen: a multicenter cohort study. *Crit Care* 26:16. <https://doi.org/10.1186/s13054-021-03881-2>
  83. Qin S, Chang W, Peng F, Hu Z, Yang Y (2023) Awake prone position in COVID-19-related acute respiratory failure: a meta-analysis of randomized controlled trials. *BMC Pulm Med* 23:145. <https://doi.org/10.1186/s12890-023-02442-3>
  84. Cao W, He N, Luo Y, Zhang Z (2023) Awake prone positioning for non-intubated patients with COVID-19-related acute hypoxic respiratory failure: a systematic review based on eight high-quality randomized controlled trials. *BMC Infect Dis* 23:415. <https://doi.org/10.1186/s12879-023-08393-8>
  85. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprizio D, Schmidt GA, Bowman A, Barr R, McCallister KE, Hall JB, Kress JP (2009) Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 373:1874–1882. [https://doi.org/10.1016/S0140-6736\(09\)60658-9](https://doi.org/10.1016/S0140-6736(09)60658-9)
  86. Wright SE, Thomas K, Watson G, Baker C, Bryant A, Chadwick TJ, Shen J, Wood R, Wilkinson J, Mansfield L, Stafford V, Wade C, Furneal J, Henderson A, Hugill K, Howard P, Roy A, Bonner S, Baudouin S (2018) Intensive versus standard physical rehabilitation therapy in the critically ill (EPICC): a multicentre, parallel-group, randomised controlled trial. *Thorax* 73:213–221. <https://doi.org/10.1136/thoraxjnl-2016-209858>
  87. Moss M, Nordon-Craft A, Malone D, Van Pelt D, Frankel SK, Warner ML, Kriekels W, McNulty M, Fairclough DL, Schenkman M (2016) A randomized trial of an intensive physical therapy program for patients with acute respiratory failure. *Am J Respir Crit Care Med* 193:1101–1110. <https://doi.org/10.1164/rccm.201505-1039OC>
  88. Ding N, Zhang Z, Zhang C, Yao L, Yang L, Jiang B, Wu Y, Jiang L, Tian J (2019) What is the optimum time for initiation of early mobilization in mechanically ventilated patients? A network meta-analysis. *PLoS ONE* 14:e0223151. <https://doi.org/10.1371/journal.pone.0223151>
  89. Matsuoka A, Yoshihiro S, Shida H, Aikawa G, Fujinami Y, Kawamura Y, Nakanishi N, Shimizu M, Watanabe S, Sugimoto K, Taito S, Inoue S (2023) Effects of mobilization within 72 h of ICU admission in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. *J Clin Med*. <https://doi.org/10.3390/jcm12185888>
  90. Daum N, Drewniok N, Bald A, Ulm B, Buyukli A, Grunow JJ, Schaller SJ (2024) Early mobilisation within 72 hours after admission of critically ill patients in the intensive care unit: a systematic review with network meta-analysis. *Intensive Crit Care Nurs* 80:103573. <https://doi.org/10.1016/j.iccn.2023.103573>
  91. Wang L, Hua Y, Wang L, Zou X, Zhang Y, Ou X (2023) The effects of early mobilization in mechanically ventilated adult ICU patients: systematic review and meta-analysis. *Front Med (Lausanne)* 10:1202754. <https://doi.org/10.3389/fmed.2023.1202754>
  92. Ruo Yu L, Jia Jia W, Meng Tian W, Tian Cha H, Ji Yong J (2024) Optimal timing for early mobilization initiatives in intensive care unit patients: a systematic review and network meta-analysis. *Intensive Crit Care Nurs* 82:103607. <https://doi.org/10.1016/j.iccn.2023.103607>
  93. Jiroutkova K, Duska F, Waldauf P (2024) Should new data on rehabilitation interventions in critically ill patients change clinical practice?

- Updated meta-analysis of randomized controlled trials. *Crit Care Med*. <https://doi.org/10.1097/CCM.00000000000006259>
94. Morris PE, Goad A, Thompson C, Taylor K, Harry B, Passmore L, Ross A, Anderson L, Baker S, Sanchez M, Penley L, Howard A, Dixon L, Leach S, Small R, Hite RD, Haponik E (2008) Early intensive care unit mobility therapy in the treatment of acute respiratory failure. *Crit Care Med* 36:2238–2243. <https://doi.org/10.1097/CCM.0b013e318180b90e>
  95. Schujmann DS, Teixeira Gomes T, Lunardi AC, Zoccoler Lamano M, Fragoso A, Pimentel M, Peso CN, Araujo P, Fu C (2020) Impact of a progressive mobility program on the functional status, respiratory, and muscular systems of ICU patients: a randomized and controlled trial. *Crit Care Med* 48:491–497. <https://doi.org/10.1097/CCM.00000000000004181>
  96. Wahab R, Yip NH, Chandra S, Nguyen M, Pavlovich KH, Benson T, Vilotijevic D, Rodier DM, Patel KR, Rychcik P, Perez-Mir E, Boyle SM, Berlin D, Needham DM, Brodie D (2016) The implementation of an early rehabilitation program is associated with reduced length of stay: a multi-ICU study. *J Intensive Care Soc* 17:2–11. <https://doi.org/10.1177/1751143715605118>
  97. Coles SJ, Erdogan M, Higgins SD, Green RS (2020) Impact of an early mobilization protocol on outcomes in trauma patients admitted to the intensive care unit: a retrospective pre-post study. *J Trauma Acute Care Surg* 88:515–521. <https://doi.org/10.1097/TA.0000000000002588>
  98. Chiarici A, Andrenelli E, Serpilli O, Andreolini M, Tedesco S, Pomponio G, Gallo MM, Martini C, Papa R, Coccia M, Ceravolo MG (2019) An early tailored approach is the key to effective rehabilitation in the intensive care unit. *Arch Phys Med Rehabil* 100:1506–1514. <https://doi.org/10.1016/j.apmr.2019.01.015>
  99. Bahouth MN, Power MC, Zink EK, Kozeniewski K, Kumble S, Deluzio S, Urrutia VC, Stevens RD (2018) Safety and feasibility of a neuroscience critical care program to mobilize patients with primary intracerebral hemorrhage. *Arch Phys Med Rehabil* 99:1220–1225. <https://doi.org/10.1016/j.apmr.2018.01.034>
  100. Sigler M, Nugent K, Alalawi R, Selvan K, Tseng J, Edriss H, Turner A, Valdez K, Krause D (2016) Making of a successful early mobilization program for a medical intensive care unit. *South Med J* 109:342–345. <https://doi.org/10.14423/SMJ.0000000000000472>
  101. Fraser D, Spiva L, Forman W, Hallen C (2015) Original research: implementation of an early mobility program in an ICU. *Am J Nurs* 115:49–58. <https://doi.org/10.1097/01.NAJ.0000475292.27985.fc>
  102. Kasotakis G, Schmidt U, Perry D, Grosse-Sundrup M, Benjamin J, Ryan C, Tully S, Hirschberg R, Waak K, Velmahos G, Bittner EA, Zafonte R, Cobb JP, Eikermann M (2012) The surgical intensive care unit optimal mobility score predicts mortality and length of stay. *Crit Care Med* 40:1122–1128. <https://doi.org/10.1097/CCM.0b013e3182376e6d>
  103. Piva S, Dora G, Minelli C, Michelini M, Turla F, Mazza S, D'Ottavi P, Moreno-Duarte I, Sottini C, Eikermann M, Latronico N (2015) The surgical optimal mobility score predicts mortality and length of stay in an Italian population of medical, surgical, and neurologic intensive care unit patients. *J Crit Care* 30:1251–1257. <https://doi.org/10.1016/j.jccr.2015.08.002>
  104. Schaller SJ, Stauble CG, Suemasa M, Heim M, Duarte IM, Mensch O, Bogdanski R, Lewald H, Eikermann M, Blobner M (2016) The German validation study of the surgical intensive care unit optimal mobility score. *J Crit Care* 32:201–206. <https://doi.org/10.1016/j.jccr.2015.12.020>
  105. Schaller SJ, Scheffenbichler FT, Bose S, Mazwi N, Deng H, Krebs F, Seifert CL, Kasotakis G, Grabitz SD, Latronico N, Houle T, Blobner M, Eikermann M (2019) Influence of the initial level of consciousness on early, goal-directed mobilization: a post hoc analysis. *Intensive Care Med* 45:201–210. <https://doi.org/10.1007/s00134-019-05528-x>
  106. McWilliams D, Weblin J, Atkins G, Bion J, Williams J, Elliott C, Whitehouse T, Snelson C (2015) Enhancing rehabilitation of mechanically ventilated patients in the intensive care unit: a quality improvement project. *J Crit Care* 30:13–18. <https://doi.org/10.1016/j.jccr.2014.09.018>
  107. Nydahl P, Dubb R, Filipovic S, Hermes C, Juttner F, Kaltwasser A, Klarmann S, Mende H, Nessizius S, Rottensteiner C (2017) Algorithms for early mobilization in intensive care units. *Med Klin Intensivmed Notfmed* 112:156–162. <https://doi.org/10.1007/s00063-016-0210-8>
  108. Hodgson CL, Bailey M, Bellomo R, Berney S, Buhr H, Denehy L, Gabbe B, Harrold M, Higgins A, Iwashyna TJ, Papworth R, Parke R, Patman S, Presneill J, Saxena M, Skinner E, Tipping C, Young P, Webb S, Trial of Early Mobilization Study I (2016) A Binational multicenter pilot feasibility randomized controlled trial of early goal-directed mobilization in the ICU. *Crit Care Med* 44:1145–1152. <https://doi.org/10.1097/CCM.0000000000001643>
  109. Paton M, Lane R, Paul E, Cuthbertson GA, Hodgson CL (2021) Mobilization During Critical Illness: A Higher Level of Mobilization Improves Health Status at 6 Months, a Secondary Analysis of a Prospective Cohort Study. *Crit Care Med* 49:e860–e869. <https://doi.org/10.1097/CCM.00000000000005058>
  110. Raurell-Torreda M, Arias-Rivera S, Marti JD, Frade-Mera MJ, Zaragoza-Garcia I, Gallart E, Velasco-Sanz TR, San Jose-Arribas A, Blazquez-Martinez E, Group MO (2021) Care and treatments related to intensive care unit-acquired muscle weakness: a cohort study. *Aust Crit Care* 34:435–445. <https://doi.org/10.1016/j.aucc.2020.12.005>
  111. Shimogai T, Izawa KP, Kawada M, Kuriyama A (2019) Factors affecting discharge to home of medical patients treated in an intensive care unit. *Int J Environ Res Public Health*. <https://doi.org/10.3390/ijerph16224324>
  112. Hodgson CL, Bailey M, Bellomo R, Brickell K, Broadley T, Buhr H, Gabbe BJ, Gould DW, Harrold M, Higgins AM, Hurford S, Iwashyna TJ, Serpa Neto A, Nichol AD, Presneill JJ, Schaller SJ, Sivasuthan J, Tipping CJ, Webb S, Young PJ (2022) Early active mobilization during mechanical ventilation in the ICU. *N Engl J Med* 387:1747–1758. <https://doi.org/10.1056/NEJMoa2209083>
  113. Vollenweider R, Manettas AI, Hani N, de Bruin ED, Knols RH (2022) Passive motion of the lower extremities in sedated and ventilated patients in the ICU—a systematic review of early effects and replicability of Interventions. *PLoS ONE* 17:e0267255. <https://doi.org/10.1371/journal.pone.0267255>
  114. Kim HJ, Lee Y, Sohng KY (2014) Effects of bilateral passive range of motion exercise on the function of upper extremities and activities of daily living in patients with acute stroke. *J Phys Ther Sci* 26:149–156. <https://doi.org/10.1589/jpts.26.149>
  115. Rahiminezhad E, Sadeghi M, Ahmadinejad M, Mirzadi Gohari SI, Dehghan M (2022) A randomized controlled clinical trial of the effects of range of motion exercises and massage on muscle strength in critically ill patients. *BMC Sports Sci Med Rehabil* 14:96. <https://doi.org/10.1186/s13102-022-00489-z>
  116. Wu RY, Yeh HJ, Chang KJ, Tsai MW (2023) Effects of different types and frequencies of early rehabilitation on ventilator weaning among patients in intensive care units: a systematic review and meta-analysis. *PLoS ONE* 18:e0284923. <https://doi.org/10.1371/journal.pone.0284923>
  117. Scheffenbichler FT, Teja B, Wongtangman K, Mazwi N, Waak K, Schaller SJ, Xu X, Barbieri S, Fagoni N, Cassavaugh J, Blobner M, Hodgson CL, Latronico N, Eikermann M (2021) Effects of the level and duration of mobilization therapy in the surgical ICU on the loss of the ability to live independently: an international prospective cohort study. *Crit Care Med* 49:e247–e257. <https://doi.org/10.1097/CCM.0000000000004808>
  118. Mazwi N, Lissak I, Wongtangman K, Platzbecker K, Albrecht L, Teja B, Xu X, Morteo NM, Sparling T, Latronico N, Barbieri S, Blobner M, Schaller SJ, Eikermann M (2023) Effects of mobility dose on discharge disposition in critically ill stroke patients. *PM R* 15:1547–1556. <https://doi.org/10.1002/pmrj.13039>
  119. Lorenz M, Fuest K, Ulm B, Grunow JJ, Warner L, Bald A, Arsene V, Verfuss M, Daum N, Blobner M, Schaller SJ (2023) The optimal dose of mobilisation therapy in the ICU: a prospective cohort study. *J Intensive Care* 11:56. <https://doi.org/10.1186/s40560-023-00703-1>
  120. Klem HE, Tveiten TS, Beitland S, Malerod S, Kristoffersen DT, Dalsnes T, Nupen-Stieng MB, Larun L (2021) Early activity in mechanically ventilated patients—a meta-analysis. *Tidsskr Nor Lægeforen*. <https://doi.org/10.4045/tidsskr.20.0351>
  121. Worraphan S, Thammata A, Chittawatanarat K, Saokaew S, Kengkla K, Prasannarong M (2020) Effects of inspiratory muscle training and early mobilization on weaning of mechanical ventilation: a systematic review and network meta-analysis. *Arch Phys Med Rehabil* 101:2002–2014. <https://doi.org/10.1016/j.apmr.2020.07.004>
  122. Anekwe DE, Biswas S, Bussieres A, Spahija J (2020) Early rehabilitation reduces the likelihood of developing intensive care unit-acquired weakness: a systematic review and meta-analysis. *Physiotherapy* 107:1–10. <https://doi.org/10.1016/j.physio.2019.12.004>
  123. Cui Z, Li N, Gao C, Fan Y, Zhuang X, Liu J, Zhang J, Tan Q (2020) Precision implementation of early ambulation in elderly patients undergoing

- off-pump coronary artery bypass graft surgery: a randomized-controlled clinical trial. *BMC Geriatr* 20:404. <https://doi.org/10.1186/s12877-020-01823-1>
124. Kayambu G, Boots R, Paratz J (2015) Early physical rehabilitation in intensive care patients with sepsis syndromes: a pilot randomised controlled trial. *Intensive Care Med* 41:865–874. <https://doi.org/10.1007/s00134-015-3763-8>
  125. Gatty A, Samuel SR, Alaparthy GK, Prabhu D, Upadya M, Krishnan S, Amaravadi SK (2020) Effectiveness of structured early mobilization protocol on mobility status of patients in medical intensive care unit. *Physiother Theory Pract*. <https://doi.org/10.1080/09593985.2020.1840683>
  126. Fuest KE, Lorenz M, Grunow JJ, Weiss B, Morgeli R, Finkenzeller S, Bogdanski R, Heim M, Kapfer B, Kriescher S, Lingg C, Martin J, Ulm B, Jungwirth B, Blobner M, Schaller SJ (2021) The functional trajectory in frail compared with non-frail critically ill patients during the hospital stay. *Front Med (Lausanne)* 8:748812. <https://doi.org/10.3389/fmed.2021.748812>
  127. Mayer KP, Joseph-Isang E, Robinson LE, Parry SM, Morris PE, Neyra JA (2020) Safety and feasibility of physical rehabilitation and active mobilization in patients requiring continuous renal replacement therapy: a systematic review. *Crit Care Med* 48:e1112–e1120. <https://doi.org/10.1097/CCM.0000000000004526>
  128. Braune S, Bojes P, Mecklenburg A, Angriman F, Soeffker G, Warnke K, Westermann D, Blankenberg S, Kubik M, Reichenspurner H, Kluge S (2020) Feasibility, safety, and resource utilisation of active mobilisation of patients on extracorporeal life support: a prospective observational study. *Ann Intensive Care* 10:161. <https://doi.org/10.1186/s13613-020-00776-3>
  129. Liu K, Ogura T, Takahashi K, Nakamura M, Ohtake H, Fujiduka K, Abe E, Oosaki H, Miyazaki D, Suzuki H, Nishikimi M, Lefor AK, Mato T (2018) The safety of a novel early mobilization protocol conducted by ICU physicians: a prospective observational study. *J Intensive Care* 6:10. <https://doi.org/10.1186/s40560-018-0281-0>
  130. Bartolo M, Bargellesi S, Castioni CA, Bonaiuti D, Intensive C, Neurorehabilitation Italian Study G, Antenucci R, Benedetti A, Capuzzo V, Gamna F, Radeschi G, Citerio G, Colombo C, Del Casale L, Recubini E, Toska S, Zanello M, D'Aurizio C, Spina T, Del Gaudio A, Di Rienzo F, Intiso D, Dallochio G, Felisatti G, Lavezzi S, Zoppellari R, Gariboldi V, Lorini L, Melizza G, Molinero G, Mandala G, Pignataro A, Montis A, Napoleone A, Pilia F, Pisu M, Semerjian M, Pagliaro G, Nardin L, Scarponi F, Zampolini M, Zava R, Massetti MA, Piccolini C, Aloj F, Antonelli S, Zucchella C (2016) Early rehabilitation for severe acquired brain injury in intensive care unit: multicenter observational study. *Eur J Phys Rehabil Med* 52:90–100
  131. Titsworth WL, Hester J, Correia T, Reed R, Guin P, Archibald L, Layon AJ, Mocco J (2012) The effect of increased mobility on morbidity in the neurointensive care unit. *J Neurosurg* 116:1379–1388. <https://doi.org/10.3171/2012.2.JNS111881>
  132. Bartolo M, Bargellesi S, Castioni CA, Intiso D, Fontana A, Copetti M, Scarponi F, Bonaiuti D, Intensive C, Neurorehabilitation Italian Study G (2017) Mobilization in early rehabilitation in intensive care unit patients with severe acquired brain injury: an observational study. *J Rehabil Med* 49:715–722. <https://doi.org/10.2340/16501977-2269>
  133. Avert Trial Collaboration Group (2015) Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. *Lancet* 386:46–55. [https://doi.org/10.1016/S0140-6736\(15\)60690-0](https://doi.org/10.1016/S0140-6736(15)60690-0)
  134. Nydahl P, Ewers A, Brodda D (2014) Complications related to early mobilization of mechanically ventilated patients on Intensive Care Units. *Nurs Crit Care*. <https://doi.org/10.1111/nicc.12134>
  135. Nydahl P, Sricharoenchai T, Chandra S, Kundt FS, Huang M, Fischill M, Needham DM (2017) Safety of patient mobilization and rehabilitation in the intensive care unit. Systematic review with meta-analysis. *Ann Am Thorac Soc* 14:766–777. <https://doi.org/10.1513/AnnalsATS.201611-843SR>
  136. Sakai T, Hoshino C, Okawa A, Wakabayashi K, Shigemitsu H (2020) The safety and effect of early mobilization in the intensive care unit according to cancellation criteria. *Prog Rehabil Med* 5:20200016. <https://doi.org/10.2490/prm.20200016>
  137. Unoki T, Hayashida K, Kawai Y, Taito S, Ando M, Iida Y, Kasai F, Kawasaki T, Kozu R, Kondo Y, Saitoh M, Sakuramoto H, Sasaki N, Saura R, Nakamura K, Ouchi A, Okamoto S, Okamura M, Kuribara T, Kuriyama A, Matsuishi Y, Yamamoto N, Yoshihiro S, Yasaka T, Abe R, Iitsuka T, Inoue H, Uchiyama Y, Endo S, Okura K, Ota K, Otsuka T, Okada D, Obata K, Katayama Y, Kaneda N, Kitayama M, Kina S, Kusaba R, Kuwabara M, Sasanuma N, Takahashi M, Takayama C, Tashiro N, Tatsuno J, Tamura T, Tamoto M, Tsuchiya A, Tsutsumi Y, Nagato T, Narita C, Nawa T, Nonoyama T, Hanada M, Hirakawa K, Makino A, Masaki H, Matsuki R, Matsushima S, Matsuda W, Miyagishima S, Moromizato M, Yanagi N, Yamauchi K, Yamashita Y, Yamamoto N, Liu K, Wakabayashi Y, Watanabe S, Yonekura H, Nakanishi N, Takahashi T, Nishida O, Committee for the Clinical Practice Guidelines of Early M, Rehabilitation in Intensive Care of the Japanese Society of Intensive Care M (2023) Japanese clinical practice guidelines for rehabilitation in critically ill patients 2023 (J-ReCIP 2023). *J Intensive Care* 11:47. <https://doi.org/10.1186/s40560-023-00697-w>
  138. Dubb R, Nydahl P, Hermes C, Schwabbauer N, Toonstra A, Parker AM, Kaltwasser A, Needham DM (2016) Barriers and strategies for early mobilization of patients in intensive care units. *Ann Am Thorac Soc* 13:724–730. <https://doi.org/10.1513/AnnalsATS.201509-586CME>
  139. Nydahl P, Gunther U, Diers A, Hesse S, Kerschensteiner C, Klarmann S, Borzikowsky C, Kopke S (2020) PROtocol-based MOBilizaTION on intensive care units: stepped-wedge, cluster-randomized pilot study (Pro-Motion). *Nurs Crit Care* 25:368–375. <https://doi.org/10.1111/nicc.12438>
  140. Collinsworth AW, Priest EL, Masica AL (2020) Evaluating the cost-effectiveness of the ABCDE bundle: impact of bundle adherence on inpatient and 1-year mortality and costs of care. *Crit Care Med* 48:1752–1759. <https://doi.org/10.1097/CCM.0000000000004609>
  141. Chen TJ, Traynor V, Wang AY, Shih CY, Tu MC, Chuang CH, Chiu HY, Chang HR (2022) Comparative effectiveness of non-pharmacological interventions for preventing delirium in critically ill adults: a systematic review and network meta-analysis. *Int J Nurs Stud* 131:104239. <https://doi.org/10.1016/j.ijnurstu.2022.104239>
  142. Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, Byrum D, Carson SS, Devlin JW, Engel HJ, Esbrook CL, Hargett KD, Harmon L, Hielsberg C, Jackson JC, Kelly TL, Kumar V, Millner L, Morse A, Perme CS, Posa PJ, Puntillo KA, Schweickert WD, Stollings JL, Tan A, D'Agostino McGowan L, Ely EW (2019) Caring for critically ill patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. *Crit Care Med* 47:3–14. <https://doi.org/10.1097/CCM.0000000000003482>
  143. Nydahl P, Schuchhardt D, Juttner F, Dubb R, Hermes C, Kaltwasser A, Mende H, Muller-Wolff T, Rothaug O, Schreiber T (2020) Caloric consumption during early mobilisation of mechanically ventilated patients in Intensive Care Units. *Clin Nutr* 39:2442–2447. <https://doi.org/10.1016/j.clnu.2019.10.028>
  144. Lee ZY, Yap CSL, Hasan MS, Engkasan JP, Barakatun-Nisak MY, Day AG et al (2021) The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. *Crit Care*. 25(1):260. <https://doi.org/10.1186/s13054-021-03693-4>
  145. Heyland DK, Patel J, Compher C, Rice TW, Bear DE, Lee ZY, Gonzalez VC, O'Reilly K, Regala R, Wedemire C, Ibarra-Estrada M, Stoppe C, Ortiz-Reyes L, Jiang X, Day AG, Team EPT (2023) The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT Protein): an international, multicentre, pragmatic, registry-based randomised trial. *Lancet* 401:568–576. [https://doi.org/10.1016/S0140-6736\(22\)02469-2](https://doi.org/10.1016/S0140-6736(22)02469-2)
  146. Nakamura K, Nakano H, Naraba H, Mochizuki M, Takahashi Y, Sonoo T, Hashimoto H, Morimura N (2021) High protein versus medium protein delivery under equal total energy delivery in critical care: a randomized controlled trial. *Clin Nutr* 40:796–803. <https://doi.org/10.1016/j.clnu.2020.07.036>
  147. de Azevedo JRA, Lima HCM, Frota P, Nogueira I, de Souza SC, Fernandes EAA, Cruz AM (2021) High-protein intake and early exercise in adult intensive care patients: a prospective, randomized controlled trial to evaluate the impact on functional outcomes. *BMC Anesthesiol* 21:283. <https://doi.org/10.1186/s12871-021-01492-6>
  148. van Delft LMM, Valkenet K, Slooter AJC, Veenhof C (2021) Family participation in physiotherapy-related tasks of critically ill patients: A mixed methods systematic review. *J Crit Care*. 62:49–57. <https://doi.org/10.1016/j.jccr.2020.11.014>



149. Waldauf P, Hruskova N, Blahutova B, Gajda J, Urban T, Krajcova A, Fric M, Jiroutkova K, Rasova K, Duska F (2021) Functional electrical stimulation-assisted cycle ergometry-based progressive mobility programme for mechanically ventilated patients: randomised controlled trial with 6 months follow-up. *Thorax* 76:664–671. <https://doi.org/10.1136/thoraxjnl-2020-215755>
150. Fossat G, Baudin F, Courtes L, Bobet S, Dupont A, Bretagnol A, Benzekri-Lefevre D, Kamel T, Muller G, Bercault N, Barbier F, Runge I, Nay MA, Skarzynski M, Mathonnet A, Boulain T (2018) Effect of in-bed leg cycling and electrical stimulation of the quadriceps on global muscle strength in critically ill adults: a randomized clinical trial. *JAMA* 320:368–378. <https://doi.org/10.1001/jama.2018.9592>
151. Eggmann S, Verra ML, Luder G, Takala J, Jakob SM (2018) Effects of early, combined endurance and resistance training in mechanically ventilated, critically ill patients: a randomised controlled trial. *PLoS ONE* 13:e0207428. <https://doi.org/10.1371/journal.pone.0207428>
152. Takaoka A, Utgikar R, Rochweg B, Cook DJ, Kho ME (2020) The efficacy and safety of in-intensive care unit leg-cycle ergometry in critically ill adults. A systematic review and meta-analysis. *Ann Am Thorac Soc* 17:1289–1307. <https://doi.org/10.1513/AnnalsATS.202001-059OC>
153. Waldauf P, Jiroutkova K, Krajcova A, Puthuchery Z, Duska F (2020) Effects of rehabilitation interventions on clinical outcomes in critically ill patients: systematic review and meta-analysis of randomized controlled trials. *Crit Care Med* 48:1055–1065. <https://doi.org/10.1097/CCM.0000000000004382>
154. Yu L, Jiang JX, Zhang Y, Chen YZ, Shi Y (2020) Use of in-bed cycling combined with passive joint activity in acute respiratory failure patients receiving mechanical ventilation. *Ann Palliat Med* 9:175–181. <https://doi.org/10.21037/apm.2020.02.12>
155. Machado ADS, Pires-Neto RC, Carvalho MTX, Soares JC, Cardoso DM, Albuquerque IM (2017) Effects that passive cycling exercise have on muscle strength, duration of mechanical ventilation, and length of hospital stay in critically ill patients: a randomized clinical trial. *J Bras Pneumol* 43:134–139. <https://doi.org/10.1590/S1806-37562016000000170>
156. Burtin C, Clerckx B, Robbeets C, Ferdinande P, Langer D, Troosters T, Hermans G, Decramer M, Gosselink R (2009) Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 37:2499–2505. <https://doi.org/10.1097/CCM.0b013e3181a38937>
157. Bianchi T, Santos LJF, Lemos O, Sachetti A, Acqua AMD, Naue WS, Júnior LAF, Dias A, Vieira SRR (2018) The effect of passive cycle ergometry exercise on diaphragmatic motion of invasive mechanically ventilated critically ill patients in intensive care unit: a randomized clinical trial. *Int J Phys Med Rehabil* 06:1–8
158. Parry SM, Berney S, Warrillow S, El-Ansary D, Bryant AL, Hart N, Puthuchery Z, Koopman R, Deney L (2014) Functional electrical stimulation with cycling in the critically ill: a pilot case-matched control study. *J Crit Care* 29(695):e691–697. <https://doi.org/10.1016/j.jcrc.2014.03.017>
159. Ribeiro BC, Poca J, Rocha AMC, Cunha C, Cunha KDC, Falcao LFM, Torres DDC, Rocha LSO, Rocha RSB (2021) Different physiotherapy protocols after coronary artery bypass graft surgery: a randomized controlled trial. *Physiother Res Int* 26:e1882. <https://doi.org/10.1002/pri.1882>
160. Medrinal C, Combret Y, Prieur G, Robledo Quesada A, Bonnevie T, Gravier FE, Dupuis Lozeron E, Frenoy E, Contal O, Lamia B (2018) Comparison of exercise intensity during four early rehabilitation techniques in sedated and ventilated patients in ICU: a randomised cross-over trial. *Crit Care* 22:110. <https://doi.org/10.1186/s13054-018-2030-0>
161. Kwakman RCH, Sommers J, Horn J, Nollet F, Engelbert RHH, van der Schaaf M (2020) Steps to recovery: body weight-supported treadmill training for critically ill patients: a randomized controlled trial. *Trials* 21:409. <https://doi.org/10.1186/s13063-020-04333-y>
162. Frazzitta G, Zivi I, Valsecchi R, Bonini S, Maffia S, Molatore K, Sebastianelli L, Zarucchi A, Matteri D, Ercoli G, Maestri R, Saltuari L (2016) Effectiveness of a very early stepping verticalization protocol in severe acquired brain injured patients: a randomized pilot study in ICU. *PLoS ONE* 11:e0158030. <https://doi.org/10.1371/journal.pone.0158030>
163. Nakanishi N, Yoshihiro S, Kawamura Y, Aikawa G, Shida H, Shimizu M, Fujinami Y, Matsuoka A, Watanabe S, Taito S, Inoue S (2023) Effect of neuromuscular electrical stimulation in patients with critical illness: an updated systematic review and meta-analysis of randomized controlled trials. *Crit Care Med* 51:1386–1396. <https://doi.org/10.1097/CCM.00000000000005941>
164. Liu M, Luo J, Zhou J, Zhu X (2020) Intervention effect of neuromuscular electrical stimulation on ICU acquired weakness: a meta-analysis. *Int J Nurs Sci* 7:228–237. <https://doi.org/10.1016/j.ijnss.2020.03.002>
165. Gutierrez-Arias RE, Zapata-Quiroz CC, Prenafeta-Pedemonte BO, Nasar-Lillo NA, Gallardo-Zamorano DI (2021) Effect of neuromuscular electrical stimulation on the duration of mechanical ventilation. *Respir Care* 66:679–685. <https://doi.org/10.4187/respcare.08363>
166. Xu C, Yang F, Wang Q, Gao W (2024) Effect of neuromuscular electrical stimulation in critically ill adults with mechanical ventilation: a systematic review and network meta-analysis. *BMC Pulm Med* 24:56. <https://doi.org/10.1186/s12890-024-02854-9>
167. Zayed Y, Kheiri B, Barbarawi M, Chahine A, Rashdan L, Chintalapati S, Bachuwa G, Al-Sanouri I (2020) Effects of neuromuscular electrical stimulation in critically ill patients: a systematic review and meta-analysis of randomised controlled trials. *Aust Crit Care* 33:203–210. <https://doi.org/10.1016/j.aucc.2019.04.003>
168. Jonkman AH, Frenzel T, McCaughey EJ, McLachlan AJ, Boswell-Ruys CL, Collins DW, Gandevia SC, Girbes ARJ, Hoiting O, Kox M, Oppersma E, Peters M, Pickkers P, Roesthuis LH, Schouten J, Shi ZH, Veltink PH, de Vries HJ, Shannon Weickert C, Wiedenbach C, Zhang Y, Tuinman PR, de Man AME, Butler JE, Heunks LMA (2020) Breath-synchronized electrical stimulation of the expiratory muscles in mechanically ventilated patients: a randomized controlled feasibility study and pooled analysis. *Crit Care* 24:628. <https://doi.org/10.1186/s13054-020-03352-0>