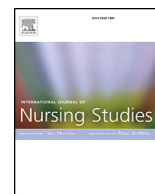




Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/locate/ns

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

Kellie Sosnowski^{a,b,c,*}, Frances Lin^d, Wendy Chaboyer^{a,c,e}, Kristen Ranse^a, Aaron Heffernan^{b,f,g}, Marion Mitchell^{a,c}

^a School of Nursing and Midwifery, Griffith University, Queensland, Australia

^b Intensive Care Unit, Logan Hospital, Queensland, Australia

^c Menzies Health Institute, Queensland, Australia

^d School of Nursing, Midwifery and Paramedicine, University of the Sunshine Coast, Queensland, Australia

^e National Health and Medical Research Council (NHMRC), Centre of Research Excellence in Wiser Wound Care, Griffith University, Queensland, Australia

^f School of Medicine and Dentistry, Griffith University, Australia

^g Faculty of Medicine, University of Queensland, Australia

ARTICLE INFO

Article history:

Received 30 May 2022

Received in revised form 4 October 2022

Accepted 22 November 2022

Keywords:

ABCDE bundle

Critical illness

Delirium

meta-analysis

Systematic review

ABSTRACT

Background: The effect of the ABCDEF bundle (Assess, prevent, and manage pain; Both spontaneous awakening and spontaneous breathing trials; Choice of analgesia and sedation; Delirium: assess, prevent, and manage; Early mobility and exercise; and Family engagement and empowerment) on patient outcomes such as delirium is potentially optimised when the bundle is implemented in its entirety.

Objective: To systematically synthesise the evidence on the effectiveness of the ABCDEF bundle delivered in its entirety on delirium, function, and quality of life in adult intensive care unit patients.

Design: Systematic review and meta-analysis.

Data source: Electronic databases including MEDLINE, CINAHL, PsycINFO, Web of Science, Cochrane Library, Joanna Briggs Institute's Evidence Based Practice, Australian New Zealand Clinical Trials Registry, and Embase were searched from 2000 until December 2021.

Review methods: Inclusion criteria included (1) adult intensive care unit patients (2) studies that described the ABCDE or ABCDEF bundle in its entirety (3) studies that evaluated delirium, functional outcomes, or quality of life. Studies were excluded if they investigated long-term intensive care unit rehabilitation patients. Two reviewers independently screened records and full text, extracted data, and undertook quality appraisals with discrepancies discussed until consensus was reached. Random effects meta-analyses were conducted for delirium but was not possible for other outcomes. The Grading of Recommendations, Assessment, Development and Evaluation approach was used to assess the certainty of the synthesised findings of the body of evidence. The study protocol was registered on PROSPERO (CRD 42019126407).

Results: A total of 18 studies (29,576 patients) were included in the descriptive synthesis. Meta-analysis of six studies (2000 patients) identified decreased delirium incidence following implementation of the ABCDEF bundle when compared with standard practice, (risk ratio = 0.57; CI, 0.36–0.90 $p = 0.02$) although heterogeneity was high ($I^2 = 92\%$). When compared with standard practice, a meta-analysis of five studies (3418 patients) showed the ABCDEF bundle statistically significantly reduced the duration of intensive care unit delirium (mean difference (days) – 1.37, 95% CI –2.61 to –0.13 $p = 0.03$; $I^2 96\%$). Valid functional assessments were included in two studies, and quality of life assessment in one.

Conclusions: Although the evidence on the effect of the ABCDEF bundle delivered in its entirety is limited, positive patient delirium outcomes have been shown in this meta-analysis. As this meta-analysis was based on only 4736 patients in eight studies, further evidence is required to support its use in the adult intensive care unit.

Registration Details: PROSPERO (CRD 42019126407).

© 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author at: School of Nursing and Midwifery, Griffith University, 170 Kessels Road, Nathan, 4111, Queensland, Australia.
E-mail address: kellie.sosnowski@griffithuni.edu.au (K. Sosnowski).

What is already known

- The ABCDEF bundle is a multidisciplinary, evidence-based bundle of care that aims to improve recovery from critical illness.
- Components of the ABCDEF bundle have been associated with positive short-term benefits for intensive care unit patients.

What this paper adds

- Analysis of the evidence suggests that effectiveness of the ABCDEF bundle increased when the bundle was implemented in its entirety.
- The ABCDEF bundle is a complex intervention that requires considered strategies to ensure successful implementation in the intensive care unit.
- This review provides further evidence of the benefit of implementing the whole ABCDEF bundle in promoting short-term outcomes in intensive care unit patient populations. Investigation of patient-centred outcomes once discharged from hospital is warranted.

1. Introduction

Complications including profound weakness, pain, agitation, and delirium are commonly experienced by patients admitted into the intensive care unit (Devlin et al., 2018; Gustafson et al., 2021). These physical and cognitive impairments associated with critical illness and treatments received in the intensive care unit negatively impact health-related quality of life following hospital discharge for many patients and their families (Rengel et al., 2019). New physical, cognitive or mental impairment following a critical illness and persisting beyond hospital discharge is identified as post-intensive care unit syndrome (Heydon et al., 2020). The syndrome may also negatively impact the caregiver (Johnson et al., 2019). Family members often become informal caregivers, which can exert a secondary toll of ill-health, altered family relationships and impacted financial security (Naaktgeboren et al., 2022).

Evidence-based recommendations for integrated, patient-centred protocols were initially proposed in 2013, with the introduction of the pain, agitation and delirium guidelines (Barr et al., 2013) and have been updated in the 2018 clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult intensive care unit patients (Devlin et al., 2018). The pain, agitation/sedation, delirium, immobility, and sleep disruption guidelines provide 37 recommendations with the quality of evidence ranging from very low to strong. These recommendations aim to reduce the duration of mechanical ventilation, optimise appropriate sedation, improve functional status and muscle strength, and reduce the adverse cognitive effects of an intensive care unit admission. Elements of the guidelines can be implemented by following a multi-component, evidence-based guide for coordinating interdisciplinary intensive care unit care, the ABCDEF bundle (Marra et al., 2017). The ABCDEF bundle has evolved from the original ABCDE bundle to include engagement with the family and significant others (Marra et al., 2017). The ABCDEF bundle components are: Assess, prevent, and manage pain; Both spontaneous awakening trials and spontaneous breathing trials; Choice of analgesia and sedation; Delirium: assess, prevent, and manage; Early mobility and exercise; and Family engagement and empowerment.

A recent systematic review and meta-analysis of studies that implemented at least three of the ABCDEF bundle components reinforced positive short-term benefits regarding the duration of coma, length of intensive care unit stay, and mortality (Zhang et al., 2021). However, the review showed that bundle implementation did not necessarily reduce the incidence or duration of delirium. As Mikkelsen and Devlin noted in their editorial, the effectiveness of the bundle may depend on both the quality and quantity of the intervention (Mikkelsen and Devlin, 2021).

Analysis of the data from the above review suggests that effectiveness increased when the bundle was implemented in its entirety

(Zhang et al., 2021). Fidelity of compliance with bundles of care is an important consideration when assessing patient outcomes (Lavallée et al., 2017). There is limited evidence on the effectiveness of the implementation of the whole ABCDEF bundle (Lavallée et al., 2017), yet positive patient outcomes have been noted when compliance to the bundle is high (Hakko et al., 2015). Research supporting the entire ABCDEF bundle adoption in the intensive care unit to prevent delirium, improve functional outcomes, and health related quality of life is growing. A comprehensive synthesis of research of the entire ABCDEF bundle of cares is warranted to assess the evidence of the effectiveness of the bundle on delirium, functional outcomes, and quality of life.

1.1. Objectives

The purpose of this systematic review and meta-analysis was to critically appraise and synthesise research on the ABCDE/F bundle in the intensive care unit. The research questions were: (1) what is the effectiveness of the ABCDE/F bundle on delirium, functional outcomes, and quality of life in adult intensive care unit patients? (2) what barriers and facilitators influence the adoption of the bundle into practice?

2. Methods

2.1. Design

A systematic review and meta-analysis of the ABCDE/F bundle in adult intensive care unit patients was conducted. This review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (Page et al., 2021). The protocol was registered on PROSPERO (CRD 42019126407) prior to the database search.

2.2. Search strategy

The final search of the following electronic databases was conducted in January 2022: MEDLINE (via OVID SP); CINAHL (via EBSCO); PsycINFO (via Ovid SP); Web of Science; Cochrane Library; Joanna Briggs Institute's Evidence Based Practice; Australian New Zealand Clinical Trials Registry; and Embase. Reference lists of systematic reviews and included studies were searched, and studies known to be relevant were checked for inclusion. The search terms were agreed upon by consensus of the review team. An experienced university health librarian reviewed the specific search strategy. Keyword searches were limited to title and abstract for the search terms 'ABCDE'; 'ABCDEF' (abbreviations and full text); 'icu', 'intensive care unit', 'critical care unit', and 'critically ill'. Boolean operators of "OR" and "AND" were applied to the search terms. These operators were consistent between the databases. The Medline search string is detailed in supplementary material Fig. 1; equivalent search strings were used to search the other databases.

2.3. Inclusion and exclusion criteria

Eligible studies were selected according to the following criteria: (1) population: critically ill adult (age ≥ 18 years) patients admitted to the intensive care unit; (2) intervention: implementation of the ABCDE/F bundle in its entirety; (3) primary outcomes: studies that reported or evaluated delirium, functional outcomes or health related quality of life in intensive care unit patients. Functional outcomes could comprise measurements of muscle strength, reaching mobility milestones including sitting on the side of the bed, standing or walking, measures of ambulation distance, or use a validated assessment tool; (4) secondary outcomes: studies that reported factors that influenced the adoption of the bundle into clinical practice were required to also report on the primary outcomes; and (5) design: quantitative and

qualitative research were included. Studies published in theses, abstracts or conference proceedings were considered if they provided sufficient relevant and reportable outcome data. Studies published in English were included, and there were no date limitations.

2.4. Study selection and data extraction

Search results were exported into an Endnote X9 library and duplicates removed. The review occurred in five phases: title and abstract screening, full-text appraisal, data extraction, quality assessment, and grading the certainty of the body of the evidence. Initially, the first author conducted the title search and abstract screening. Inclusion and exclusion criteria were considered, and articles deemed not relevant were excluded following consultation with two authors. A data extraction tool was developed using an excel spreadsheet. Full text included articles were reviewed and data extracted by the first author, which included: author and country, year of publication, study setting, study design, patient characteristics, ABCDE/F bundle implementation details, sample size, outcome measure, main findings, and study limitations identified by study authors. Two authors verified extracted data. Discrepancies were discussed and consensus achieved before assessing the methodological quality of the articles.

2.5. Quality assessment of included studies

Joanna Briggs Institute Critical Appraisal tools (Tufanaru et al., 2017) for quasi-experimental studies, cohort studies, and randomised controlled trials were used to systematically analyse and rigorously evaluate the methodological quality of the included research studies. Two authors independently assessed the risk of bias. Each study was reviewed to determine if a study had minimised the possibility of bias in its design, conduct and analysis. Missing data were noted within the assessment. Discussion among the authors resolved uncertainty regarding the quality or risk of bias if required. Each study was scored based on adherence to the appraisal tools (Yes = 1, Unclear or No = 0), and an overall percentage was applied.

The Grading of Recommendations, Assessment, Development and Evaluation approach (Guyatt et al., 2011) was used to assess the certainty of the synthesised findings of the body of evidence. We focussed on the primary outcomes used in the meta-analyses of delirium incidence and delirium duration. The assessment was conducted in GRADEpro by the primary author and verified by a second author.

2.6. Statistical analysis

Analysis of data from the included studies was conducted using Review Manager v5.4 (Review Manager, 2020). Dichotomous outcomes were analysed by calculating the risk ratio of improvement and were reported with a 95% confidence interval (CI). Continuous outcomes were reported as mean difference with 95% CI. Pooled means were presented as weighted effect sizes with 95% CI. Random effects models were used to interpret high heterogeneity ($p < 0.1$ or $I^2 > 50\%$). Sensitivity analysis was performed to assess the impact of each study on the overall result. Outcome data not suitable for the meta-analysis are summarised and reported narratively.

3. Results

3.1. Study selection

Initially, 717 citations were identified, and 271 duplicates were removed. Titles and abstracts screening against the inclusion/exclusion criteria resulted in 50 articles for full text review. A further 35 studies were excluded following full text review because the study design did not meet the inclusion criteria ($n = 30$), the article reported a secondary analysis of an included study ($n = 2$), or the

article did not present sufficient evidence ($n = 3$). Three additional studies were identified from searches of reference lists from included articles. Eighteen papers that included fourteen distinct studies met the criteria for inclusion in this review. A preferred reporting items for systematic reviews and meta-analyses flow diagram illustrates the screening process and study selection (Fig. 1).

3.2. Study characteristics

Characteristics of the 18 included studies are reported in Table 1. They were published between 2014 and 2021 and comprised 13 journal articles (Balas et al., 2014; Barnes-Daly et al., 2017; Bounds et al., 2016; DiSabatino and Grami, 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Malik et al., 2021; Negro et al., 2018; Patel et al., 2014; Pun et al., 2019; Schallom et al., 2020; Sosnowski et al., 2018), four conference abstracts (Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018), and one dissertation (Jacob, 2017). A total of 102 intensive care units and 29,576 participants were included in the review. Study sample sizes ranged from 30 to 15,226 participants. There were seven multi-centred studies (Balas et al., 2014; Barnes-Daly et al., 2017; Bounds et al., 2016; DiSabatino and Grami, 2016; Hsieh et al., 2019; Pun et al., 2019; Schallom et al., 2020) and 11 single-centre studies (Kram et al., 2015; Lee et al., 2020; Malik et al., 2021; Negro et al., 2018; Patel et al., 2014; Sosnowski et al., 2018; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018; Jacob, 2017). Most participants ($n = 22,911$ [77.5%]) were recruited from general intensive care units ($n = 90$) that admitted a mix of medical and surgical patients. Thirteen studies were conducted in the United States Of America (USA) (Balas et al., 2014; Barnes-Daly et al., 2017; Bounds et al., 2016; DiSabatino and Grami, 2016; Hsieh et al., 2019; Kram et al., 2015; Pun et al., 2019; Schallom et al., 2020; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018; Jacob, 2017), while one each was conducted in Korea (Lee et al., 2020), Italy (Negro et al., 2018), India (Malik et al., 2021), United Kingdom (Patel et al., 2014) and Australia (Sosnowski et al., 2018).

Of these studies, two were clinical trials (Malik et al., 2021; Sosnowski et al., 2018), one was quasi-experimental (DiSabatino and Grami, 2016), three were cohort studies (Barnes-Daly et al., 2017; Negro et al., 2018; Pun et al., 2019) and 12 were before-after studies (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Patel et al., 2014; Schallom et al., 2020; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018; Jacob, 2017). Five studies (Pun et al., 2019; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018) related to the Society of Critical Care Medicine intensive care units liberation initiative (www.iculiberation.org) with the parent study by Pun et al. (2019). The Society of Critical Care Medicine intensive care units' liberation sub-studies detail different methodology and outcome data and have been included in the review (Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018). Data reported by the parent study (Pun et al., 2019) was not duplicated in this review.

The ABCDE bundle was implemented in nine studies (Balas et al., 2014; Bounds et al., 2016; DiSabatino and Grami, 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Negro et al., 2018; Patel et al., 2014; Sosnowski et al., 2018). The ABCDEF bundle incorporating the addition of family engagement was delivered in a further nine studies (Barnes-Daly et al., 2017; Malik et al., 2021; Pun et al., 2019; Schallom et al., 2020; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018; Jacob, 2017). Usual care was reported in five studies (Balas et al., 2014; Bounds et al., 2016; Malik et al., 2021; Negro et al., 2018; Sosnowski et al., 2018) and generally comprised some, though not all, components of the bundles. In these instances, elements of the bundle were implemented at the discretion of the treating consultant or physiotherapist.

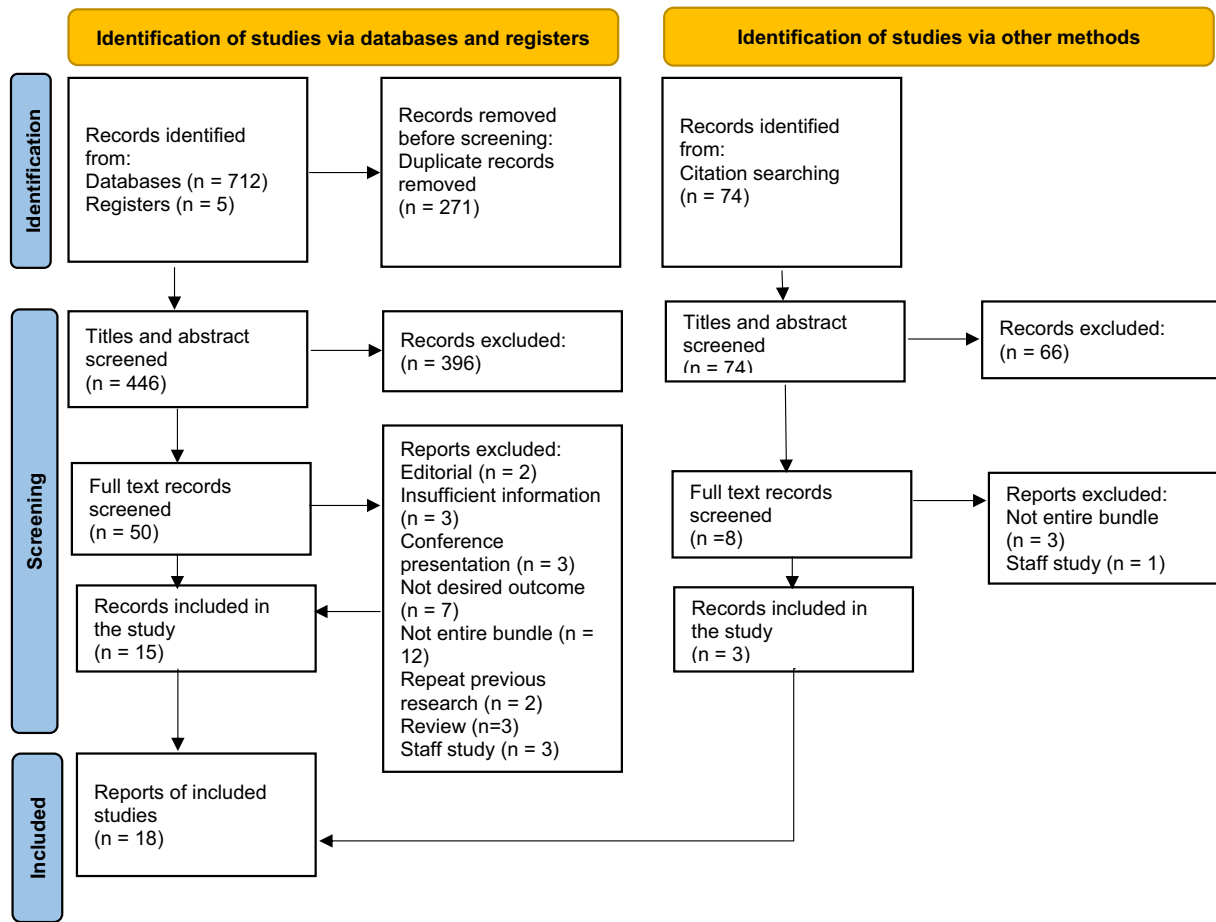


Fig. 1. Prisma 2020 Flow Diagram for the ABCDE/F bundle effect of delirium, functional outcomes, and quality of life in adult ICU patients.

3.3. Results of individual studies

Twelve studies that recruited 29,188 participants evaluated intensive care unit delirium following the implementation of the ABCDE bundle (Balas et al., 2014; Bounds et al., 2016; DiSabatino and Grami, 2016; Hsieh et al., 2019; Lee et al., 2020; Sosnowski et al., 2018) or the ABCDEF bundle (Barnes-Daly et al., 2017; Pun et al., 2019; Schallom et al., 2020; Loffink et al., 2018; Zhorne et al., 2018; Jacob, 2017). Four studies reported both the incidence and duration of delirium (Balas et al., 2014; Bounds et al., 2016; Lee et al., 2020; Loffink et al., 2018), six studies reported incidences of delirium only (Barnes-Daly et al., 2017; DiSabatino and Grami, 2016; Hsieh et al., 2019; Pun et al., 2019; Sosnowski et al., 2018; Jacob, 2017); and two studies reported the duration of delirium only (Schallom et al., 2020; Zhorne et al., 2018). Of the twelve studies, four reported delirium as the primary outcome (Barnes-Daly et al., 2017; Bounds et al., 2016; DiSabatino and Grami, 2016; Jacob, 2017). Eleven studies described screening delirium using a validated tool with eight using the Confusion Assessment Method for the intensive care unit (Balas et al., 2014; Barnes-Daly et al., 2017; DiSabatino and Grami, 2016; Hsieh et al., 2019; Lee et al., 2020; Schallom et al., 2020; Sosnowski et al., 2018; Jacob, 2017), one used the Intensive Care Delirium Screening Checklist (Bounds et al., 2016), and one multi-site study used both screening tools in different sites (Pun et al., 2019). The remaining two studies did not specify the tool (Loffink et al., 2018; Zhorne et al., 2018).

Ten of the studies described patients' physical functioning in the intensive care unit (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Negro et al., 2018; Schallom et al., 2020; Sosnowski et al., 2018; Cape et al., 2018; Zheng et al., 2016). Seven studies described the patient's ability to sit in bed, sit

out of bed, stand or walk (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Negro et al., 2018; Cape et al., 2018). Two studies reported the use of validated functional assessment tools, including the intensive care unit mobility scale (Schallom et al., 2020), the functional independence measure, and the physical function in intensive care unit test – scored (Sosnowski et al., 2018).

One study evaluated the participant's quality of life using a validated tool, the Short Form (36) Health Survey, for the assessments at baseline and 90 days post-discharge from hospital (Sosnowski et al., 2018).

3.4. Methodological quality and risk of bias within studies

Risk of bias assessments are reported in supplementary material Table 1. Three controlled studies (DiSabatino and Grami, 2016; Malik et al., 2021; Sosnowski et al., 2018) scores were reduced as the studies were exposed to bias due to the inability to blind participants, staff delivering the intervention, and some outcome assessors. Randomisation was reported in two trials (Q1) (Malik et al., 2021; Sosnowski et al., 2018). The cohort studies (Barnes-Daly et al., 2017; Negro et al., 2018; Pun et al., 2019) scored highly, meeting the Joanna Briggs Institute assessment criteria. These trials reported valid and reliable exposure measurements (Q3), identified confounders, and described strategies to deal with them (Q4, Q5), valid and reliable measurements were used to evaluate outcomes (Q7), follow up was complete (Q8, Q9), and appropriate statistical tests were used (Q11). The before-after studies (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Patel et al., 2014; Schallom et al., 2020; Cape et al., 2018; Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018; Jacob, 2017) failed to meet all assessment criteria, although components

Table 1
Characteristics of the included studies.

Author/year/country/article type	Study design and setting	Participants	Intervention	Results	Key findings
Balas et al. (2014) 2014 USA Journal Article	Before/after study Prospective cohort Setting: Tertiary medical centre (n = 1) ICU - Multi-centre: 5 general medical/surgical, 1 progressive care unit, 1 dedicated ICU for immune-compromised patients (n = 7)	n = 296 (ventilated and non-ventilated) Pre n = 146 Post n = 150 Age: Similar (not described) Severity of illness score -APACHE II: similar, not detailed Inclusion: Adult ICU Exclusion: not described	ABCDE bundle	Delirium incidence n (%): pre 91 (62.3%) vs post 73 (48.7%); p = 0.02 Delirium duration, days, median (IQR): pre 3 (1–6) vs post 2 (1–4); p = 0.52 Delirium duration pre 50% (IQR 30 to 64.3) vs. post 33.3% (IQR 18.8 to 50); p = 0.003 Odds of delirium incidence reduced after adjusting for age, severity of illness score, sex, mechanical ventilation (OR: 0.55; 95% CI, 0.33–0.93 p = 0.03) Function - mobilised during ICU admission pre 48% vs. post 66%; p = 0.002 Function - twice the odds of mobilising out of bed for the post group (95% CI, 1.30–3.45; p = 0.003)	Implementation of the ABCDE bundle resulted in reduced duration of ventilation, reduced incidence and duration of delirium, and more time out of bed. No difference in coma prevalence, coma duration, mean RASS score, ICU or hospital time to discharge or change in residence.
Barnes-Daly et al. (2017) 2017 USA Journal article	Prospective cohort study Setting: Community hospitals (n = 7) ICU - Multi-centre (n = 7)	n = 6064 (ventilated and non-ventilated) Age: (mean/SD): 63.1 (17.4) Severity of illness score - APACHE III: (mean/SD): 92.0 (26.0) Inclusion: Ventilated and non-ventilated general medical and surgical adult ICU patients. Exclusion: active alcohol or drug withdrawal; open abdomen; significant haemodynamic or respiratory instability; new coronary ischaemia; therapeutic neuromuscular blockade; intubation within the previous 6 hours without stabilisation.	ABCDEF bundle	Delirium incidence: patients experienced more days free of delirium and coma with total bundle compliance (IRR 1.02; 95% CI 1.01–1.04; p = 0.004) compared to partial bundle compliance (IRR 1.15; 95% CI 1.09–1.22; p = 0.001)	Implementation of the SCCM's PAD guidelines using the ABCDEF was successfully implemented in 7 community hospital ICUs. Higher bundle compliance was independently associated with improved survival and more days free of delirium and coma after adjusting for age, severity of illness, and presence of mechanical ventilation. Even when delivered incompletely, positive patient outcomes were evident.
Bounds et al. (2016) 2016 USA Journal article	Before/after study Retrospective cohort Setting: Rural hospital (n = 2) ICU - Multi-centre: general medical/surgical (n = 2)	n = 159 (ventilated and non-ventilated) Pre n = 80 Post n = 79 Age: (mean/SD) pre - 67.2 (14.6), post - 65.3 (15.5) Severity of illness score -Charlson Comorbidity Index: (mean/SD): Pre- 3.03 (2.48) Post - 5.88 (2.85) Inclusion: 18 years or older, ICU stay >24 h Exclusion: increased ICP > 50% from 1st ICU measure; quadriplegia; GCS < 8 without sedatives; palliative care; CPR resulting in death	ABCDE bundle	Delirium incidence: decreased in mechanically ventilated patients 38% to 23%, p = 0.01 Delirium duration decreased in all patients 3.8 days to 1.72 days; p = <0.001 Delirium duration in mechanically ventilated patients decreased 2.96 to 0.56 days, p < 0.001 Delirium free days increased 62% to 77%; p = 0.01 Function - the number of patients assisted to a sitting position, either in a chair position using the bed or sitting on the edge of the bed, increased significantly (from 1% to 10%, p = 0.01) Function - the percentage of patients assisted out of bed during their ICU stay did not change (35% before vs 33% after, p = 0.62)	Implementation of the ABCDE bundle led to significant decreases in the prevalence and duration of delirium. Length of mechanical ventilation, duration of ICU and hospital stay did not differ between groups. ABCDE bundle can be implemented by an interprofessional team in smaller ICUs.
Cape et al. (2018). 2018 USA Conference Presentation Part of the SCCM ICU Liberation Collaborative	Before/after study Prospective cohort Setting: Academic medical centre (n = 1) ICU - Medical ICU (n = 1) Part of the SCCM ICU Liberation Collaborative	n = 15–30 patients per month for 12 months (precise number not described). (ventilated and non-ventilated) Pre n = not described Post n = not described Age: not described Severity of illness score - APACHE II: similar, not detailed	ABCDE bundle	Function: Of 1273 days assessed, 250 had mobility sessions (24.4%). A subgroup of 646 days on mechanical ventilation had 40 mobility days (6.2%). Completion of a spontaneous awakening trial or spontaneous breathing trial positively	Patients were more likely to be mobilised on days when other elements of the ABCDE bundle were completed.

(continued on next page)

Table 1 (continued)

Author/year/country/article type	Study design and setting	Participants	Intervention	Results	Key findings
DiSabatino and Grami (2016) 2017 USA Journal article	Controlled interventional cohort study. Setting: Tertiary medical centre (n = 1) ICU – general medical/surgical (n = 2)	Inclusion: not described Exclusion: not described n = 447 (ventilated and non-ventilated) ICU (1) (18 bed) – Control n = 149 ICU (2) (10 bed) Intervention n = 298 Age: Control - majority aged 45–64 (n%) n = 116 (38.9) Intervention majority aged 45–64 (n%) n = 66 (44.3) Severity of illness score - not described Inclusion: Adult ICU Exclusion: not described	ABCDE bundle Called Delirium Prevention Bundle (DPB) by the authors	predicted mobility (6.1% vs 1.1%, p = 0.01 and 9.0% vs 3.4%, p = 0.01 respectively). Variables found to negatively predict mobility included receiving IV sedation (11.5% vs 31.6%, p < 0.01), IV or oral benzodiazepines (10.1% vs 24.2%, p < 0.01), mechanical ventilation (6.2% vs 33.3%, p < 0.01), coma (RASS ≤ -4) (2.5% vs 24.9%, p < 0.01), and delirium (6.9% vs 38.0%, p < 0.01). Risk of delirium: Longitudinal (repeated measures) multivariate logistic regressions indicate that patients in the intervention group experienced highly significant reductions (78%) in the relative risk for delirium (odds ratio 0.22; 95% CI 0.08–0.56; p = 0.001).	Reduction in the odds of delirium include the DPB and age less than 64 years. Use of the DPB is an effective and feasible strategy to prevent delirium in medical-surgical ICU patients. Contamination may have occurred as nurses worked across departments.
Hsieh et al. (2019) 2019 USA Journal article	Before/after study between 2 ICU groups: Partial bundle ICU – ABD Full bundle ICU - ABCDE Prospective cohort Setting: Urban university hospital (n = 1) ICU – Medical ICU (n = 2)	Partial bundle ICU n = 819 Baseline n = 267 Period 1 n = 271 Period 2 n = 281 Full Bundle ICU n = 1036 Baseline n = 356 Period 1 n = 314 Period 2 n = 366 Age: Baseline: (mean [range]) Partial bundle ICU 64 (54–74) Full bundle ICU 64 (53–75) Severity of illness score - APACHE IV: baseline: (median [IQR]) Partial bundle ICU 59 (43–76) Full bundle ICU 59 (43–77) Inclusion: all adult patients admitted for >24 h Exclusion: not described	ABCDE bundle Staged implementation of full vs partial ABCDE bundle in 2 ICUs	Delirium incidence pre 71% vs post 45% p = 0.02 Function - Full bundle ICU pre 95% patient days were spent resting in bed vs post 65% of patients stood and 54% walked at least once during their ICU stay	The addition of early mobilisation and structured coordination of ABCDE bundle components to a spontaneous breathing, awakening, and delirium management background led to substantial reductions in delirium and increased mobilisation. The results support the concept that the entire bundle is greater than its individual parts.
Jacob (2017). 2017 USA Dissertation	Before/after study Prospective cohort Setting: Community hospital (n = 1) ICU –Single centre: general medical/surgical (n = 1)	n = 301 (ventilated and non-ventilated) Pre n = 151 Post n = 150 Age: (mean/SD) Pre- 65.7 (17.4) Post – 64.8 (18.3) Severity of illness score - not described Inclusion: Adult >18 years Exclusion: No exclusions	ABCDEF bundle	Delirium incidence n (%): day -pre 77 (51%) vs post 16 (11%); p < 0.001; night - pre 89 (18%) vs post 27 (18%) p < 0.001	The ABCDEF bundle was successfully implemented into everyday ICU care. Patients who received the ABCDEF bundle had statistically significant reduction in the incidence of delirium in the day and night.
Kram et al. (2015) 2015 USA Journal article	Before/after study Retrospective cohort Setting: Rural community hospital (n = 1) ICU – Single centre: general medical/surgical (n = 1)	n = 83 (ventilated) Pre n = 47 Post n = 36 Age: Not described Severity of Illness score - not described Inclusion: All adult patients Exclusion: Not described	ABCDE bundle	Delirium incidence: 19% of patients in the post implementation group had positive delirium measure. Function: Patients received 92% of prescribed early exercises including passive range of motion (37%) and sitting or ambulation (55%).	Multidisciplinary collaboration and education using multiple educational delivery methods were essential for sustained culture change. The ABCDE bundle was successfully implemented in a rural, community-based hospital. The bundle provided a safe, cost-effective method for enhancing ICU patient outcomes. Pre-bundle delirium measure was not available, post-bundle data was compared with the literature. Pre-bundle early mobility was not measured/reported, so it is difficult to assess effectiveness.

Table 1 (continued)

Author/year/country/article type	Study design and setting	Participants	Intervention	Results	Key findings
Lee et al. (2020) 2020 Republic of Korea Journal Article	Before/after QI study Retrospective cohort Setting: Urban hospital (n = 1) ICU – Medical (n = 1)	n = 185 (ventilated and non-ventilated) Group 1 Early ABCDE bundle (n = 91) Group 2 Modified ABCDE bundle following QI (n = 94) Age: mean (SD) Group 1: 64.4 (13.9) Group 2: 64.8 (16.6) Severity of illness score - APACHE II: mean (SD) Group 1: 26.3 (7.7) Group 2: 26.6 (7.6). Inclusion: Adult, admitted for ≥48 h, 1st admission to ICU only. Exclusion: Not described	ABCDE bundle	Delirium incidence n (%) Group 1: Early ABCDE 60 (67%) vs Group 2 Modified ABCDE 71 (75.5%) p = 0.20 Delirium duration (days) – mean (SD) Group 1: 5.9 (10.8) vs Group 2: 6.1 (8.8) p = 0.89 Sedation level (RASS - alert) mean (SD) – Group 1: 1938 (58.2) vs Group 2: 2410 (72) RASS (RASS -deeply sedated) mean (SD) – Group 1: 485 (14.6) vs Group 2: 397 (11.9) Function: Early mobility (frequency (%)) Group 1: 10 (11.0) vs Group 2: 51 (54.3) p < .001	An increase in the incidence and duration of delirium was observed in the modified ABCDE bundle. Modified ABCDE bundle reduced deep sedation and improved mobility in the ICU. Percentage of calm and alert patients increased significantly in the modified group. Implementation of the bundle is complex. Multidisciplinary team that includes various medical personnel can contribute to positive outcomes for patients.
Loffink et al. (2018) 2018 USA Conference Abstract Part of the SCCM ICU Liberation Collaborative	Before/after study Retrospective and prospective cohort Setting: Urban university hospital ICU (n = 1) ICU – Medical/surgical ICU (n = 1) Part of the SCCM ICU Liberation Collaborative	n = 270 (ventilated and non-ventilated) Pre 6 months of retrospective data (Jan – June 2015) First 5 patients admitted to site per month. n = not described. Post: 14 months of prospective data (Jan 2016 – Mar 2017) First 15 patients admitted to site per month. n = not described Age: not described Severity of illness score - not described. Inclusion: All adult ICU patients Exclusion: Patients who died or were discharged from the participating ICU within 24 h of ICU admission, were undergoing active life support withdrawal, and/or “comfort care-only” within 24 h of ICU admission	ABCDEF bundle	Delirium incidence pre 23% vs post 18% Delirium duration pre 3.14 vs post 2.24 days Deep sedation incidence (RASS -4 or -5) pre 47% vs 29% Deep sedation duration (RASS -4 or -5) pre 2.2 days vs post 1.8 days	Critical care nurse practitioners were ideally positioned to lead this complex quality improvement project. No p values reported, so statistical significance cannot be inferred.
Malik et al. (2021) 2021 India Journal article	Randomised controlled trial Setting: Tertiary urban hospital (n = 1) ICU – Medical/surgical ICU (n = 1)	n = 50 (ventilated) Intervention n = 25 Control n = 25 Age mean (SD): Intervention 37.7 (15.9) Control 46.4 (18.1) Severity of illness score - APACHE II: mean (SD): Intervention 19.4 (5.9) Control 19.52 (5.0) Inclusion: Adult (over 18 years old), mechanically ventilated for ≥24 h. Exclusion: prior neurological or psychiatric disorders, poor irreversible neurological status at ICU admission, traumatic brain injury and delirium at ICU admission.	ABCDEF bundle (called “Delirium prevention protocol”)	Delirium incidence n (%): Intervention 9 (36) vs Control 14 (56) p = 0.156 Delirium duration (mean ± SD): Intervention 1.92 ± 3.0 vs Control 3.88 ± 6.3 p = 0.219	This study recruited mechanically ventilated, severely ill patients. An independent physician performed delirium assessment. Strict adherence to the bundle of cares was achieved. The incidence and duration of delirium were reduced, though results were not significant.
Negro et al. (2018) 2018 Italy Journal Article	Prospective cohort study Setting: Teaching hospital (n = 1) ICU - Mixed medical/surgical (n = 1)	n = 482 (ventilated and non-ventilated). Non mobilised patients (n = 388). Mobilised patients (n = 94) Age: mean 79.5 years Severity of illness score -SAPS II: mean 31.33. SOFA mean 5.25 Inclusion: Adult ICU Exclusion: Dying patients, patients discharged in the next hours	ABCDE bundle	Functional outcomes: 94 patients (19.5%) of the entire cohort were mobilised 34 (7%) ventilated patients were mobilised No patients were mobilised with non-invasive ventilation 16 (3.3%) patients were mobilised on vasopressors	Non- mobilised patients were on average admitted with a surgical diagnosis, had shorter length of stay, and lower severity of illness scores. Average staffing requirement was 2 staff. The results may be generalisable to other ICUs that lack dedicated physiotherapy service.
Patel et al. (2014) 2014 UK Journal Article	Before/after study Prospective cohort Setting: Tertiary medical centre (n = 1) ICU – Mixed medical/surgical (n = 1)	n = 338 (ventilation status not described) Pre n = 167 Post n = 171 Age: (mean/SD) pre – 60.0 (13.7), post – 60.6 (16.3) Severity of illness score -APACHE II: (mean/SD): Pre- 15.0 (7.6) Post – 14.2 (6.6) Inclusion: 18 years or older, ICU	ABCDE bundle (called “Multi -component bundle of interventions”)	Delirium incidence n (%): pre 55 (33) vs post 24 (14%) p < 0.001 Delirium duration (days): pre (3.4 (1.4) days vs post 1.2 (0.9) days, p = 0.021) Patient reporting high sleep efficiency index scores demonstrated a significantly	The introduction of a multicomponent MDT bundle of interventions was effective in reducing sleep deprivation and delirium. Patients reporting high sleep efficiency index scores demonstrated a significantly reduced risk of delirium

(continued on next page)

Table 1 (continued)

Author/year/country/article type	Study design and setting	Participants	Intervention	Results	Key findings
Pun et al. (2019) 2019 USA Journal article	Before/after study Retrospective before and prospective after cohort Setting: Academic, community and federal ICUs throughout the USA and Puerto Rico ICU – Multi-centre (n = 68) SCCM ICU Liberation Collaborative	stay > one night Exclusion: Pre-existing history of sleep pathology, severe visual or hearing impairment, alcohol addiction or illicit drug abuse, history of cognitive dysfunction, previously discharged from the ICU in this hospital admission, neurosurgical patients, developed delirium at any point during the study, received sedative medications within 24 h of consent. n = 15,226 (mechanically ventilated (n = 8089 (54%) and non-mechanically ventilated patients (n = 7137 (46%)) Pre: 6 months of retrospective data (Jan – June 2015) First 5 patients admitted to each site per month. Post: 14 months of prospective data (Jan 2016 – Mar 2017) First 15 patients admitted to each site per month. Age: Majority of patients were aged 50–79 (n = 9874 (66%)) Severity of illness score - not described Inclusion: Adult ICU patients Exclusion: Patients who died or were discharged from the participating ICU within 24 h of ICU admission, active life support withdrawal and/or "comfort care-only" within 24 h of ICU admission	ABCDEF bundle	reduced risk of delirium (OR 0.90, 95% CI 0.84–0.97). Compliance with the interventions was >90% Complete ABCDEF bundle performance was associated with lower likelihood of seven outcomes: delirium (AOR 0.60; CI 0.49–0.72), There was a consistent dose–response relationship between higher proportional bundle performance and improvements in each of the above-mentioned clinical outcomes (all p < 0.002)	The performance of the ABCDEF bundle results in significant and dose-related improvements in survival, duration of mechanical ventilation, brain organ dysfunction (i.e., delirium and coma), physical restraint use, ICU readmission rates, and discharge disposition of ICU survivors. Data was collected for 7 days and there was no ICU follow-up.
Schallom et al. (2020) 2020 USA Journal article	Before/after study Retrospective cohort Setting: Tertiary medical centre (n = 1) ICU –Surgical, trauma, burn, cardiothoracic, cardiac, neurosurgical, medical (n = 7)	n = 4625 (ventilation status: not described) Phase 1 Pre n = 1266 Post n = 1420. Phase 2 Pre n = 258 Post n = 1681 Age: not described Severity of illness score: not described Inclusion: not described Exclusion: not described	Adding the E component to an established ABCDF protocol	Delirium duration pre - 1.65 (3.68) vs post 1.37 (3.47) (p = not significant) Mobility level (Level 1 –passive range of motion, Level 2 – sitting, Level 3 – standing, Level 4 – walking) (mean (SD) pre 1.45 (1.03) vs post 1.64 (1.03) (p < 0.001). ICU Mobility Scale scores (mean (SD) at ICU discharge pre 6.4 (2.5) vs post 6.8 (2.3) (p = 0.04); at hospital discharge pre 7.2 (2.5) vs post 7.3 (2.3) (p = not significant). ICU LOS mean (SD) pre 7.8 (7.3) days vs post 6.8 (5.9) days (p = 0.03).	Implementing early mobility protocol in an ICU with embedded ABCDEF components can increase mobility levels, decrease incidence and duration of delirium, and length of stay. Interdisciplinary approach is vital for successful implementation of the bundle. Retrospective review of medical records increased risk of missing data. Intervention fidelity was not reported.
Sosnowski et al. (2018) 2018 Australia Journal article	RCT feasibility study Prospective cohort Setting: Metropolitan hospital (n = 1) ICU – Single centre (n = 1) Mixed medical/surgical ICU	n = 30 (ventilated) Intervention n = 30 Control n = 30 Age mean (SD): Intervention 54.9 (15.9) Control 60.6 (11.0) Severity of illness score - APACHE II: mean (SD): Intervention 14.9 (5.9) Control 13.7 (5.0) Inclusion: Adult (over 18 years old), invasively ventilated for 48 h and expected to require ventilation for a further 24 h. Exclusion: inability to mobilise 3 m before the current ICU illness; were diagnosed with neuromuscular disease that could impair ventilator weaning; had suffered an acute	ABCDE bundle	Delirium incidence: 100% of patients in both groups suffered delirium at a mean of 36.9% of ventilated days. Function: FIM at ICU discharge mean (SD)– Intervention 46.7 (16.8) vs Control 44.6 (20.2). FIM at hospital discharge mean (SD)– Intervention 95.8 (29.6) vs Control 95.2 (24.7). PFFT at ICU discharge mean (SD)– Intervention 7.0 (1.1) vs Control 6.15 (1.2). SF-36 PCS at baseline mean (SD)– Intervention 32.7 vs (11.1) Control 41.6 (11.4). SF-36 PCS at 90-day follow-up mean (SD)– Intervention vs 43.8 (12.0) Control 37.9 (10.7).	ABCDE bundle can be reliably implemented in an Australian ICU with good intervention fidelity. Small single site study may limit generalisability of results.

Table 1 (continued)

Author/year/country/article type	Study design and setting	Participants	Intervention	Results	Key findings
Zheng et al. (2016) 2016 USA Conference abstract Part of the SCCM ICU Liberation Collaborative	Before/after study Prospective cohort Setting: Urban university hospital (n = 1) ICU –Medical (n = 1) Part of the 20-month SCCM ICU Liberation Collaborative	stroke; were not for active resuscitation; had been readmitted to ICU within the current hospitalisation; or were not expected to survive the current ICU admission n = 88 (ventilation status: not described) Pre n = 25 Post n = 63 The first 15–20 patients admitted per month from Jan – May 2016. Age: Similar -not described Severity of illness score - not described Inclusion: First 5 adult ICU patients admitted each month from Jan – Jun 2015 were included in the pre group. The first 15–20 adult ICU patients admitted per month from Jan – May 2016 were included in the post implementation group. Exclusion: Patients were excluded if they died during the ICU admission.	ABCDEF bundle	SF-36 MCS at baseline mean (SD)– Intervention 45 (14.4) vs Control 41.8 (14.1). SF-36 MCS at 90-day follow-up mean (SD)– Intervention 47.4 (16.0) vs Control 40.3 (15.9). Barriers to E component – Haemodynamic/respiratory instability (21.6%), sleeping (18.9%), procedures (16.2%), dialysis (8.1%), agitation delirium (5.4%), other (2.7%) Function: Patients without mobility restrictions at discharge: pre 52.5% vs post 93.5% (p < 0.0001). Discharge destination: Discharged to a long-term acute care hospital or skilled nursing facility: pre 20% vs post 3.2% (p = 0.018)	Implementing the ABCDEF bundle with an inter-professional healthcare team during teaching rounds consistently reinforced early mobility and significantly improved the functional status of patients at discharge.
Zhorne et al. (2018) 2018 USA Conference abstract	Before/after study Prospective and retrospective cohort Setting: Urban community hospital (n = 1) ICU - not described Part of the 20-month SCCM ICU Liberation Collaborative	n = 300 (ventilated and non-ventilated patients) Pre: n = not described Post n = not described Age: not described Severity of illness score - not described Inclusion: First 15 adult ICU patients admitted each month from August 2015 – March 2017 Exclusion: not described	ABCDEF bundle	Delirium duration: 75% of patients with delirium experienced two or fewer days compared to the before group.	The implementation of the ABCDEF bundle in a large community hospital resulted in fewer comatose days, fewer days of delirium, and improved hospital survival.

APACHE – Acute Physiology and Chronic Health Evaluation; CPR- Cardi-pulmonary resuscitation; DPB – Delirium Prevention Protocol; FIM – Functional Independence Measure; GCS- Glasgow Coma Scale; ICP- Intracranial pressure; ICU- Intensive Care Unit; LOS – Length of stay; MDT- Multidisciplinary team; PAD- Pain, Agitation, Delirium; PFIIT- The Physical Function in ICU Test; QI-Quality Improvement; RASS – Richmond Agitation Sedation Scale; SCCM – Society of Critical Care Medicine; SF-36 MCS – Short Form 36 Health Survey Mental Component Summary; SF-36 PCS – Short Form 36 Health Survey Physical Component Summary; USA – United States of America.

were completed, thus providing important preliminary evidence for the effectiveness of the ABCDE/F bundle. Participant groups differed in two studies with higher severity of illness scores in the after-group scores (Q2) (Bounds et al., 2016; Hsieh et al., 2019), one study did not assess delirium in the before-group and the after group was compared to literature (Q7) (Kram et al., 2015), two studies failed to discuss whether outcomes were measured using the same method between groups or measured reliably (Q7, Q8) (Loffink et al., 2018; Zheng et al., 2016; Zhorne et al., 2018). Statistical analysis was not reported in two studies (Loffink et al., 2018; Zhorne et al., 2018).

3.5. Incidence and duration of delirium

3.5.1. Incidence of delirium

Six before–after studies (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Lee et al., 2020; Patel et al., 2014; Jacob, 2017) with 2000 participants provided sufficient information to perform a meta-analysis using a random-effects model. When compared with standard practice, the ABCDEF bundle interventions resulted in statistically

significant reduced risk of intensive care unit delirium (Risk Ratio = 0.57; CI, 0.36–0.90; p = 0.02). Although there was considerable heterogeneity between studies ($I^2 = 92\%$), most studies reported reduced delirium incidence following implementation of the ABCDEF bundle (Fig. 2). Using the Grading of Recommendations, Assessment, Development and Evaluation approach, the certainty of the evidence was assessed as low and was downgraded for inconsistency (supplementary material Table 2).

One study not included in the pooled results reported longitudinal multivariate logistic regressions, which indicated that patients in the intervention group experienced statistically significant reductions (78%) in the relative risk for delirium (odds ratio, 0.22; 95% CI, 0.08–0.56; P = 0.001) (DiSabatino and Grami, 2016). Pun et al. (2019) reported that complete ABCDEF bundle performance was associated with lower likelihood of delirium (adjusted odds ratio (AOR) 0.60; CI, 0.49–0.72). Trial participants received a positive Confusion Assessment Method for the intensive care unit assessment on 39.6% of mechanically ventilated days in a feasibility randomised controlled trials (Sosnowski et al., 2018).

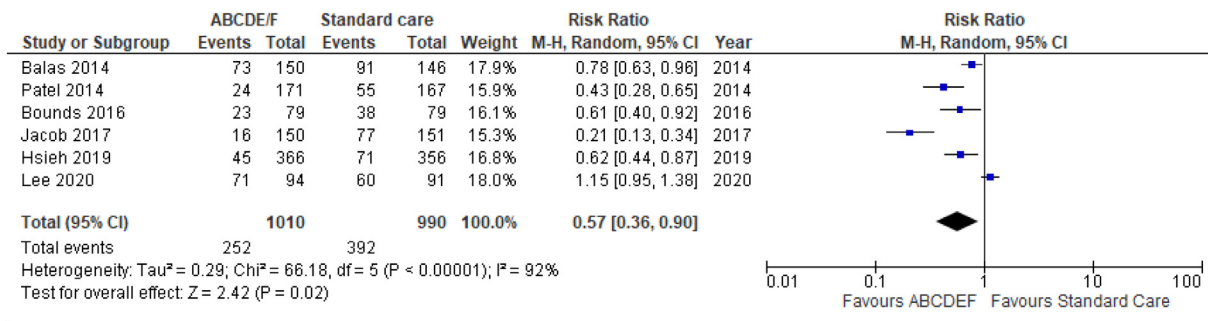


Fig. 2. Delirium incidence: Forest plot comparison ABCDEF versus standard care.

3.5.2. Duration of delirium

Four studies (Bounds et al., 2016; Lee et al., 2020; Patel et al., 2014; Schallom et al., 2020) and one randomised controlled trial (Malik et al., 2021) with 3418 participants provided sufficient information to perform a meta-analysis using a random-effects model. When compared with standard practice, the ABCDEF bundle intervention resulted in statistically significant reduction in the duration of intensive care unit delirium (mean difference (days) - 1.37, 95% CI -2.61 to -0.13 p = 0.03; I² 96%). Although there was considerable heterogeneity between studies (I² = 91%); most studies reported reduced delirium incidence following implementation of the ABCDEF bundle. One study that demonstrated an increased duration of delirium compared an early ABCDEF bundle (before) with a modified ABCDEF bundle (after) (Lee et al., 2020) (See Fig. 3). Using the Grading of Recommendations, Assessment, Development and Evaluation approach, the quality of the evidence was assessed as low and was downgraded for inconsistency (See supplementary material Table 2).

One study (Loffink et al., 2018) did not report statistical significance and was not included in the pooled results. This study showed decreased duration of delirium of 3.14 days to 2.24 days. Delirium was reduced by one day in the post-implementation period, and the percent of intensive care unit days delirious decreased by 17% in one study (pre 50% [IQR 30 to 64.3] versus post 33.3% [IQR 18.8 to 50]; (p = 0.003)) (Balas et al., 2014). Barnes-Daly et al. (2017) reported that a 10% increase in total bundle compliance resulted in a 2% increase in delirium free days and coma-free days (IRR, 1.02; 95% CI, 1.01-1.04; p = 0.004).

3.6. Sensitivity analysis

The impact of each individual study on the overall results in the meta-analysis was assessed by removing a study from the analysis one at a time. Considerable heterogeneity between studies of delirium incidence was heavily influenced by one study (Schallom et al., 2020), although re-analysis following removal of the study did not change the overall result. No single study was found to influence the pooled results of the statistically significant duration of delirium.

3.7. Functional outcomes

Ten studies described participants' physical function during their intensive care unit admission (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Negro et al., 2018; Schallom et al., 2020; Sosnowski et al., 2018; Cape et al., 2018; Zheng et al., 2016). Mobility milestones including sitting on the side of the bed, standing beside the bed, or walking were significantly improved in the intervention group compared to standard care in four before after studies (Balas et al., 2014; Bounds et al., 2016; Hsieh et al., 2019; Schallom et al., 2020) and one randomised controlled trial (Sosnowski et al., 2018) Although Bounds et al. (2016) increased sitting position in or on the side of the bed (from pre 1% vs. post 10%, p = 0.01), they found that the number of patients assisted out of bed during their intensive care unit stay did not change (pre 35% vs. post 33%, p = 0.62). Hsieh et al. (2019) reported that participants spent 95% of their admission days resting in bed pre-bundle implementation versus post-implementation, where 65% of patients stood, and 54% walked at least once during their intensive care unit stay. Two groups of authors reported the use of validated tools to assess function (Schallom et al., 2020; Sosnowski et al., 2018). One study (Sosnowski et al., 2018) provided comparisons using the Functional Independence Measure at both intensive care unit discharge (mean [SD] intervention 46.7 [16.8] vs. control 44.6 [20.2]) and hospital discharge (mean [SD] Intervention 95.8 [29.6] vs. control 95.2 [24.7]). They measured the Physical Function in intensive care unit test at intensive care unit discharge (mean [SD] intervention 7.0 [1.1] vs. control 6.15 [1.2]). Higher scores indicated a higher level of physical function, although statistical significance was not reported in this feasibility study. Another pre and post-study reported that the intensive care unit mobility scale scores resulted in statistically significant increase from the initial evaluation of 4.4 (2.8) to 5.0 (2.8) (p = 0.01) and at intensive care unit discharge of 6.4 (2.5) to 6.8 (2.3) (p = 0.04) (Schallom et al., 2020). Zheng et al. (2016) reported more patients discharged without mobility restrictions in the ABCDEF bundle group compared to the pre-ABCDEF bundle group (93.5% vs. 52.5%, p < 0.0001). However, the nature of these restrictions was not identified in the article.

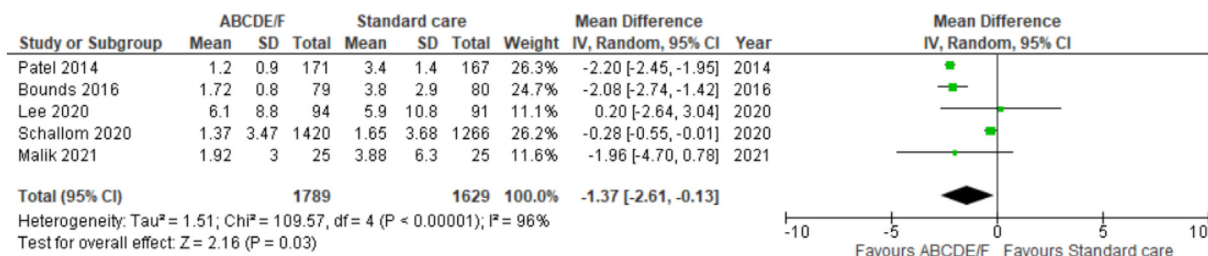


Fig. 3. Delirium duration: Forest plot comparison ABCDEF versus standard care.

3.8. Health related quality of life

Only one study reported health related quality of life outcomes using a validated tool (Sosnowski et al., 2018). Improved scores at 90 days after hospital discharge using the Short Form 36 Health Survey version 2™ were reported, which provided a baseline and post-discharge measure of participants' health-related quality of life (Sosnowski et al., 2018). Improved physical and mental components following discharge from hospital were noted in the group that received the ABCDE bundle. However, statistical analysis was not reported in this feasibility study, thus making it difficult to assess patient benefit.

3.9. Barriers and facilitators

Facilitators and barriers that influenced successful ABCDEF bundle adoption were identified within the included studies and are outlined in Table 2. As the reviewed study's primary focus was patient outcomes, most articles described facilitators and barriers informally within the methods or discussion sections. Detail was not provided regarding how the information was attained except for one study where nursing staff provided reasons for not completing components of the bundle on a case report form (Sosnowski et al., 2018).

4. Discussion

Eighteen studies that evaluated delirium, physical function, and health-related quality of life of 29,576 adult intensive care unit patients from 102 intensive care units who had received the ABCDE/F bundle in its entirety were synthesised in this review. Study outcome measures were highly variable, so not all data could be pooled. Combining data from eight studies demonstrated that implementing the ABCDE/F bundle resulted in statistically significant reduction of the incidence and/or the duration of delirium in adult intensive care unit patients. However, these results should be interpreted cautiously, as there was considerable heterogeneity among the studies suggesting variability in the potential benefit of the intervention, and the certainty of the evidence was assessed as low. Such variability suggests that the magnitude of the potential benefit for the ABCDE/F bundle implementation may vary depending on the quality of each intervention, patient specific factors, and the specific clinical setting. Nonetheless, the current evidence suggests a likely benefit for patients following the implementation of the ABCDE/F bundle in its entirety.

In this review, delirium incidence before bundle implementation was reported in 38% (Bounds et al., 2016) to 71% (Hsieh et al., 2019) of the participants, consistent with reported delirium incidence in mechanically ventilated patients (Zhang et al., 2021; Arumugam et al.,

Table 2
Facilitators and barriers to bundle implementation.

Facilitators	Description
Patient related facilitators	Family engagement and involvement (Sosnowski et al., 2018)
Clinician related facilitators	Collaboration between members of the interdisciplinary team (Balas et al., 2014; Barnes-Daly et al., 2017; Bounds et al., 2016; Hsieh et al., 2019; Kram et al., 2015; Lee et al., 2020; Patel et al., 2014; Pun et al., 2019; Schallom et al., 2020; Sosnowski et al., 2018; Loffink et al., 2018; Zheng et al., 2016) Expertise within the interdisciplinary team (Kram et al., 2015) Dedicated ABCDEF interdisciplinary team to champion bundle compliance (Barnes-Daly et al., 2017; Pun et al., 2019) Unit champions to support education, serve as a resource, and assist to overcome barriers (Patel et al., 2014) Simulation training and skill development (Sosnowski et al., 2018) Multimodal interdisciplinary education, practice to embed skill and knowledge, collaboration, and shared decision making (Barnes-Daly et al., 2017; Bounds et al., 2016; Kram et al., 2015; Patel et al., 2014; Sosnowski et al., 2018; Jacob, 2017)
Protocol related facilitators	Discussion of the bundle during interdisciplinary teaching round (Barnes-Daly et al., 2017; Bounds et al., 2016; Patel et al., 2014; Loffink et al., 2018; Zheng et al., 2016) Nurse led implementation (Negro et al., 2018; Loffink et al., 2018) Physician led implementation (Malik et al., 2021) Early introduction of the E component (within 24 h of admission) (Hsieh et al., 2019) Adjusting existing policies and procedures (Kram et al., 2015) Focus on non-pharmacological management of delirium (Bounds et al., 2016; Patel et al., 2014) Interdisciplinary mobility protocol with prescribed roles and responsibilities (Hsieh et al., 2019)
Intensive care unit facilitators	Encouraging bed-side nurses to engage in the multidisciplinary round (Loffink et al., 2018) Dedicated rehabilitation staff (Barnes-Daly et al., 2017) Mobilisation was more likely to occur when other components of the bundle were performed (Schallom et al., 2020; Cape et al., 2018) Organisational support from key stakeholders (Kram et al., 2015) Organisational support to change existing policies and procedures (Kram et al., 2015) Clinical information system (Sosnowski et al., 2018) Dedicated physiotherapist to foster collaboration and improve outcomes (Negro et al., 2018; Schallom et al., 2020)
Barriers	Description
Patient related barriers	Medical issues including haemodynamic or respiratory instability (Lee et al., 2020; Schallom et al., 2020; Sosnowski et al., 2018) Procedure or tests (Schallom et al., 2020; Sosnowski et al., 2018) Patient fatigue or patient sleeping (Schallom et al., 2020; Sosnowski et al., 2018) Agitation or delirium (Sosnowski et al., 2018; Cape et al., 2018) Deep sedation (Cape et al., 2018) (Sosnowski et al., 2018; Cape et al., 2018) Patient refusal (Schallom et al., 2020) Lack of glasses, hearing aids (DiSabatino and Grami, 2016) Patient receiving dialysis (Sosnowski et al., 2018)
Clinician related barriers	Lack of knowledge (Lee et al., 2020) Staff communication issues (Lee et al., 2020) Negative attitude (Lee et al., 2020)
Intensive care unit related barriers	Lack of equipment (DiSabatino and Grami, 2016; Schallom et al., 2020) Nurse staffing resource issues (Lee et al., 2020; Negro et al., 2018; Schallom et al., 2020) Lack of dedicated physiotherapist and team for mobilisation (DiSabatino and Grami, 2016; Negro et al., 2018; Schallom et al., 2020) Lack of allied health team (Balas et al., 2014; DiSabatino and Grami, 2016; Negro et al., 2018; Schallom et al., 2020) Light and noise (DiSabatino and Grami, 2016) Limited time (Lee et al., 2020)

2017). In a recent meta-analysis of studies that implemented at least three components of the ABCDEF bundle, the authors reported no statistically significant difference in reducing the prevalence and duration of intensive care unit delirium (Zhang et al., 2021). However, on closer inspection, delirium was reduced by 40% in the one reviewed study that implemented the bundle in its entirety (Mikkelsen and Devlin, 2021). Our review also supported this result where entire bundle implementation resulted in delirium reduction between 13.6% (Balas et al., 2014) and 40% (Jacob, 2017). Compliance with the care bundle is an important consideration when assessing patient outcomes. A “bundle of care” comprises a set of interventions that should be performed collectively to improve the effectiveness and quality of patient care (Clarkson, 2013). Full implementation of bundles has been reported as rare (Lavallée et al., 2017), yet positive patient outcomes have been noted when compliance is high (Hakko et al., 2015). Future research of the effect of the ABCDEF bundle on delirium would benefit from well-designed randomised controlled trials that optimise fidelity and adherence of all components.

Throughout the review, it was evident that collaboration and shared decision-making among a dedicated interdisciplinary team improved the adherence to the bundle in its entirety and was considered a key component contributing to improved patient outcomes (Barnes-Daly et al., 2017; Hsieh et al., 2019; Sosnowski et al., 2018). Success was further enhanced by incorporating discussion of the bundle into the interdisciplinary round (Hsieh et al., 2019; Zheng et al., 2016; Jacob, 2017). This reinforced the importance of adherence to the ABCDEF bundle for each patient every day. Although more challenging, studies in our review demonstrated that smaller, less-resourced units could successfully implement this complex intervention (Bounds et al., 2016; DiSabatino and Grami, 2016; Kram et al., 2015; Lee et al., 2020; Sosnowski et al., 2018; Loffink et al., 2018; Zheng et al., 2016). In this case, nurse leadership was essential for success (DiSabatino and Grami, 2016; Kram et al., 2015; Loffink et al., 2018). Deeper exploration of the methods used by smaller and less-resourced units to implement complex interventions like the ABCDEF bundle would benefit the wider intensive care unit community.

In some reviewed studies, ABCDEF bundle adherence was hampered by a lack of allied health support staff (Balas et al., 2014; DiSabatino and Grami, 2016; Negro et al., 2018; Schallom et al., 2020). In Australia, physiotherapy and occupational therapy are generally established roles within intensive care unit teams. Despite this, a multi-centre study in Australia and New Zealand intensive care units with dedicated physiotherapy services found early mobilisation and exercise of ventilated patients was uncommon (The, 2015). More than 50% of the cohort had developed intensive care unit acquired weakness which was associated with an increased risk of mortality between intensive care unit discharge and day 90 post-intensive care unit discharge (The, 2015). These outcomes may relate to business hours physiotherapy and allied health services. The ABCDEF bundle's successful implementation relies on more than office-hours interventions. Interdisciplinary team collaboration and planning ensure that the bundle can continue during the hours when the allied health team is absent. One reviewed study showed that it was safe and feasible for intensive care unit nursing staff to continue ABCDEF bundle implementation, including exercise regimes out of office hours (Sosnowski et al., 2018). Future studies should examine the impact of the ABCDEF bundle delivered consistently regardless of the day of the week or the time of day.

The consequence of cognitive, physical and functional impairment associated with an intensive care unit admission can be devastating for the patient, and the effects may last well after discharge from hospital (Herridge et al., 2011). The loss of independence related to a critical illness may dramatically affect the patient's return to pre-admission functional status and, therefore, post-admission quality of life. Of the 18 reviewed studies, only the randomised controlled trial's feasibility study provided post-hospital discharge quality of life assessments (Sosnowski et al., 2018). A recent systematic review of randomised

controlled trials outcome measures (Gaudry et al., 2017) found that merely 10% of 112 studies performed in intensive care units assessed at least one non-mortality patient-important outcome following discharge. Patient-important outcomes are defined as characteristics that reflect how a patient feels, functions, or survives (Pino et al., 2012) and summarise how an event, critical illness, for example, has impacted the patient's life. Although Guyatt et al. (2004) suggest that it may be more important to recommend an intervention when it results in improvements to patient-important outcomes rather than producing a clinically relevant effect, a mix of clinical importance and patient-centric outcomes would benefit both intensive care unit clinicians and the intensive care unit survivor. This idea places the patient at the centre of their care and highlights the importance of their values and preferences.

Longitudinal studies to examine the impact of the bundle on long-term cognition, mental health, and physical function are limited (Mikkelsen and Devlin, 2021). The reported physiological endpoints within the reviewed intensive care unit literature fail to link improvements in the primary outcome with quality of life after discharge from the intensive care unit. Patient-reported outcome measures provide insight into the impact of interventions on the patient. There is increasing support for patient-reported outcome measures in measuring the effectiveness of healthcare and guiding improvement in health service delivery (Kingsley and Patel, 2017). However, evidence of measurement of patient-reported outcome measures in intensive care unit survivors is limited (Robinson et al., 2017). Therefore, this would be an important area to consider in future research of the ABCDEF bundle. Since research of the ABCDEF bundle has been chiefly confined to short-term clinical outcomes, it would seem a logical progression to investigate if benefits are realised following discharge from hospital.

United States researchers have primarily led implementation research on the ABCDEF bundle, with 13 of the 18 reviewed studies conducted in various intensive care units within the United States. However, there is variability in intensive care unit staff to patient ratio internationally (Bakhru et al., 2016). In intensive care units in the United States, nurse-patient ratios are generally 1:2 (Bakhru et al., 2016); in contrast, Australia (ACCCN, 2016) and the United Kingdom advocate a 1:1 nurse-patient ratio for mechanically ventilated patients. This differs from the French model, where a 1:3 nurse-patient ratio is the norm (Bakhru et al., 2016). Allied health support in intensive care units varies internationally, with respiratory therapists managing oxygenation and ventilation in Canada and the US (Parker et al., 2013; West et al., 2016). In contrast, physicians, physiotherapists, and registered nurses perform this role in many other parts of the world, including Australia. Dedicated physiotherapists are available in 34% of United States units (Bakhru et al., 2016), whereas it is often a standard service delivered in many other parts of the world. These differences may impact routine intensive care unit patient care and the use of the bundle and may alter patient outcomes. Further examination of outcomes related to the ABCDEF bundle in intensive care units outside of the United States will provide a global perspective and add to the generalisability of the intervention.

Staff resources, patient population, ward culture within intensive care units, and workload have been described as significant barriers to successful patient rehabilitation (Lin et al., 2020; Sosnowski et al., 2015) and positive patient outcomes (Neuraz et al., 2015). Translating new treatment and knowledge and embedding these into clinical practice can be challenging. The gap between research evidence and embedded clinical practice is problematic, particularly in complex interventions like the ABCDEF bundle. Although qualitative methods are ideal for understanding processes required to embed complex interventions into real-world settings, they were not evident in this review. Formal measures of staff satisfaction and engagement were not reported in any studies. However, several studies described barriers to the implementation of the bundle. The review highlighted challenges consistent with other systematic reviews and studies (Balas et al., 2013; Costa et al., 2017), which identified four classes of barriers and facilitators (1) patient-related factors; (2) clinician-related factors; (3) protocol associated factors; and

(4) intensive care unit contextual factors. The experience and knowledge of staff involved in embedding complex interventions in diverse settings warrants further exploration. Process evaluations as described within the Medical Research Council framework for developing and evaluating complex interventions (Craig et al., 2008) provide additional understanding of the effect of interventions in various contexts and potential confounders related to organisational or professional performance.

5. Limitations

Our systematic review has several limitations. Although these results are promising, limitations of the mostly before-after designs of the reviewed studies and the associated threats to internal validity should be considered.

Including experimental, quasi-experimental, and observational studies meant that differences in study design existed and variable eligibility criteria limiting our ability to draw reliable conclusions. Many reviewed studies were single-centre and recruited participants such as mechanically ventilated and non-ventilated patients or patients with lower severity of illness scores. Standard care was not often reported limiting the generalisability of the outcomes. Many sources of bias occurred within the included studies related to patient selection and appropriate blinding methods. Conference abstracts were included in the review. To meet our selection criteria, the abstracts needed to provide sufficient information to appraise the design, methods, risk of bias, outcomes, and results of the studies. However, the dependability of results in the abstracts may be uncertain as they may not have been peer-reviewed. Finally, heterogeneity existed related to the types of outcomes assessed, which limited the possibility of performing an extensive meta-analysis. Publications were only in English which may have limited the inclusion of important studies from relevant non-English speaking countries.

6. Conclusion

The current body of evidence measuring the effect of the ABCDEF bundle in the intensive care unit patients is small. However, positive patient outcomes including reduced incidence and duration of delirium have been demonstrated in the available research. The ABCDEF bundle differs from other evidence-based, multicomponent intensive care unit interventions as it applies to every intensive care unit patient every day, regardless of mechanical ventilation status or admitting diagnosis. Although limited and of varying quality, a growing body of research supports implementing the ABCDEF bundle in its entirety for both ventilated and non-ventilated intensive care unit patients. There is a paucity of high-quality research evidence relating to the ABCDEF bundle. High quality randomised controlled trials are required to formally determine the relationship between the ABCDEF bundle and delirium outcomes in real-world intensive care units.

Funding

No external funding.

CRediT authorship contribution statement

Kellie Sosnowski: Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Frances Lin:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing, Supervision. **Wendy Chaboyer:** Formal analysis, Writing - original draft, Writing - review & editing, Supervision. **Kristen Ranse:** Writing - original draft, Writing - review & editing, Supervision. **Aaron Heffernan:** Formal analysis, Writing - original draft, Writing - review & editing, Supervision. **Marion Mitchell:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing, Supervision.

Declaration of Competing Interest

Conflicts of interest: none.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijnurstu.2022.104410>.

References

- ACCCN, 2016. Workforce Standards for Intensive Care Nursing.
- Arumugam, S., El-Menyar, A., Al-Hassani, A., Strandvik, G., Asim, M., Mekkodithal, A., Mudali, I., Al-Thani, H., 2017. Delirium in the intensive care unit. *J. Emerg. Trauma Shock* 10 (1), 37–46.
- Bakhr, R.N., McWilliams, D.J., Wiebe, D.J., Spuhler, V.J., Schweickert, W.D., 2016. Intensive care unit structure variation and implications for early mobilization practices. An international survey. *Ann. Am. Thorac. Soc.* 13 (9), 1527–1537.
- Balas, M.C., Burke, W.J., Gannon, D., Cohen, M.Z., Colburn, L., Bevil, C., Franz, D., Olsen, K.M., Ely, E.W., Vasilevskis, E.E., 2013. Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into everyday care: opportunities, challenges, and lessons learned for implementing the ICU pain, agitation, and delirium guidelines. *Crit. Care Med.* 41 (9 Suppl 1), S116–S127.
- Balas, M.C., Vasilevskis, E.E., Olsen, K.M., Schmid, K.K., Shostrom, V., Cohen, M.Z., Peitz, G., Gannon, D.E., Sisson, J., Sullivan, J., et al., 2014. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit. Care Med.* 42 (5), 1024–1036.
- Barnes-Daly, M.A., Phillips, G., Ely, E.W., 2017. Improving hospital survival and reducing brain dysfunction at seven California community hospitals: implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. *Crit. Care Med.* 45 (2), 171–178.
- Barr, J., Fraser, G.L., Puntillo, K., Ely, E.W., Gelinas, C., Dasta, J.F., Davidson, J.E., Devlin, J.W., Kress, J.P., Joffe, A.M., et al., 2013. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit. Care Med.* 41 (1), 263–306.
- Bounds, M., Kram, S., Speroni, K.G., Brice, K., Luschinski, M.A., Harte, S., Daniel, M.G., 2016. Effect of ABCDE bundle implementation on prevalence of delirium in intensive care unit patients. *Am. J. Crit. Care* 25 (6), 535–544.
- Cape, K., Elefritz, J., Ryder, L., Doepker, B., Weber, M., Carey, C., Exline, M., Byrd, C., 2018. ABCDEF bundle improves mobility in the medical intensive care unit. *Crit. Care Med.* 46 (1).
- Clarkson, D.M., 2013. The role of 'care bundles' in healthcare. *Br. J. Healthc. Manag.* 19 (2), 63–68.
- Costa, D.K., White, M.R., Ginier, E., Manojlovich, M., Govindan, S., Iwashyna, T.J., Sales, A.E., 2017. Identifying barriers to delivering the awakening and breathing coordination, delirium, and early exercise/mobility bundle to minimize adverse outcomes for mechanically ventilated patients: a systematic review. *Chest* 152 (2), 304–311.
- Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., Petticrew, M., 2008. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 337, a1655.
- Devlin, J.W., Skrobik, Y., Gelinas, C., Needham, D.M., Slooter, A.J.C., Pandharipande, P.P., Watson, P.L., Weinhouse, G.L., Nunnally, M.E., Rochweg, B., et al., 2018. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit. Care Med.* 46 (9), e825–e873.
- DiSabatino, Smith C., Grami, P., 2016. Feasibility and effectiveness of a delirium prevention bundle in critically ill patients. *Am. J. Crit. Care* 26 (1), 19–27.
- Gaudry, S., Messika, J., Ricard, J.-D., Guillo, S., Pasquet, B., Dubief, E., Boukertouta, T., Dreyfuss, D., Tubach, F., 2017. Patient-important outcomes in randomized controlled trials in critically ill patients: a systematic review. *Ann. Intensive Care* 7 (1) 28–28.
- Gustafson, O.D., Williams, M.A., McKechnie, S., Dawes, H., Rowland, M.J., 2021. Musculoskeletal complications following critical illness: a scoping review. *J. Crit. Care* 66, 60–66.
- Guyatt, G., Montori, V., Devereaux, P.J., Schunemann, H., Bhandari, M., 2004. Patients at the center: in our practice, and in our use of language. *ACP J. Club* 140 (1), A11–A12.
- Guyatt, G., Oxman, A.D., Akl, E.A., Kunz, R., Vist, G., Brozek, J., Norris, S., Falck-Ytter, Y., Glasziou, P., DeBeer, H., et al., 2011. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J. Clin. Epidemiol.* 64 (4), 383–394.
- Hakko, E., Guvenc, S., Karaman, I., Cakmak, A., Erdem, T., Cakmakci, M., 2015. Long-term sustainability of zero central-line associated bloodstream infections is possible with high compliance with care bundle elements. *East Mediterr. Health J.* 21 (4), 293–298.
- Herridge, M.S., Tansey, C.M., Matte, A., Tomlinson, G., Diaz-Granados, N., Cooper, A., Guest, C.B., Mazer, C.D., Mehta, S., Stewart, T.E., et al., 2011. Functional disability 5 years after acute respiratory distress syndrome. *N. Engl. J. Med.* 364 (14), 1293–1304.
- Heydon, E., Wibrow, B., Jacques, A., Sonawane, R., Anstey, M., 2020. The needs of patients with post-intensive care syndrome: a prospective, observational study. *Aust. Crit. Care* 33 (2), 116–122.
- Hsieh, S.J., Otusanya, O., Gershengorn, H.B., Hope, A.A., Dayton, C., Levi, D., Garcia, M., Prince, D., Mills, M., Fein, D., et al., 2019. Staged implementation of awakening and breathing, coordination, delirium monitoring and management, and early mobilization bundle improves patient outcomes and reduces hospital costs. *Crit. Care Med.* 47 (7), 885–893.
- Jacob, C., 2017. The Effect of the ABCDEF Bundle on Incidence of Delirium in Critically Ill Patients. ProQuest Dissertations Publishing.

- Johnson, C.C., Suchyta, M.R., Darowski, E.S., Collar, E.M., Kiehl, A.L., Van, J., Jackson, J.C., 2019. Hopkins RO: psychological sequelae in family caregivers of critically ill intensive care unit patients. A systematic review. *Ann. Am. Thorac. Soc.* 16 (7) pp. 894–894–909.
- Kingsley, C., Patel, S., 2017. Patient-reported outcome measures and patient-reported experience measures. *Bj. Educ.* 17 (4), 137–144.
- Kram, S.L., DiBartolo, M.C., Hinderer, K., Jones, R.A., 2015. Implementation of the ABCDE bundle to improve patient outcomes in the intensive care unit in a rural community hospital. *Dimens. Crit. Care Nurs.* 34 (5), 250–258.
- Lavallée, J.F., Gray, T.A., Dumville, J., Russell, W., Cullum, N., 2017. The effects of care bundles on patient outcomes: a systematic review and meta-analysis. *Implement. Sci.* 12 (1), 142.
- Lee, Y., Kim, K., Lim, C., Kim, J.S., 2020. Effects of the ABCDE bundle on the prevention of post-intensive care syndrome: a retrospective study. *J. Adv. Nurs.* 76 (2), 588–599.
- Lin, F., Phelan, S., Chaboyer, W., Mitchell, M., 2020. Early mobilisation of ventilated patients in the intensive care unit: a survey of critical care clinicians in an Australian tertiary hospital. *Aust. Crit. Care* 33 (2), 130–136.
- Loffink, A., Barr, J., Zimmerman, L., 2018. 1262: ICU liberation: nurse practitioner-led implementation of the ABCDEF bundle in a VA hospital. *Crit. Care Med.* 46 (1), 614.
- Malik, A.K., Baidya, D.K., Anand, R.K., Subramaniam, R., 2021. A new ICU delirium prevention bundle to reduce the incidence of delirium: a randomized parallel group trial. *Indian J. Crit. Care Med.* 25 (7), 754–760.
- Marra, A., Ely, E.W., Pandharipande, P.P., Patel, M.B., 2017. The ABCDEF bundle in critical care. *Crit. Care Clin.* 33 (2), 225–243.
- Mikkelsen, M.E., Devlin, J.W., 2021. The A2F bundle: quantity and quality matter*. *Crit. Care Med.* 49 (2).
- Naaktgeboren, R., Zegers, M., Peters, M., Akkermans, R., Peters, H., van den Boogaard, M., van de Laar, F.A., 2022. The impact of an intensive care unit admission on the health status of relatives of intensive care survivors: a prospective cohort study in primary care. *Eur. J. Gen. Pract.* 28 (1), 48–55.
- Negro, A., Cabrini, L., Lembo, R., Monti, G., Dossi, M., Perduca, A., Colombo, S., Marazzi, M., Villa, G., Manara, D., et al., 2018. Early progressive mobilization in the intensive care unit with out dedicated personnel. *Can. J. Crit. Care Nurs.* 29 (3), 26–31.
- Neuraz, A., Guerin, C., Payet, C., Polazzi, S., Aubrun, F., Dailler, F., Lehot, J.J., Piriou, V., Neidecker, J., Rimmele, T., et al., 2015. Patient mortality is associated with staff resources and workload in the ICU: a multicenter observational study. *Crit. Care Med.* 43 (8), 1587–1594.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., et al., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372, n71.
- Parker, A.M., Liu, X., Harris, A.D., Shanholtz, C.B., Smith, R.L., Hess, D.R., Reynolds, M., Netzer, G., 2013. Respiratory therapy organizational changes are associated with increased respiratory care utilization. *Respir. Care* 58 (3), 438–449.
- Patel, J., Baldwin, J., Bunting, P., Laha, S., 2014. The effect of a multicomponent multidisciplinary bundle of interventions on sleep and delirium in medical and surgical intensive care patients. *Anaesthesia* 69 (6), 540–549.
- Pino, C., Boutron, I., Ravaut, P., 2012. Outcomes in registered, ongoing randomized controlled trials of patient education. *PLoS One* 7 (8) e42934–e42934.
- Pun, B.T., Balas, M.C., Barnes-Daly, M.A., Thompson, J.L., Aldrich, J.M., Barr, J., Byrum, D., Carson, S.S., Devlin, J.W., Engel, H.J., et al., 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 (1), 3–14.
- Rengel, K.F., Hayhurst, C.J., Pandharipande, P.P., Hughes, C.G., 2019. Long-term cognitive and functional impairments after critical illness. *Anesth. Analg.* 128 (4), 772–780.
- Review Manager, 2020. Review Manager (RevMan) In., Version 5.4. The Cochrane Collaboration.
- Robinson, K.A., Davis, W.E., Dinglas, V.D., Mendez-Tellez, P.A., Rabiee, A., Sukrithan, V., Yalamanchilli, R., Turnbull, A.E., Needham, D.M., 2017. A systematic review finds limited data on measurement properties of instruments measuring outcomes in adult intensive care unit survivors. *J. Clin. Epidemiol.* 82, 37–46.
- Schallom, M., Tymkew, H., Vyders, K., Prentice, D., Sona, C., Norris, T., Arroyo, C., 2020. Implementation of an interdisciplinary AACN early mobility protocol. *Crit. Care Nurs.* 40 (4), e7–e17.
- Sosnowski, K., Lin, F., Mitchell, M.L., White, H., 2015. Early rehabilitation in the intensive care unit: an integrative literature review. *Aust. Crit. Care* 28 (4), 216–225.
- Sosnowski, K., Mitchell, M.L., White, H., Morrison, L., Sutton, J., Sharratt, J., Lin, F., 2018. A feasibility study of a randomised controlled trial to examine the impact of the ABCDE bundle on quality of life in ICU survivors. *Pilot Feasibility Stud.* 4 (1), 32.
- The, T.S.I., 2015. Early mobilization and recovery in mechanically ventilated patients in the ICU: a bi-national, multi-centre, prospective cohort study. *Crit. Care* 19 (1), 81.
- Tufanaru, C., Munn, Z., Aromataris, E., Campbell, J., Hopp, L., 2017. Systematic reviews of effectiveness. In: Aromataris, E. (Ed.), *Joanna Briggs Institute Reviewer's Manual*. Z. M. The Joanna Briggs Institute.
- West, A.J., Nickerson, J., Breau, G., Mai, P., Dolgowicz, C., 2016. Staffing patterns of respiratory therapists in critical care units of Canadian teaching hospitals. *Can. J. Respir. Ther.* 52 (3), 75–80.
- Zhang, S., Han, Y., Xiao, Q., Li, H., Wu, Y., 2021. Effectiveness of bundle interventions on ICU delirium: a meta-analysis*. *Crit. Care Med.* 49 (2).
- Zheng, M., Tan, M., Tang, L., Rogan, J., Colborn, B., Singh, E., McDaniel, C., Baram, M., 2016. Implementation of the ABCDEF bundle leads to increased patient mobility and improved disposition. *Crit. Care Med.* 44 (12), 359.
- Zhorne, M., Schuh, C., Wright, J., Chapman, D., 2018. Improving survival through the implementation of the ABCDEF bundle in a large community hospital. *Crit. Care Med.* 46 (1), 615.