

ABCDE and ABCDEF care bundles

A systematic review of the implementation process in intensive care units

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Abstract

Background: The ABCDE (Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise) and ABCDEF (Assessment, prevent and manage pain, Both spontaneous awakening and spontaneous breathing trials, Choice of analgesia and sedation, assess, prevent and manage Delirium, Early mobility and exercise, Family engagement) care bundles consist of small sets of evidence-based interventions and are part of the science behind Intensive Care Unit (ICU) liberation. This review sought to analyse the process of implementation of ABCDE and ABCDEF care bundles in ICUs, identifying barriers, facilitators and changes in perception and attitudes of healthcare professionals; and to estimate care bundle effectiveness and safety.

Methods: We selected qualitative and quantitative studies addressing the implementation of ABCDE and ABCDEF bundles in the ICU, identified on MEDLINE, Embase, CINAHL, The Cochrane Library, Web of Science, Epistemonikos, PsycINFO, Virtual Health Library and Open Grey, without restriction on language or date of publication, up to June 2018. The outcomes measured were ICU and hospital length of stay; mechanical ventilation time; incidence and prevalence of delirium or coma; level of agitation and sedation; early mobilization; mortality in ICU and hospital; change in perception, attitude or behaviour of the stakeholders; and change in knowledge of health professionals. Two reviewers independently selected the studies, performed data extraction, and assessed risk of bias and methodological quality. A meta-analysis of random effects was performed.

Results: Twenty studies were included, 13 of which had a predominantly qualitative and 7 a quantitative design (31,604 participants). The implementation strategies were categorized according to the taxonomy developed by the Cochrane Effective Practice and Organization of Care Group and eighty strategies were identified. The meta-analysis results showed that implementation of the bundles may reduce length of ICU stay, mechanical ventilation time, delirium, ICU and hospital mortality, and promoted early mobilization in critically-ill patients.

Conclusion: This study can contribute to the planning and execution of the implementation process of ABCDE and ABCDEF care bundles in ICUs. However, the effectiveness and safety of these bundles need to be corroborated by further studies with greater methodological rigor.

Protocol registration: PROSPERO CRD42019121307.

Abbreviations: ABCDE = awakening and breathing coordination of daily sedation and ventilator removal trials, delirium monitoring and management, and early mobility and exercise, ABCDEF = assessment, prevent and manage pain, both spontaneous awakening and spontaneous breathing trials, choice of analgesia and sedation, assess, prevent and manage delirium, early mobility and exercise, family engagement, ICU = intensive care unit, PAD = clinical practice guideline for the management of pain, agitation, and delirium.

Keywords: care bundles, effectiveness, implementation, intensive care units

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1. Introduction

Intensive care units (ICUs) are characterized by being an environment that provides care and continuous monitoring of critically-ill patients, with a specialized multidisciplinary team, dedicated technology and equipment, considered highly complex, and typically classified according to patient age or medical specialty.^[1]

Furthermore, ICU admissions are usually due to clinical instability or involve surgical patients that require continuous monitoring and predominantly invasive ventilator support. Despite its benefits, mechanical ventilation is not devoid of complications for the patient, who, after an extended period of inactivity, may present respiratory muscle weakness, muscular atrophy in the limbs and decreased ability to perform daily activities.^[2,3]

Although intensive care professionals work to ensure the best conditions, ICU culture does not always prepare the patient to return home and resume the life they had before hospitalization.^[4] In this sense, the science of ICU liberation seeks to strengthen the identity and dignity of the user, in order to reduce the factors that threaten their beliefs, values and needs.^[5]

Some studies represent a milestone in that field, for instance, in 2010, Vasilevskis et al adopted the acronym ABCDE (awakening and breathing coordination of daily sedation and ventilator removal trials, delirium monitoring and management, and early mobility and exercise) in a study that addressed a screening, prevention and recovery model to treat ICU survivors.^[6] In 2013, the clinical practice guideline for the management of pain, agitation, and delirium (PAD guideline) emerged, which incorporated the available evidence in critical care.^[7] In 2014, the first studies were conducted using the ABCDEF bundle (assessment, prevent and manage pain, both spontaneous awakening and spontaneous breathing trials, choice of analgesia and sedation, assess, prevent and manage delirium, early mobility and exercise, family engagement) with a focus on delirium and family inclusion.^[8]

Although these interventions are the result of research and recommendations that improve the quality of services, they are not always translated properly into practice.^[9] This issue is due to several factors and represents an obstacle to the implementation of interventions and changes in clinical practice.^[10]

In order to bridge the gap between theory and practice in the field of implementation, two issues have been a focus of research: the design and improvement of the planning process so that the most promising interventions can be applied in their specific context; and the identification of optimal interventions and critical components for success.^[11]

In this context, the aim of the present study was to analyse the process of implementation of ABCDE and ABCDEF care bundles in ICUs, identifying barriers, facilitators and changes in the perception and attitude of healthcare professionals, and to estimate care bundle effectiveness and safety.

2. Methods

2.1. Protocol and registration

This systematic review was reported according to the items in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.^[12] The protocol was registered in the International Prospective Register of Systematic Reviews CRD42019121307 (<https://www.crd.york.ac.uk/PROSPERO/dis>

[play_record.php?RecordID=121307](https://www.crd.york.ac.uk/PROSPERO/dis/play_record.php?RecordID=121307)) and previously published.^[13] There were no significant amendments in relation to the primary protocol.

2.2. Search strategy

The following terms were combined: ABCDE; ABCDEF; PAD guideline; ICU liberation; PAD care bundle (see table, Supplemental Content 1, <http://links.lww.com/MD/G767>, which demonstrates the search strategies). There was no restriction on language restriction or publication status. Other studies described in full text and grey literature (OpenGrey European database) were checked to identify whether they contained sufficient and relevant data.

The MEDLINE (PubMed), Embase (Ovid), CINAHL (EBSCO), The Cochrane Library (Wiley), Web of Science, Epistemonikos, PsycINFO and Virtual Health Library databases were consulted up to June, 2018.

2.3. Inclusion criteria

Qualitative and quantitative studies addressing experiences of implementing ABCDE or ABCDEF care bundles were included. The inclusion criteria were:

Participants: Adults aged >18 years admitted to ICUs.

Interventions: Implementation of ABCDE or ABCDEF care bundles, in whole or part.

Comparators: Usual care.

Patient-important outcomes: ICU length of stay; mechanical ventilation time; incidence and prevalence of delirium or coma; level of agitation and sedation; early mobilization; ICU and hospital mortality; hospital length of stay.

Process implementation outcomes: Qualitative studies provided relevant information on barriers, facilitators, changes in health professionals perception and attitudes, helping to guide clinical practice, formulation of policies and decision-making.

Study design: To estimate the effectiveness of bundle implementation, preferentially controlled quantitative studies were searched (randomized controlled trials [RCTs], non-RCTs, controlled before-after studies, interrupted time series and repeated measurement studies). Although in the absence of these methodological designs, uncontrolled studies were considered and the limitations of this methodological design were discussed. For qualitative studies that addressed the implementation process of the ABCDE and ABCDEF care bundles, the study design was not an inclusion criteria.

2.4. Exclusion criteria

Studies were excluded based on the following criteria: (i) conference abstracts; (ii) systematic review protocols; reviews (systematic review, scoping review, umbrella review, narrative review, and other reviews); and overviews of systematic reviews; (iii) other care bundles or protocols implemented in the ICU or in the process of implementation; (iv) evaluation or validation of instruments and clinical tools.

2.5. Eligibility determination and data extraction

Initially, titles and abstracts of the studies retrieved were evaluated, to identify those that met the eligibility criteria.

Full texts were then evaluated and reference lists reviewed to identify further relevant articles. Both steps were carried out by two independent reviewers (FSM and LLM) and differences were resolved by consensus.

Data extraction was based on three previously defined and tested spreadsheets, collecting the following variables:

1. Characteristics of the studies included: authors; year of publication; data collection period; country and institution in which the study was conducted; environment; study design; care bundle implemented; characteristics of the patient/ICU.
2. Qualitative data: implementation strategies; barriers and facilitators; perception of health professionals; benefits and risks for the patient (safety) associated with bundle implementation; implications for policies, practices and research; limitations of the studies.
3. Quantitative data: size of groups; outcomes assessed and respective measures; measurement of effects and safety.

Data extraction was performed by the first reviewer (FSM) and the information collected was subsequently verified by a second reviewer (SB-F). Differences were resolved by consensus.

2.6. Quality assessment

For before-after studies, the Quality Assessment Tool for Before-After (Pre-Post) Studies with no Control Group was used with 12 quality assessment criteria. Studies selected were classified based on the number of positive responses and defined as low quality (0–4 points); moderate quality (5–8 points) or high quality (9–12 points).^[14]

To assess the quality of qualitative studies, the Checklist for Qualitative Research tool developed by The Joanna Briggs Institute was chosen. This tool comprises ten quality assessment criteria.^[15] All qualitative studies were included, regardless of the quality assessment result.

For cohort studies, the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies with 14 quality assessment criteria was used. The studies selected were classified based on the number of positive responses and defined as low quality (0–5 points); moderate quality (6–10 points) or high quality (11–14 points).^[14]

To assess the quality of clinical trial evidence, the Cochrane Handbook for Systematic Reviews (The Cochrane Collaboration's tool for assessing risk of bias) tool was used independently and for seven different domains related to risk of bias: randomization sequence generation, allocation concealment, masking (blinding) of participants and staff, masking (blinding) of outcome assessment, incomplete outcome data, selective reporting of outcomes and other sources of bias. The risk of bias was assessed for each domain and classified as high, unclear or low.^[16]

The articles included were independently assessed for quality and risk of bias by two reviewers (FSM and LLM). Disagreements between reviewers were resolved by consensus.

2.7. Data synthesis

The implementation strategies refer to the formal steps taken by different institutions to implement ABCDE and ABCDEF care bundles. Qualitative data such as the implementation strategies identified in the included studies were classified according to the

taxonomy developed by the Cochrane Effective Practice and Organization of Care Group. This taxonomy provides criteria for different interventions using four main domains: (i) organization; (ii) financial; (iii) governance; and (iv) implementation strategies.^[17] This categorization and the number of strategies were presented in a table.

The Cochrane Effective Practice and Organization of Care Group recognizes that there may be overlap between categories and subcategories and that some interventions can be classified into more than one category.^[17] In this systematic review, the authors chose to classify each strategy into a single category.

Implementation strategies involve the formal steps adopted by different institutions to implement the ABCDE and ABCDEF care bundles. As described in the literature, structured implementation processes with a greater number of strategies may indicate a more complete implementation process.^[18]

Information related to barriers and facilitators was identified and described in a table. Whenever reported in primary studies, bundle adherence, savings generated and the theoretical model used to guide the implementation process were recorded.

The selected outcomes and the methodology to categorize the strategies were previously defined in the systematic review protocol.^[13] Data from quantitative studies were initially grouped based on the outcomes selected in a worksheet (Microsoft Office, Excel 14.0).

For dichotomous outcomes, odds ratio was calculated with a 95% confidence interval, using a random effects of inverse variance model. For continuous variables, standardized mean difference was calculated using the inverse variance random-effects model. When standard deviation was not reported, the confidence interval was used to estimate this, employing the method described by Higgins and Green (2011). All results were grouped according to type of bundle implemented (ABCDE or ABCDEF).

The number of studies was insufficient to assess publication bias using a funnel plot^[19] or Egger's regression test.^[20] The I^2 statistic indicated by the Cochrane Handbook for Systematic Reviews of Interventions was used to indicate the level of heterogeneity affecting the meta-analysis findings: 0% to 40% (may not be important), 30% to 60% (moderate heterogeneity), 50% to 90% (substantial heterogeneity) and 75% to 100% (considerable heterogeneity).^[16]

The RevMan 5.3.5^[21] system was used to perform the meta-analysis. In cases where the meta-analysis could not be executed (due to the heterogeneity of the population, intervention, comparator, result or method), a narrative synthesis of the evidence was produced.

3. Results

A total of 4287 records were identified on the databases and two relevant studies were further identified by manual search, of which 2177 were screened for title and abstract. This initial screening led to the rejection of 2132 studies for not meeting the selection criteria. After full text reading of the 45 eligible studies, 25 were excluded for not meeting the eligibility criteria (see table, Supplemental Content 2, <http://links.lww.com/MD/G768>, which demonstrates the articles excluded and reasons for exclusion.), giving a total of 20 studies selected.

The flow diagram shown in Figure 1 illustrates the study selection process.

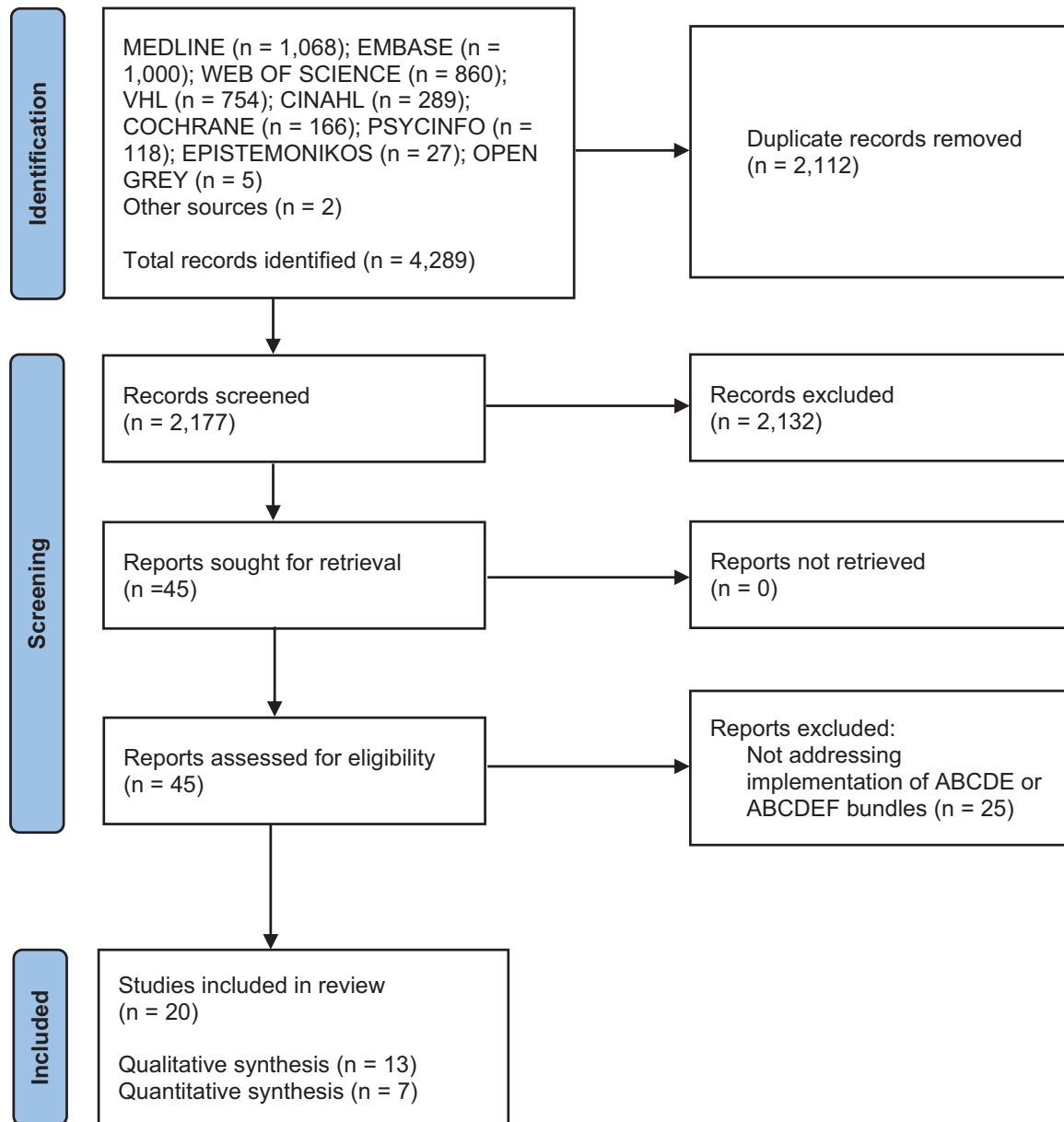


Figure 1. Study selection process.

3.1. Study selection and characteristics

Table 1 presents the characteristics of the studies included. Fifteen studies involved the ABCDE bundle and five the ABCDEF bundle and were published between 2013 and 2018.

Thirteen studies had a predominantly qualitative design while seven used a quantitative approach. Of the qualitative studies, survey-type studies prevailed, whereas quantitative were predominantly before-after studies.

Studies conducted in university (n=8) and rural (n=2) hospitals were identified. Most studies were performed in the United States (n=15), followed by China (n=1), Australia (n=1), and Italy (n=1).

The results systematized in this study encompassed about 31,604 participants from primary studies, carried out in

different scenarios using different methodological designs (quantitative and qualitative).

All studies' characteristics are presented in Table 1.

3.2. Synthesis of findings

Strategies for implementing ABCDE and ABCDEF care bundles

The main strategies adopted in the process of implementing the ABCDE and ABCDEF bundles included the distribution of educational materials, educational meetings, customized interventions, interventions aimed at service providers, and structural interventions. Other less frequent strategies included outreach visits, patient-mediated intervention, patient-oriented interventions and expert review.

Educational meetings, supported by materials such as leaflets, cards and posters, were important initiatives for promoting

Table 1**Characteristics of studies included.**

Author, y (bundle, N)	Study design	Environment, country	Aim	Outcome
Balas et al, 2013 (ABDCE, n=328)	Before and after (predominantly qualitative design)	University Hospital, United States	To identify facilitators and barriers to the adoption of the ABCDE bundle and assess whether the implementation of the bundle was effective, sustainable and contributed to the dissemination of practices	Prior knowledge and challenges in implementing the bundle Acceptance of participants Aspects to consider when implementing
Balas et al, 2014 (ABCDE, n=296)	Before and after (predominantly quantitative design)	Not reported	To assess the effectiveness and safety of implementing the ABCDE bundle in the daily routine	28 d free from mechanical ventilation Prevalence and duration of days of <i>delirium</i> and coma in the ICU Number of patients mobilized out of bed while in the ICU Total hospital mortality Time to discharge from the ICU and hospital in days Number of patients who have undergone "change of residence" Unplanned extubations, reintubations, tracheostomy procedure Physical restraint time in the ICU, in days Changes in mental status
Barnes-Daly et al, 2018 (ABCDE, n=17,000)	Survey-type exploratory (predominantly qualitative design)	Several hospitals, adult and pediatric ICUs, United States	To describe the history of the ICU Liberation ABCDEF Bundle Improvement Collaborative, its implementation strategies to promote change and teamwork, as well as the performance metrics used to monitor progress	Evolution Dissemination Implementation Strategies Compliance with protocols Performance by metric
Barnes-Daly et al, 2017 (ABCDEF, n=6064)	Cohort (predominantly quantitative design)	Community hospitals, post-surgical ICU, United States	To study the association between compliance of the ABCDEF bundle with a focus on adherence	Survival Length of stay in the ICU in days Length of hospital stay in days Days free of coma and <i>delirium</i> in days Proportion of days on mechanical ventilation Proportion of compliance and total and partial adherence
Boehm et al, 2017a (ABCDE, n=315)	Survey-type exploratory (predominantly qualitative design)	University hospitals and study centers, United States	To understand the relation between organizational factors and attitudes generated for the domains: policies and protocols, work unit, amount of work, quality of work, activities carried out and physical environment	Professional team by performance class Perception of ease of executing the bundle Perception of safety Confidence in the outcome of the bundle Perception of strength of evidence
Boehm et al, 2017b (ABCDE, n=101)	Survey-type exploratory (predominantly qualitative design)	University hospitals and study centers, United States	To examine the relation between attitudes and adherence to the ABCDE bundle	Professional team by performance class Perception of ease of executing the bundle Perception of security Confidence in the outcome of the bundle Perception of strength of evidence Adherence

Table 1
(continued).

Author, y (bundle, N)	Study design	Environment, country	Aim	Outcome
Boehm et al, 2016 (ABCDE, n = 16)	Descriptive (predominantly qualitative design)	University Hospital, United States	To describe the organizational domains that contribute to the variation in the implementation of the ABCDE bundle and examine the performance of a theoretical model to identify changes in the implementation of the bundle with a focus on reducing mechanical ventilation, <i>delirium</i> and increasing early mobility	Organizational factors Physical environment Quantity and quality of work Task load Attitudes Patient characteristics
Bounds et al, 2016 (ABCDE, n = 159)	Before and after (predominantly quantitative design)	Rural and university hospital, surgical ICU, United States	To quantify the prevalence and duration of <i>delirium</i> in ICU patients before and after the implementation of the ABCDE bundle	Patients with <i>delirium</i> Duration of <i>delirium</i> in days Patients with zero day of <i>delirium</i> Patients on mechanical ventilation Patients on mechanical ventilation with <i>delirium</i> Duration of <i>delirium</i> in patients on mechanical ventilation in days Patients on mechanical ventilation with zero days of <i>delirium</i> Patients without mechanical ventilation with <i>delirium</i> Duration of <i>delirium</i> in patients without mechanical ventilation in days Daily RASS score Length of hospital stay in days Length of stay in the ICU in days Mechanical ventilation time in days Patients with zero days of mechanical ventilation
Carrothers et al, 2013 (ABCDE, n = 81)	Survey-type exploratory (predominantly qualitative design)	University and Community Hospital, United States	To identify which contextual factors facilitate and/or hinder the implementation of the ABCDE bundle for guidance in future studies	Length of stay in the ICU in days Mechanical ventilation time in days
Chai, 2017 (ABCDEF, n = 301)	Before and after (predominantly quantitative design)	Not reported, United States	To study the effect of multiple components of ABCDEF on the incidence of <i>delirium</i> , number of days of mechanical ventilation and length of stay in the ICU	Reduced incidence of <i>delirium</i> Mechanical ventilation time in days Length of stay in the ICU for a period of 30 d
Collinsworth et al, 2014 (ABCDE, n = 3018)	Descriptive (predominantly qualitative design)	Several hospitals, adult ICU, United States	To examine the percentage of ABCDE bundle elements recorded in a computerized system and verify compliance with data entry procedures	Implementation of element A in the computerized system Data recording for element B Data visualization by patient Data entry in the system Data not documented in the system
Costa et al, 2018 (ABCDE, n = 293)	Survey-type exploratory (predominantly qualitative design)	Representative Association of Hospitals, United States	To measure the involvement of intensive care professionals in spontaneous awakening tests, spontaneous breathing attempts, management of <i>delirium</i> and in the execution of mobility	Application Involvement Perception

Table 1
(continued).

Author, y (bundle, N)	Study design	Environment, country	Aim	Outcome
Kram et al, 2015 (ABCDE, n=83)	Before and after (predominantly quantitative design)	Rural hospital, not reported	To implement the ABCDE bundle in a general adult ICU with six beds in a rural community hospital	Incidence of <i>delirium</i> Length of patient stay in the ICU in days Total hospital stay of the patient in days Mechanical ventilation time in days
Louzon et al, 2017 (ABCDE, n=935)	Case study (predominantly qualitative design)	University Hospital, United States	To describe a two-phase program to increase the pharmacist's involvement in the treatment of pain, agitation and <i>delirium</i>	Involvement of the pharmacist Inter-professional collaboration
Miller et al, 2015 (ABCDE, n=212)	Survey-type exploratory (predominantly qualitative design)	Not reported, United States	To evaluate the self-reported rates of implementation of ABCDE components and their association with the results in collaboration for quality improvement	Patients engaged in breathing exercises Patients who received mobility physiotherapy Frequency of data collection Association of the hospital with other entities supporting critical care
Morandi et al, 2017 (ABCDEF, n= 1521)	Survey-type exploratory (predominantly qualitative design)	Various hospitals, Europe, South America, North America, Oceania, Africa	To assess knowledge and use of the elements of the ABCDEF bundle to implement the PAD Guideline guidelines	Bundle implementation Conformity Use of measurement scales related to the bundle Monitoring of <i>delirium</i> Execution of early mobility Assessment of weakness acquired in the ICU Family involvement
Pinto et al, 2016 (ABCDE, n=108)	Survey-type exploratory (predominantly qualitative design)	University hospital, Italy	To evaluate nursing knowledge, practice and perception about the ABCDE bundle	Cognizance of the bundle Agreement on the bundle's ability to improve patient outcomes Understanding the testing for elements A and B Relevance of scales to assess <i>delirium</i> Execution of mobility Execution of multidisciplinary rounds Applicability of the bundle
Ren et al, 2017 (ABCDE, n=143)	Before and after (predominantly quantitative design)	Not reported, China	To investigate the effects of the ABCDE bundle on hemodynamics in patients on mechanical ventilation	Duration of mechanical ventilation in days Length of stay in the ICU in days 28-d survival rate
Sosnowski et al, 2018 (ABCDE, n=30)	Pilot study for randomized clinical trial (predominantly quantitative design)	Not reported, adult ICU, Australia	To evaluate the feasibility of conducting a large-scale randomized controlled study comparing the ABCDE bundle to standard ICU treatment through a pilot study	Organic and cognitive functional status Physical functional status and potential physical limitations Quality of life before and after hospitalization Feasibility of conducting a randomized clinical trial
Weber et al, 2017 (ABCDEF, n= 600)	Descriptive (predominantly qualitative design)	University Hospital, United States	To describe the relevant points of the implementation of the ABCDEF bundle with a focus on mobility	Accuracy in assessing pain, agitation and <i>delirium</i> Adherence to guidelines, protocols and instruments of clinical practice

ABCDE=awakening and breathing coordination of daily sedation and ventilator removal trials, delirium monitoring and management, and early mobility and exercise; ABCDEF=assessment, prevent and manage pain, both spontaneous awakening and spontaneous breathing trials, choice of analgesia and sedation, assess, prevent and manage delirium, early mobility and exercise, family engagement; ICU=intensive care unit; PAD=clinical practice guideline for the management of pain, agitation, and delirium; RASS=Richmond Agitation-Sedation Scale.

better understanding of bundles, supporting training on the elements related to the management of delirium, sedation and early mobility.^[22] As many professionals reported low confidence in their ability to use delirium scales, continuing education actions, case studies and applications in practice proved essential to ensure all participants held the same level of knowledge, guided by clear protocols and well-defined work structures.^[23]

The quantity and the type of strategy found for each study are presented in Table 2.

3.3. Barriers, facilitators and changes in perception and attitude of implementation process actors

The most frequent barriers identified in the implementation process were: challenges with communication; lack of planning; excessive documentation; and the fear of risks to the patient. The most cited facilitators were: leadership involvement and support; existence of a multidisciplinary team; training; and practice-oriented training.

Resistance to change is a crucial point to be identified.^[24] Perceptions held about this behaviour revealed that some members, despite high performance, did not become actively involved until the end of the process. This can be explained by the fact that there were no employees exclusively dedicated to the implementation and obstacles took time to resolve, albeit due to inefficient communication flows, centralized coordination or lack of sufficient support for the process.^[25,26]

When factors related to acceptance, practical application and project safety are not guaranteed by leaders and not supported by organizational culture and values, even the best employees tend to favour other projects, which may influence the speed of implementation.^[24] This obstacle is not straightforward, because it may involve institutional issues that need to be harmonized with the philosophy of patient liberation from the ICU. This should ideally take place before the beginning of the process, where communication and transparency are fundamental for change.^[22]

Lack of bundle knowledge is also an obstacle which needs to be identified and overcome through training and clear protocols.^[27] Workload is a recurrent concern, mainly in relation to the amount of documentation to be filled in during the process.^[24]

Implementation is also facilitated when those involved believe and feel safe and supported during execution.^[28] This is due to a consequent strengthening of interdisciplinary communication, multidisciplinary actions and autonomy of nursing and other intensive care professionals.^[29]

Collaboration between professionals can be a key point influencing the way activities are conducted, promoting greater adherence to spontaneous awakening and breathing tests and more appropriate use of scales for assessing pain, agitation, sedation and delirium.^[30] For early mobility exercises, screening and interprofessional assessment can favour patient safety and result in a more confident attitude among professionals.^[24]

The component involving the family must adopt a comprehensive and humanized approach, including social care professionals, occupational therapists and psychologists. The lack of professionals from other disciplines trained in intensive care makes it difficult to form a capable team for implementation of this element.^[29] In addition, to the difficulty inherent to the process of communicating with family, there is a fear that their presence may compromise the professionals' routine in the

Table 2
The quantity and the type of strategy identified per study for implementing ABCDE and ABCDEF care bundles.

Intervention	Balas et al (2013)	Balas et al (2014)	Barnes-Daly et al (2016)	Barnes-Daly et al (2018)	Barnes-Daly et al (2017)	Bounds et al (2016)	Carrothers et al (2013)	Chai (2017)	Collinsworth et al (2014)	Kram et al (2015)	Louzon et al (2017)	Ren et al (2017)	Sosnowsky et al (2018)	Weber et al (2017)	Total
IS															
Distribution of educational materials	3	1	1	1	1	2	2	5	2	2	1	1	1	1	19
Educational meetings	1	1	1	1	1	2	1	2	1	2	1	1	1	1	15
Local consensus processes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	6
Disclosure visits	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Local leader opinion	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Patient-mediated intervention	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Audit and alignment with participants	3	1	1	1	1	1	1	1	1	1	1	1	1	1	6
Reminders	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Customized interventions	2	1	1	1	1	1	1	1	1	1	1	1	1	1	8
Supplier-oriented interventions	3	1	1	1	1	1	1	1	1	1	1	1	1	1	7
Patient-oriented interventions	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Structural interventions	1	1	1	1	1	3	3	1	1	1	1	1	1	1	7
Expert review	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
TOTAL	12	6	1	5	9	10	4	7	3	5	2	80			

ABCDE = awakening and breathing coordination of daily sedation and ventilator removal trials, delirium monitoring and management, and early mobility and exercise; ABCDEF = assessment, prevent and manage pain, both spontaneous awakening and spontaneous breathing trials, choice of analgesia and sedation, assess, prevent and manage delirium, early mobility and exercise, family engagement; D = delivery arrangements; EPOC = Cochrane Effective Practice and Organization of Care taxonomy categories; G = governance arrangements; IS = implementation strategies.

critical environment.^[23] These perceptions can be addressed with clear and well-defined protocols, by the institution adopting a holistic, humanized approach in the ICU, and with the proper inclusion of visitors in the procedures and objectives for this element.^[28]

All barriers and facilitators concerning this process are presented in Table 3.

3.4. Effectiveness and safety of ABCDE and ABCDEF bundles

The outcomes found in the studies were: time on mechanical ventilation (n=5), incidence or prevalence of delirium (n=5), length of stay in the ICU (n=4), sedation (n=2), length of stay in the hospital (n=2), ICU mortality (n=2), early mobilization (n=1), coma incidence (n=1), and hospital mortality (n=1). They were measured as follows: Time on mechanical ventilation, ICU and hospital length of stay were measured in number of days. ICU and hospital mortality, coma, and early mobilization were presented in percentage. The patients' level of arousal was assessed with the Richmond Agitation-Sedation Scale and duration of coma was defined as the number of ICU days that patients had a Richmond Agitation-Sedation Scale score of -4 or -5. Delirium was assessed with Confusion Assessment Method in Intensive Care Unit or Intensive Care Delirium Screening Checklist. Early mobilization was recorded whether patients were mobilized out of bed anytime in ICU.

Meta-analysis was performed for only 5 of the 7 studies, because two measured different effectiveness and safety outcomes. Implementing of the ABCDE and ABCDEF bundles resulted in a lower incidence of delirium, shorter time on mechanical ventilation and in the ICU, increased early mobility and decreased mortality in both the ICU and hospital compared to patients who received usual care.

Sosnowski et al (2018) conducted a prospective, single-centre, randomised controlled feasibility study. Thirty mechanically-ventilated adults were randomized to the intervention group (n=15) or control group (n=15).^[31] Of these participants, 23

(76.6%) successfully completed the 90-day post-discharge assessment. Although some favourable results were obtained for the implementation of the ABCDE bundle, it is important to emphasize that this feasibility study was not designed or appropriately powered to test a hypothesis.

Barnes-Daly et al (2017) analysed data from 6064 patients for total and partial ABCDEF bundle compliance measured daily and concluded that implementing this bundle was associated with significant marked improvements for both in-hospital survival and days alive and free of delirium and coma.^[8] Further, even when delivered incompletely, bundle implementation results showed improvements in patient outcomes.

The forest plots shown in Figures 2–10 summarize the effects of ABCDE and ABCDEF bundles implementation for the selected outcomes.

3.5. Risk of bias

The assessment of the methodological quality of the five before-after studies.^[32–36] revealed that all had scores indicating moderate quality. Barnes-Daly et al (2017) cohort study was defined as moderate classification.^[7]

The main limitations of the before-after and cohort studies were similar: sample size, blinding of evaluators, and analysis of loss to follow-up and limited outcome measures.

The results for methodological quality of the 13 qualitative studies^[22–30,37–40] and the RCT^[31] are summarised (see table, Supplemental Content 3, <http://links.lww.com/MD/G769>, which demonstrates the Risk of bias).

The main limitations of the qualitative studies were related to: a statement locating the researcher culturally or theoretically; the influence of the researcher on the research, and vice-versa; the representation of participants; and prior ethical approval. In the feasibility RCT, it was not possible to blind the research team or participants to group assignment.^[31]

4. Discussion

4.1. Main findings

This systematic review has found that, in the implementation process, strategies supported by a theoretical model which guides all stages and defines the responsibilities of each of the actors involved seem to be associated with better results. Collaborative, comprehensive leadership that offers educational training and transparency in the process contributes to more receptive behavior of teams and facilitates adherence and understanding of key implementation points. Models that are applicable regardless of the size of the hospital and ICU, with more rigorous methodological designs, and make results reproducible across various types of critical environments can be useful.

The meta-analysis demonstrated that implementation of ABCDE and ABCDEF bundles may be important for the management of critical patients, since it resulted in a lower incidence of delirium, reduced time on mechanical ventilation and in the ICU, increased early mobility and decreased both ICU and hospital mortality relative to patients receiving usual care. However, the design and quality of the studies, which was predominantly moderate, do not allow assertive conclusions to be drawn regarding the effectiveness and safety of the bundles, as studies had methodological bias and/or limitations that may affect the interpretation of the results.

Table 3
Barriers and facilitators concerning perceptions and attitudes of health professionals in the implementation process.

Barriers	Facilitators
Communication challenges (n=7)	Leaders' involvement (n=7)
Lack of planning (n=6)	Training (n=6)
Excess documentation (n=5)	Multidisciplinarity (n=5)
Fear of risks to the patient (n=5)	Practice-oriented training (n=3)
Lack of formalization of the bundle (n=3)	Carrying out planning (n=3)
Lack of professional staff (n=3)	Protocol consolidation (n=3)
High workload (n=3)	Strengthening organizational culture (n=2)
Methodological problem (n=2)	Performance evaluation (n=2)
High staff turnover (n=2)	Continuing education (n=2)
Process resistance (n=2)	Interdisciplinarity (n=2)
Lack of motivation (n=1)	Strengthening communication (n=2)
	Checking records (n=1)
	Audit (n=1)
	Family involvement (n=1)
	Dedicated team (n=1)

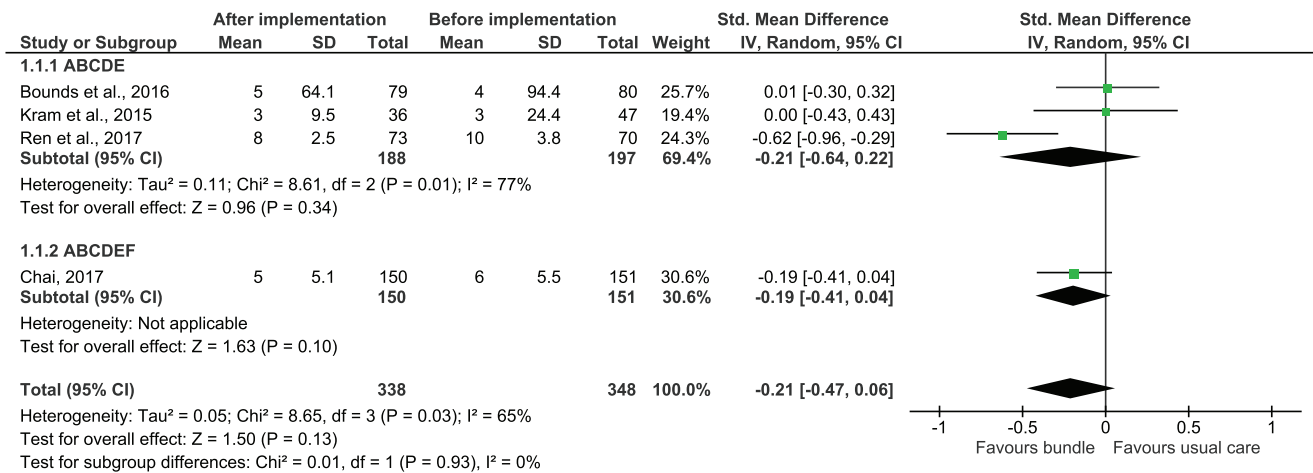


Figure 2. Forest plot summarizing the effects of ABCDE and ABCDEF bundles implementation for ICU length of stay outcome, in number of days. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise; ABCDEF=Assessment, prevent and manage pain, Both spontaneous awakening and spontaneous breathing trials, Choice of analgesia and sedation, assess, prevent and manage Delirium, Early mobility and exercise, Family engagement; ICU=intensive care unit.

4.2. Interpretation of findings in relation to literature

Leadership involvement and support, the existence of a multidisciplinary team and training have represented relevant facilitators in the implementation process of the ABCDE and ABCDEF care bundles, whereas challenges with communication, lack of planning, excessive documentation have appeared as barriers to be mitigated. Strategies as distribution of educational materials, educational meetings, and customized interventions were quite usual to the bundles implement.

Effective planning well as support and resources shall be guaranteed on the part of the institution must take place before the implementation, as during the process of implementation the attention must be paid to compliance and documentation so as to ensure adherence and help the practice over time.^[26] It is important to emphasize that interventions such have been

executed shall be based on evidence and embraced by the multidisciplinary team to instill security and ensure everyone involved holds the same level of knowledge of the clinical protocol.^[22]

Many of the hospitals that have proved successful in this practice were characterized as small institutions, able to more readily adopt changes and carry out tests promptly during implementation.^[32] This success is also due to the implementation of actions in a staggered manner and through interprofessional rounds.^[24]

The importance of assessing, preventing, and managing delirium in the ICU is a consensus in the literature, however there still is a lack of robust evidence to support the best clinical practices. Trogrlic et al (2015) summarized what types of strategies of implementation have been tested to improve ICU

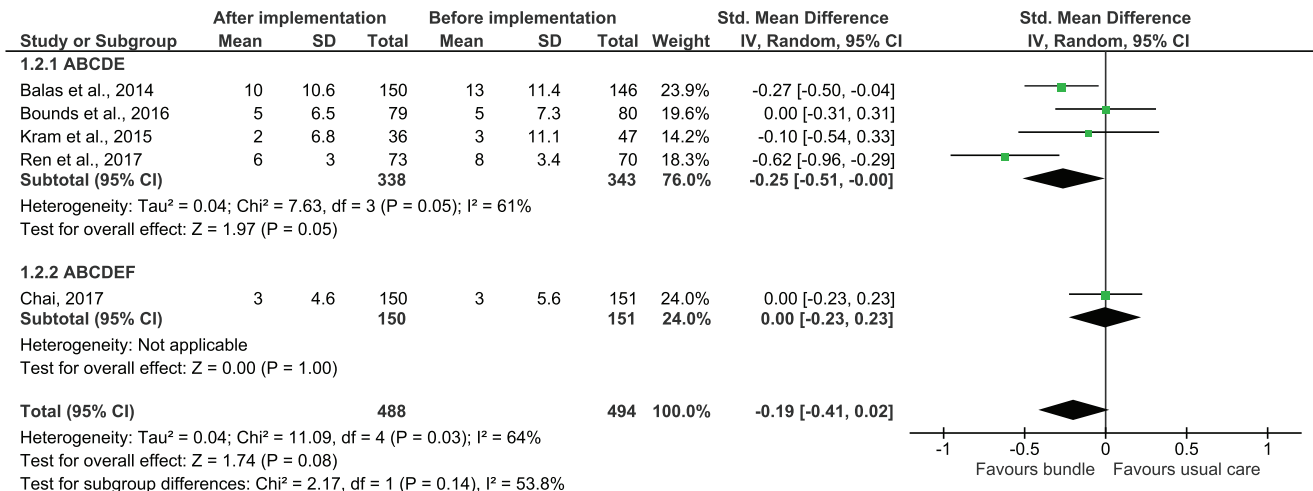
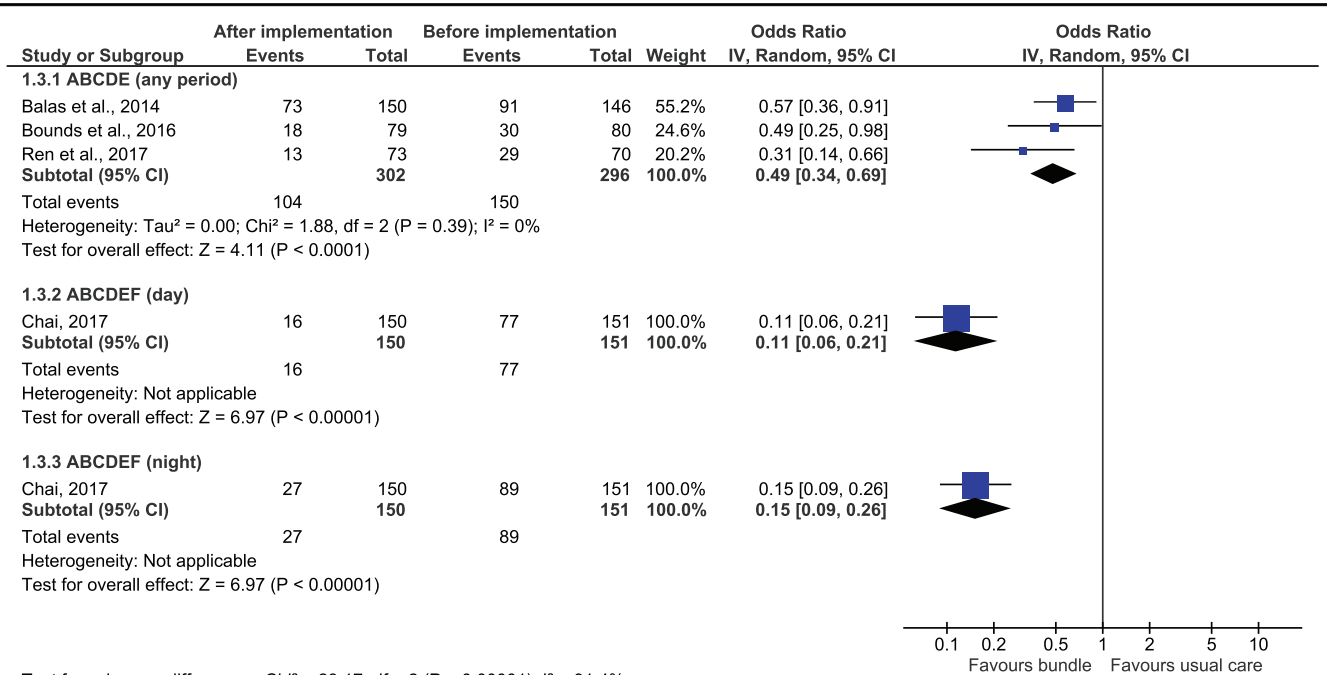


Figure 3. Forest plot summarizing the effects of ABCDE and ABCDEF bundles implementation for mechanical ventilation time outcome, in number of days. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise; ABCDEF=Assessment, prevent and manage pain, Both spontaneous awakening and spontaneous breathing trials, Choice of analgesia and sedation, assess, prevent and manage Delirium, Early mobility and exercise, Family engagement.



Test for subgroup differences: Chi² = 23.17, df = 2 (P < 0.00001), I² = 91.4%

Figure 4. Forest plot summarizing the effects of ABCDE and ABCDEF bundles implementation for delirium outcome, assessed with Confusion Assessment Method in Intensive Care Unit (CAM-ICU) or Intensive Care Delirium Screening Checklist (ICDSC). ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise; ABCDEF=Assessment, prevent and manage pain, Both spontaneous awakening and spontaneous breathing trials, Choice of analgesia and sedation, assess, prevent and manage Delirium, Early mobility and exercise, Family engagement.

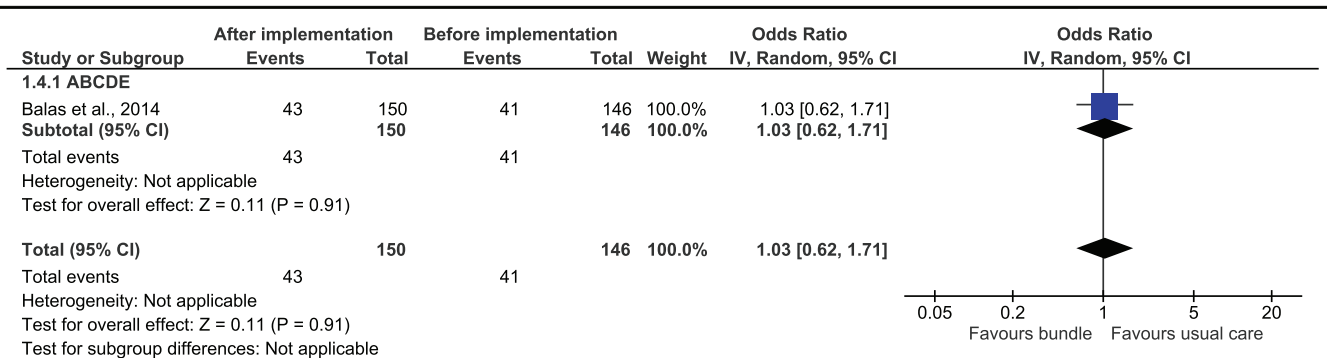


Figure 5. Forest plot summarizing the effects of ABCDE bundle implementation for coma outcome, in percentage. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise.

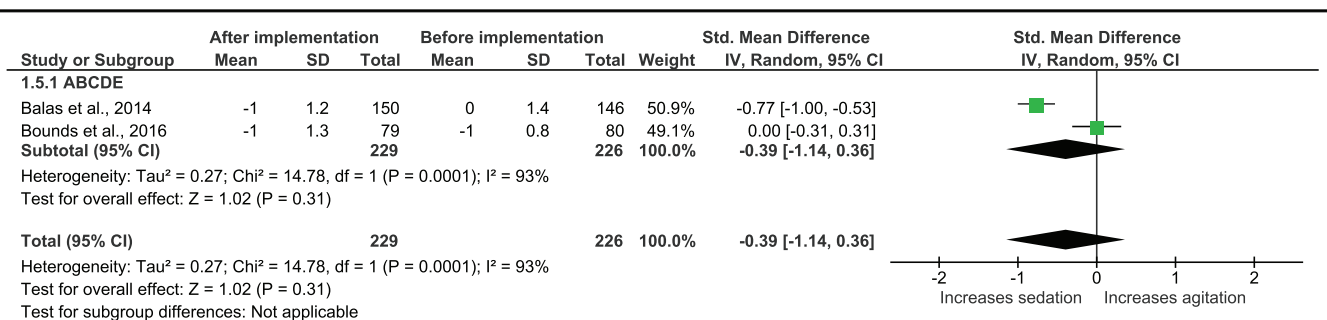


Figure 6. Forest plot summarizing the effects of ABCDE bundle implementation for sedation outcome, assessed with the Richmond Agitation-Sedation Scale (RASS). ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise.

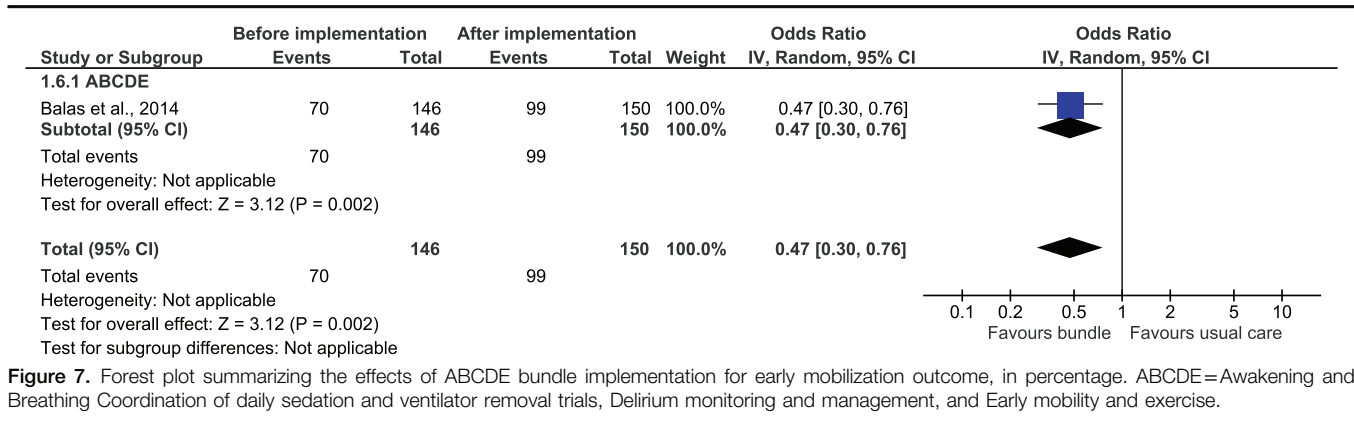


Figure 7. Forest plot summarizing the effects of ABCDE bundle implementation for early mobilization outcome, in percentage. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise.

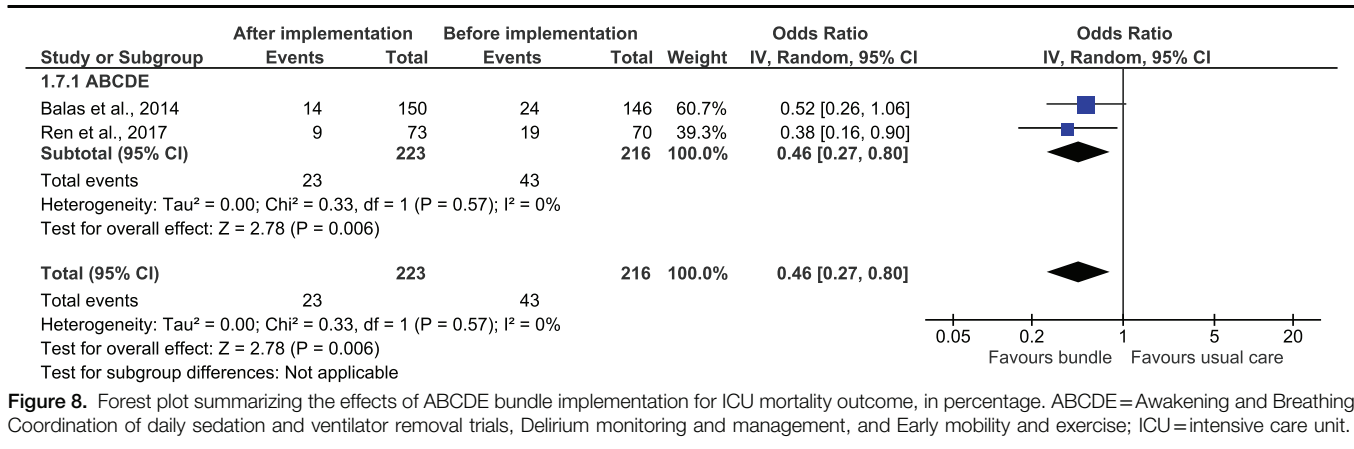


Figure 8. Forest plot summarizing the effects of ABCDE bundle implementation for ICU mortality outcome, in percentage. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise; ICU=intensive care unit.

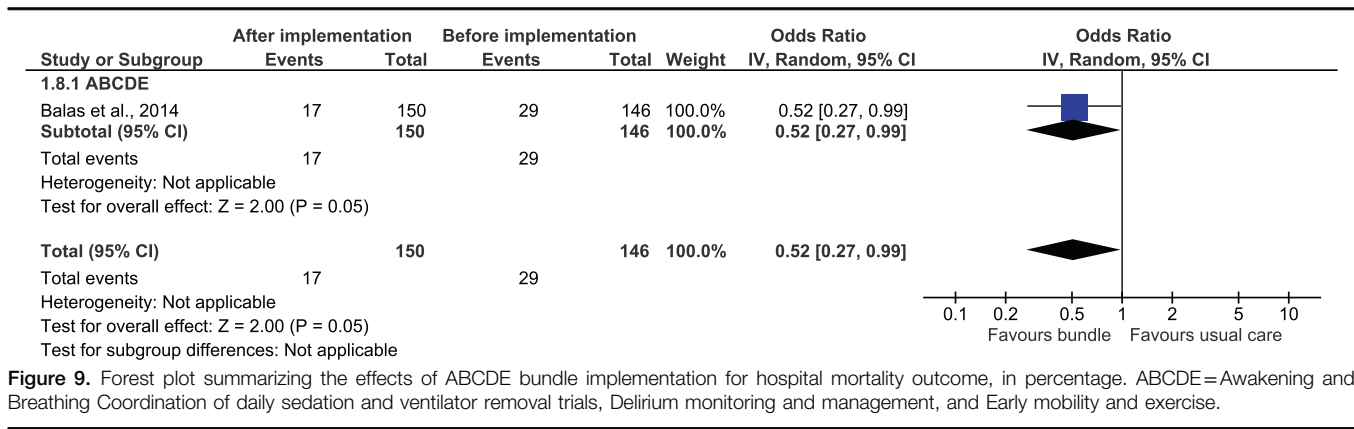


Figure 9. Forest plot summarizing the effects of ABCDE bundle implementation for hospital mortality outcome, in percentage. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise.

clinicians' ability to effectively assess, prevent and treat delirium well as to evaluate the effect of these interventions on clinical outcomes while the main objective of our study has been to analyse the implementation process to ABCDE and ABCDEF bundles in terms of effectiveness, experiences and behaviors.^[18] Furthermore, in this systematic review, we have summarized the effects of the care bundles on ten clinical outcomes, including delirium.

A recent study has shown a low implementation of the ABCDEF bundle for critically ill patients with COVID-19

infection.^[41] The combination of a novel disease, resource limitations, and risks to medical personnel health have created new barriers and opportunities to implementing the ABCDEF bundle.^[42]

4.3. Strengths and limitations

The strengths of this study include the description of intervention strategies, barriers and facilitators that can reduce possible obstacles to implementation and promote more effective

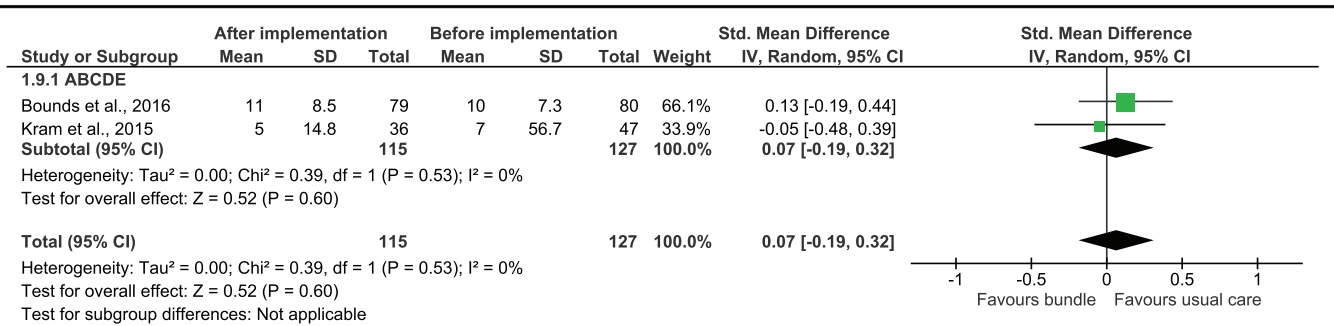


Figure 10. Forest plot summarizing the effects of ABCDE bundle implementation for hospital length of stay outcome, in number of days. ABCDE=Awakening and Breathing Coordination of daily sedation and ventilator removal trials, Delirium monitoring and management, and Early mobility and exercise.

planning. Twenty primary studies were included, involving about 31,604 participants, including interviewed professionals and patients, with possible overlaps, carried out in different contexts and on five continents.

Limitations to discuss the implementation process, barriers, facilitators, changes in health professionals perception and attitudes have come predominantly from methodological designs once that for qualitative approach the outcomes were many times self-reported and not directly observed, surveys may have interpretation bias and the timing of the site visits may have influenced participant's perceptions of barriers and facilitators.

To evaluate the effectiveness and safety of the ABCDE and ABCDEF care bundles, methodological limitations were predominantly due to the fact that most of the quantitative studies included had a before-after design, without a control group, and failed to analyse the risks for patients. Given the quality of the studies included, their conclusions should be confirmed by future studies involving larger samples, confounders control, and designs with greater methodological rigor, especially randomized controlled trials. Also, primary studies did not always detail the guidelines implemented in each institution.

It is important to highlight these points are especially relevant for the ABCDEF bundle since few studies have been published regarding it.

4.4. Implications for clinical practice

The importance of care bundles stems from the evidence that supports best practices. Since the proposed interventions are supported by the best evidence, the uncertainties and controversies about implementation are reduced.

Although meta-analysis indicated benefits of implementing ABCDE and ABCDEF care bundles for most of the outcomes evaluated, it was not possible to make assertive conclusions about the effectiveness and safety of the bundles.

However, more relevant than the choice between one care bundle or another, it is each institution to ensure the effective project planning and the resources for the implementation process, in order to guarantee adherence to and support of the practice over time.

The effort to implement the bundles from an inter and multidisciplinary perspective, involving (besides physicians and nursing team) other professionals (physiotherapists, occupational therapists, pharmacists, social workers, psychologists, and managers), is highly recommended and improves both attitudes and behaviour, promoting better clinical results.

4.5. Implications for research

More appropriate study designs are needed to adequately measure the effectiveness of the bundles to reduce confounders related to the clinical condition and prognosis of patients. The conducting of randomized controlled trials involving a greater number of patients can better determine the effectiveness and safety of these care bundles.

Studies need to involve not only managers of ICU areas, but professionals involved in the daily routine, besides direct observation of ICU practices. Investigations assessing larger samples of physical therapists, pharmacists, nursing assistants and technicians, as well as exploring the relationship between personal and institutional attitudes towards bundle implementation could also increase knowledge about the process. In the case of implementation of the ABCDEF bundle, the involvement of family members, their beliefs and behaviours should also be taken into account, along with the participation of psychologists, occupational therapists and social workers.

Studies extrapolating these findings, regardless of hospital or ICU size, are also necessary. Prospective studies, in turn, can determine whether interventions influencing professionals' attitudes in relation to workload and the viability of the implementation process result in better adherence to bundles.

Other important gaps are research based on adequate theoretical models and conceptual frameworks, the lack of studies incorporating economic evaluations, comparing other ICU care protocols, and involving outcomes with longer follow-up after ICU liberation.

5. Conclusion

The primary studies included in this systematic review demonstrated potential benefits of the processes of implementing the ABCDE and ABCDEF care bundles in the ICU.

The qualitative information can contribute to implementation process planning and execution, based on the body of evidence and knowledge gathered.

Strategies involving distribution of educational materials, educational meetings and interventions tailored to the desired objective proved the most common. These strategies should be supported by an appropriate theoretical model for the institution's scenario, considering factors such as organizational culture, willingness to change and its technical and human resources that can influence implementation. Therefore, ways of overcoming communication barriers, lack of planning, excessive documentation and fear of risks to patients should be sought. On

the other hand, greater involvement and support of the management, existence of a multiprofessional team, investment in training and capacity-building oriented to practice can lead to successful implementation.

The process of implementing the ABCDE and ABCDEF bundles is likely to provide better results than usual care, especially for the outcomes ICU length of stay, time on mechanical ventilation, delirium, ICU and hospital mortality and early mobilization. However, further studies with greater methodological rigor should be conducted to corroborate these findings.

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