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Care bundles for improving outcomes in patients with COVID-19 or related conditions in intensive care – a rapid scoping review (Review)

Smith V, Devane D, Nichol A, Roche D

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[Prototype Review]

Care bundles for improving outcomes in patients with COVID-19 or related conditions in intensive care – a rapid scoping review

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ABSTRACT

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the strain of coronavirus that causes coronavirus disease 2019 (COVID-19) can cause serious illness in some people resulting in admission to intensive care units (ICU) and frequently, ventilatory support for acute respiratory failure. Evaluating ICU care, and what is effective in improving outcomes for these patients is critical. Care bundles, a small set of evidence-based interventions, delivered together consistently, may improve patient outcomes. To identify the extent of the available evidence on the use of care bundles in patients with COVID-19 in the ICU, the World Health Organization (WHO) commissioned a scoping review to inform WHO guideline discussions. This review does not assess the effectiveness of the findings, assess risk of bias, or assess the certainty of the evidence (GRADE). As this review was commissioned to inform guideline discussions, it was done rapidly over a three-week period from 26 October to 18 November 2020.

Objectives

To identify and describe the available evidence on the use of care bundles in the ICU for patients with COVID-19 or related conditions (acute respiratory distress syndrome (ARDS) viral pneumonia or pneumonitis), or both. In carrying out the review the focus was on characterising the evidence base and not evaluating the effectiveness or safety of the care bundles or their component parts.

Search methods

We searched MEDLINE, Embase, the Cochrane Library (CENTRAL and the Cochrane COVID-19 Study Register) and the WHO International Clinical Trials Registry Platform on 26 October 2020.

Selection criteria

Studies of all designs that reported on patients who are critically ill with COVID-19, ARDS, viral pneumonia or pneumonitis, in the ICU setting, where a care bundle was implemented in providing care, were eligible for inclusion. One review author (VS) screened all records on title and abstract. A second review author (DR) checked 20% of excluded and included records; agreement was 99.4% and 100% respectively on exclude/include decisions. Two review authors (VS and DR) independently screened all records at full-text level. VS and DR resolved any disagreements through discussion and consensus, or referral to a third review author (AN) as required.

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Data collection and analysis

One review author (VS) extracted the data and a second review author (DR) checked 20% of this for accuracy. As the review was not designed to synthesise effectiveness data, assess risk of bias, or characterise the certainty of the evidence (GRADE), we mapped the extracted data and presented them in tabular format based on the patient condition; that is patients with confirmed or suspected COVID-19, patients with ARDS, patients with any influenza or viral pneumonia, patients with severe respiratory failure, and patients with mixed conditions. We have also provided a narrative summary of the findings from the included studies.

Main results

We included 21 studies and identified three ongoing studies. The studies were of variable designs and included a systematic review of standardised approaches to caring for critically ill patients in ICU, including but not exclusive to care bundles (1 study), a randomised trial (1 study), prospective and retrospective cohort studies (4 studies), before and after studies (7 studies), observational quality improvement reports (4 studies), case series/case reports (3 studies) and audit (1 study). The studies were conducted in eight countries, most commonly China (5 studies) and the USA (4 studies), were published between 1999 and 2020, and involved over 2000 participants in total. Studies categorised participant conditions patients with confirmed or suspected COVID-19 (7 studies), patients with ARDS (7 studies), patients with another influenza or viral pneumonia (5 studies), patients with severe respiratory failure (1 study), and patients with mixed conditions (1 study).

The care bundles described in the studies involved multiple diverse practices. Guidance on ventilator settings (10 studies), restrictive fluid management (8 studies), sedation (7 studies) and prone positioning (7 studies) were identified most frequently, while only one study mentioned chest X-ray.

None of the included studies reported the prespecified outcomes ICU-acquired weakness (muscle wasting, weight loss) and users' experience adapting care bundles. Of the remaining prespecified outcomes, 14 studies reported death in ICU, nine reported days of ventilation (or ventilator-free days), nine reported length of stay in ICU in days, five reported death in hospital, three reported length of stay in hospital in days, and three reported adherence to the bundle.

Authors' conclusions

This scoping review has identified 21 studies on care bundle use in critically ill patients in ICU with COVID-19, ARDS, viral influenza or pneumonia and severe respiratory failure. The data for patients with COVID-19 specifically are limited, derived mainly from observational quality improvement or clinical experiential accounts. Research is required, urgently, to further assess care bundle use and optimal components of these bundles in this patient cohort. The care bundles described were also varied, with guidance on ventilator settings described in 10 care bundles, while chest X-ray was part mentioned in one care bundle in one study only. None of the studies identified in this scoping review measured users' experience of adapting care bundles. Optimising care bundle implementation requires that the components of the care bundle are collectively and consistently applied. Data on challenges, barriers and facilitators to implementation are needed. A formal synthesis of the outcome data presented in this review and a critical appraisal of the evidence is required by a subsequent effectiveness review. This subsequent review should further explore effect estimates across the included studies.

PLAIN LANGUAGE SUMMARY

What evidence is there that care bundles improve outcomes for patients with COVID-19 in the intensive care setting?

What are care bundles?

Care bundles are a set of care practices that are carried out together (as a bundle) when delivering care to patients with the same condition or in the same healthcare setting. There are usually three to five practices in a bundle. Practices could include any aspect of patient care. For example, a bundle might include guidance on inserting breathing tubes, ventilator settings and care of ventilated patients. All the practices are ‘evidence-based’, that is, they are based on evidence that shows they are useful.

Why might care bundles help?

Some people with COVID-19 can become seriously ill and need intensive care. They will require respiratory (breathing) support and may need to be placed on a ventilator. Recent information suggests that around 26% of people with COVID-19 around the world have been admitted to an intensive care unit (ICU), and of these people, almost one-third have died.

For people with COVID-19 and related conditions (such as viral pneumonia, which also causes serious breathing difficulties), using care bundles will mean that practitioners carry out each care practice in the bundle, each time. Implementing the practices together, rather than individually, should result in better outcomes for patients. Use of care bundles should also reduce variation in how care is delivered and can improve the teamwork needed to provide high-quality health care, which also results in better patient outcomes.

Purpose of the review

The World Health Organization (WHO) commissioned this 'scoping' review to identify how much and what type of evidence is available on the use of care bundles for patients in the ICU setting suffering from COVID-19, acute respiratory distress syndrome (ARDS) or viral

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pneumonia. We wanted to identify and describe the studies that have been done and what they assessed, but not to appraise their quality or analyse their findings as we would usually do in a standard review. The WHO wanted to use this review to help develop their guidelines, so we prepared it quickly, over a three-week period from 26 October to 18 November 2020.

How did we identify and map the evidence?

We searched for all types of studies that reported on patients who were seriously ill with COVID-19, ARDS or viral pneumonia in the ICU setting, where a care bundle was used. Study participants could be any age. The care bundles could include any practices, but there had to be at least three in a bundle, they had to be evidence-based, and delivered together in the same way each time.

We grouped the studies according to their participants' health condition: confirmed or suspected COVID-19; ARDS; viral pneumonia; severe respiratory failure; and patients with a variety of these conditions.

What did we find?

We included 21 studies and identified three ongoing studies. The studies were conducted in eight countries, most commonly China and the USA, and were published between 1999 and 2020. Over 2000 participants in total were involved in the studies. Seven studies included patients with COVID-19, seven with ARDS, five with viral pneumonia, one with severe respiratory failure and one with a mixture of conditions.

The descriptions of the care bundles were varied, but most involved care practices related to breathing support or ventilator settings, or the positioning of a patient (e.g. face down), for ARDS and COVID-19. COVID-19-specific studies also focused on infection control and use of personal protective equipment (PPE). Some care bundles were specific to parts of the body such as eye or skin care.

Some of the 'evidence gaps' we identified were a lack of care bundles focused on preparing patients to leave the ICU, preventing infections caused by giving medicines intravenously (by drip), and the long-term effects of COVID-19. None of the studies looked at healthcare workers' experience of adapting care bundles.

Authors' conclusions

Information specific to patients with COVID-19 that compares patients receiving care bundles and not receiving care bundles is limited, and more research is needed. We also need information on how care bundles can best be implemented in practice, and the difficulties that might be associated with this. A separate review that assesses the quality of the evidence that we found in this review, and that combines and analyses the data, is required

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BACKGROUND

Description of the condition under consideration

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), was declared by the World Health Organization (WHO) to be a Public Health Emergency of International Concern in January 2020 and a pandemic in March 2020. The virus has since spread rapidly across the globe. As of 1 December 2020, around 64.2 million cases have been confirmed with almost 1.5 million associated deaths. Disease manifestation is variable, with some infected people remaining asymptomatic, and others suffering mild flu-like symptoms. For others however, the infection can cause serious illness, with organ dysfunction requiring admission to intensive care units (ICU) and frequently, ventilatory support for acute respiratory failure. A recent systematic review and meta-analysis identified a global ICU admission rate of 26% and an ICU mortality of 31% based on pooled data from 26 studies of patients with SARS-CoV-2 infection (Abate 2020).

Although a novel disease, COVID-19 shares some similarities with other pathological processes that intensive care clinicians are familiar with. For example, 60% to 70% of patients with COVID-19 admitted to the ICU will develop acute respiratory distress syndrome (ARDS), an inflammatory condition or 'pneumonitis', where the lung tissue becomes stiff and the transfer of oxygen and carbon dioxide across lung tissue is reduced (Fanelli 2013). In many cases for patients with COVID-19, ARDS manifestation is similar in nature to that of non-COVID-19-related ARDS (Grasselli 2020), as defined using the Berlin definition (The ARDS Definition Task Force 2012). Furthermore, management of COVID-19 in the ICU also shares many common processes and goals with the management of previous pandemic-associated viral pneumonias such as SARS-CoV-1 and the H1N1 virus. This is particularly so in relation to isolation precautions and prevention of viral spread.

Considering the impact of severe COVID-19 infection on both patients and ICU resources, understanding how care processes for these patients are organised and delivered is critical to improving outcomes. This scoping review will identify and describe the available evidence on the use of care bundles in the ICU for patients with COVID-19 and, given the similarities described above, for patients with ARDS, pneumonitis and viral pneumonia.

Description of the intervention

The concept of care bundles was introduced by the Institute for Health Improvement (IHI) in 2001 and is defined as;

“A small set of evidence-based interventions for a defined patient segment/population and care setting that, when implemented together, will result in significantly better outcomes than when implemented individually” (Resar 2012)

Care bundles are a way of re-organising and restructuring care processes by introducing a package of evidence-based practices, usually three to five practices (Homer 2012), aimed at reducing variability in how care is provided and delivered. It has been suggested also that they may be used as a tool to help bridge the gap between research and clinical practice (Fullbrook 2003). Care bundles may help improve the teamwork required to improve the reliability of care (Resar 2005). The most common implementation strategies used for care bundles include education sessions, reminders, and audit and feedback. A systematic review of implementation strategies, however, was unable to determine the most effective implementation strategy (Borgert 2015).

How the intervention might work

Previous systematic reviews have suggested that care bundles are effective in managing a range of conditions including ventilator-associated pneumonia (Resar 2005), sepsis, pressure ulcers and central line-associated blood stream infections (Lavallée 2017). It is important to note that a care bundle does not constitute comprehensive care; instead, a care bundle is an intervention where compliance with a core set of accepted evidence-based care interventions in a particular clinical setting are measured, incorporating the reorganisation of infrastructure, communication and team dynamics. The goal of a care bundle intervention is to improve overall patient care and patient outcomes (Resar 2012). The COVID-19 pandemic has required the restructuring of care processes in relation to isolation precautions and personal protective equipment (PPE) as well as the increased frequency of prone positioning of ventilated and non-ventilated patients in the ICU. Care bundles may have a role in reducing the variability of care and ensuring that patients with COVID-19 who require treatment in the ICU receive the same package of evidence-based interventions to improve outcomes.

Rationale for undertaking a scoping review

The WHO commissioned this scoping review as a means of identifying and describing the extent of the available evidence on the use of care bundles in the ICU (e.g. type of care bundles, type of studies, etc.) in patients with COVID-19, ARDS, viral pneumonia or pneumonitis. The purpose of this commissioned work was to inform WHO guideline discussions. The review was thus not designed to synthesise effectiveness data, assess risk of bias, or characterise the certainty of the evidence (GRADE); instead, the review focused on examining broadly the use of care bundles in the populations of interest, collating and mapping the types of published evidence on the topic, and examining the emerging evidence to determine whether a future effectiveness review should be considered (Lockwood 2019). The commissioned review, to have the information available for the Guideline Group's discussion meeting (2 December 2020), was conducted rapidly over a three-week period (26 October to 18 November 2020).

OBJECTIVES

To identify and describe the available evidence on the use of care bundles in the ICU for patients with COVID-19 or related conditions (ARDS, viral pneumonia or pneumonitis), or both. In carrying out the review the focus was on characterising the evidence base and not evaluating the effectiveness or safety of the care bundles or their component parts.

METHODS

Some methodological expectations for Cochrane intervention reviews are not necessary or suitable for scoping reviews, such as those relating to the synthesis of effectiveness data (with or without meta-analysis), assessment of bias across study results, and application of GRADE to assess confidence in synthesised results. In carrying out this scoping review, we primarily drew on methodological guidance from The *Joanna Briggs Institute (JBI)*

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Manual for Evidence Synthesis, Chapter 11: Scoping reviews (Godfrey 2020). Due to the condensed timeframe for this scoping review, we also consulted guidance to conduct rapid reviews developed by Cochrane Rapid Reviews Methods Group (Garritty 2020), to assist us in deciding which steps to abbreviate to expedite the review process. The review is reported using the PRISMA for Scoping Reviews extension (Tricco 2018; Appendix 1). The protocol for the review was peer reviewed in advance of commencing the review (Appendix 2).

Criteria for considering studies for the review

Types of studies

As this is a rapid scoping review, which sought to identify the scope and type of available evidence on the use of care bundles, we included studies of all designs: randomised controlled trials (RCTs), including quasi-RCTs and cluster-RCTs; prospective and retrospective observational cohort studies; controlled before-and-after studies; case-controlled studies; cross-sectional studies; case series; and systematic reviews. We considered studies of any duration and follow-up periods for inclusion. We excluded narrative literature reviews, letters, and correspondence reports unless they provided detailed information about a care bundle based on the results from either research or experiential clinical practice.

Types of participants

Patients with COVID-19, ARDS, viral pneumonia or pneumonitis who are critically ill in ICU, with or without invasive ventilation. We included populations of children (defined as under 18 years) and adult patients (v 18 years) and categorised them accordingly.

Types of interventions

The intervention of interest to the review was a care bundle. For the purposes of this review, we defined a care bundle as per the IHI definition of at least three (or more) evidence-informed practices delivered collectively and consistently to improve patient outcomes (Resar 2012). We excluded practices that may have been described as a bundle but did not meet the IHI minimum definition. Conversely, we considered for inclusion practices that were not explicitly defined as a 'bundle' but were implemented collectively as a bundle of care and met our definition of at least three evidence-informed practices. We also excluded care bundles that were designed and implemented for settings other than the ICU, or the ICU setting but for patients that did not have COVID-19, ARDS, viral pneumonia or pneumonitis. The comparator (where relevant) was no care bundle/standard care.

Types of outcome measures

The 'critical' and 'important' outcomes listed below were required by the WHO, who commissioned this review. We also included two 'additional scoping' outcomes that we considered relevant given the scoping nature of the review.

Critical outcomes

1. Death in ICU (within 30, 60, 90 days, and longer if data available), listed as one of three proposed minimal core outcomes by the WHO Working Group in the Clinical Characterisation and Management of COVID-19 infections (WHO 2020); accessible also via the COMET database (comet-initiative.org/Studies/Details/1538)
2. Days of ventilation (or ventilator-free days)
3. Length of stay in ICU (in days)

Important outcomes

1. Length of stay in hospital (in days)
2. Death in hospital (within 30 days, within 90 days, and longer if data available)
3. ICU-acquired weakness (muscle wasting, weight loss)

Additional 'scoping' outcomes

1. Rates of adherence to all components of the care bundle
2. User experiences in adapting care bundles

Electronic searches

We searched the following electronic sources for potentially relevant records on 26 October 2020.

1. Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 10) in the Cochrane Library (searched 26 Oct 2020)
2. OVID MEDLINE (R) (1946-October 2020) searched 26 October 2020
3. Embase via OVID Sp (1974-Oct 2020) searched 26 October 2020
4. Cochrane COVID-19 Study Register (covid-19.cochrane.org), searched 26 October 2020
5. World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch), searched 26 October 2020)
6. Epistemonikos (for systematic reviews; October 2020)

The electronic search strategy for this review was developed by a Cochrane Information Specialist, J Vendt, Cochrane Anaesthesia and Cochrane Emergency and Critical Care Groups. The search strategy was peer-reviewed (R Featherstone), and refined before implementation. The complete search strategy is presented in Appendix 3.

Searching other sources

As per interim guidance on the conduct of rapid reviews (Garritty 2020), we reviewed the reference lists of all included records to identify any additional, potentially eligible studies not captured by the electronic searches. We also examined the reference lists of systematic reviews, which were included for full-text screening to identify any additional, potentially relevant records. Although our intention in this scoping review was to include primary studies reporting on the topic of interest only, to assess the relevance of including Guidelines in our search strategy, we additionally searched the ECRI (Emergency Care Research Institute) guideline database (guidelines.ecri.org) on 29 October 2020. Initially, we searched the database using the term 'bundle', which yielded zero returns, and then 'COVID', which yielded 150 returns. We reviewed the first 20 of these records, none of which we deemed eligible for inclusion. We therefore did not proceed with searching guideline-specific databases.

Selection criteria

We selected all complete study records that met our inclusion criteria. In addition to these, we included records published in abstract format only if they were eligible and had usable data. If relevant, we also included ongoing studies, identifiable via MEDLINE and Embase 'ahead of print' records, the World Health

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Organization International Clinical Trials Registry Platform and the Cochrane COVID-19 Study Register, which also includes preprints. Although we did not apply any language restrictions to our search, we included relevant records where at least the abstract was in English and classified the report as 'abstract only, full text not in English' to highlight any non-English language full-text publications.

We initially screened all records on title and abstract as follows; one review author (VS) independently assessed for inclusion all the potential studies identified as a result of the search strategy. A second review author (DR) screened 20% of included and excluded abstracts to corroborate the accuracy of screening at this level. If agreement was less than 80%, the second review author would have dual-screened all abstracts. However, as agreement was 99.4% on excluded records and 100% on included records, this was not required. Two review authors (VS and DR) independently screened all records at full-text level. They resolved any disagreements through discussion and consensus. Given the rapid and scoping nature of this review, we did not contact individual study authors with eligibility queries; however, where necessary we consulted a third review author (AN) to confirm record inclusion/exclusion. All decisions taken during screening are documented and reported as per PRISMA for Scoping Reviews extension guidance (Tricco 2018; Appendix 1).

Data collection and analysis

One review author (VS) performed data extraction, which was checked by a second review author (DR), based on initially assessing a random selection of 20% of studies for data extraction accuracy. Had inaccuracies of more than 80% been identified, we would have conducted independent dual data extraction of all records. As accuracy agreement was almost 100%, with one data item only requiring a recheck, this was not needed. We extracted the following data, where available, from the included studies.

1. Record details, which included year, authors, title, journal and funding source
2. Study design, which included study methods, follow-up times, location of study/description of the study setting, study groups and sample sizes
3. Participant characteristics, which included age, gender, invasive/non-invasive ventilation and time in ICU
4. Intervention characteristics, which included a description of the care bundle, application, compliance to the care bundle and duration of the intervention
5. Comparator characteristics, where relevant, which included a description of standard care in the study setting
6. Outcomes assessed and the measurement tool used where relevant
7. Numerical data for outcomes of interest, or narrative data where relevant
8. Confounding factors (NRS) controlled for in each appropriate analysis presented

We extracted all data from the study records as reported or presented. We did not contact the study authors for additional details. If we identified a conflict between data reported across multiple sources for a single study; for example, between an abstract and full study record, we used the data from the main study report.

As per scoping review guidance (Godfrey 2020), we mapped the extracted data in tabular form and have provided a descriptive summary of the findings from the included studies. We mapped and reported the results as follows.

1. Description of included studies: summary descriptions and tabular presentation of the characteristics of the included studies are presented in the Characteristics of included studiestables. These details are also presented in aggregated format by patient condition (i.e. patients with suspected or confirmed COVID-19, patients with ARDS, patients with other influenza or pneumonia, patients with severe respiratory failure and patients with mixed conditions) (see Appendix 4). Details described include study aim, study design, dates studies were conducted, description of study settings, including country, description of study population, and funding sources (if any). A narrative summary of these details is also provided.
2. Description of the care bundles and comparators, where relevant: summary descriptions of the components of the care bundles described in the studies are provided in this section. We categorised the tabular details by type of patient condition for which the bundle was applied, by care bundle component, that is, the discrete practices involved across the care bundles, and by study design. An Additional File (osf.io/mfc6z), which provides the complete descriptions of the care bundles used in each included study has been provided to the WHO for purposes of completeness.
3. Descriptive summary and tabular presentation of results: this section maps the number of studies that reported each of the review's prespecified outcome measures, and presents this in tabular format. We categorised the results reported in the included studies and presented them according to the type of patient condition for which the care bundle was applied and by outcome. Detailed results, that is, data from numerical/statistical results, are provided in an Additional File to the WHO (osf.io/mfc6z). We did not apply GRADE assessments to the results and the numerical/statistical results do not form part of this scoping review to avoid the risk of interpretations of 'effectiveness'. A subsequent effectiveness review to formally synthesis the results and to explore these in-depth is required.

RESULTS

Results of the search

We identified 6399 records from the database searches and an additional nine records from other sources; six from reference lists of studies and three from reference lists of systematic reviews. Following removal of duplicate records (n = 1242), we screened 5166 records on title and abstract. Of these, we excluded 5031 as irrelevant, and assessed 135 at full-text level. Of these 135 records, we excluded 109 for the following reasons: 43 did not include participants with COVID-19 or a related condition; 31 were editorials, letters or literature reviews with no meaningful data; 15 did not describe a care bundle(s) as per the IHI definition; seven were further identified as duplicate records; six were not specific to an ICU setting; four were not in English, nor had they an abstract in English that we deemed eligible for inclusion; and three were abstracts that had insufficient information to determine their eligibility clearly. The Characteristics of excluded studies tables contains the references to these 109 studies, and the reasons for their exclusion. This resulted in the inclusion of 26 records reporting

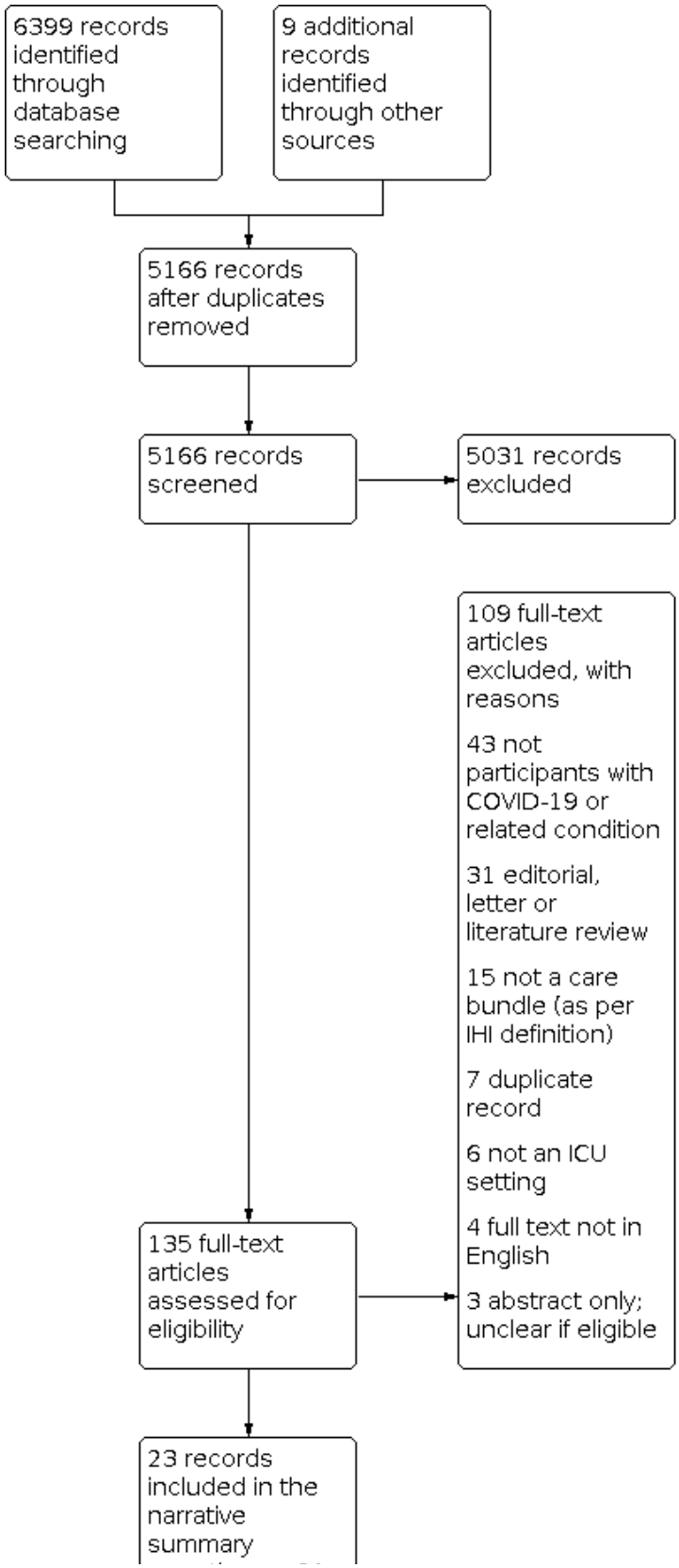
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on 24 studies; information on two studies were reported in multiple papers and we merged these with the overall main study reports (Peek 2009; Duggal 2020).

Of the 24 included studies, six were abstract reports only (Mellor 1999; Jung 2012; Thomas 2014; Yang 2014; Yue 2015; Wang 2018). Three of these had associated full-text papers, but as these were published in Chinese, we extracted data from the English language abstract publication only (Yang 2014; Yue 2015; Wang 2018). A further three studies were trial registration records and we identified them as ongoing studies (NCT04070053; NCT04459819; NCT03504176). We subsequently removed these records from further analyses and provide details of them in the Ongoing studies section. We thus extracted and summarised data from 21 studies in this rapid scoping review. Figure 1 illustrates the searching and selection process.

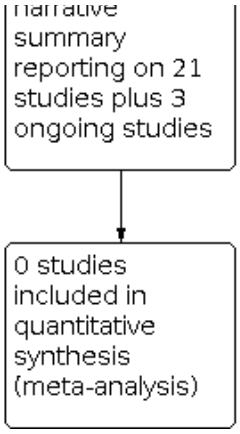
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Figure 1. Study flow diagram



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Figure 1. (Continued)



Description of included studies

Of the 21 studies included in the review, five were conducted in China (Guo 2014; Yang 2014; Yue 2015; Wang 2018; Peng 2020), four in the USA (Albutt 2020; Duggal 2020; Janz 2020; Singh 2020), three in the UK (Peek 2009; Thomas 2014; Ting 2020), two in Chile (Cornejo 2011; Diaz 2018), and one study in each of India (Balakrishnan 2020), Germany (Luedike 2015), France (Georges 2013) and Korea (Choi 2020). For the remaining three studies, two did not describe the setting (Mellor 1999; Jung 2012), and the third was a systematic review that evaluated the impact of standardised care management measures implemented within the first 24 hours in the ICU or emergency department settings (Phua 2016). Although the Phua 2016 review targeted populations with severe community-acquired pneumonia, the patient conditions described in the included studies (n = 14 key studies) varied from community-acquired pneumonia, ARDS and septic shock.

The reported number of patients in the 19 studies in this review that provided participant numbers was 2102 critically ill patients. The dates that the studies were published ranged from 1999 to 2020 and the study conduct dates ranged from 1995 to April 2020. Six studies reported funding sources (Peek 2009; Cornejo 2011; Guo 2014; Luedike 2015; Diaz 2018; Janz 2020), two stated that their work was unfunded (Phua 2016; Balakrishnan 2020), and the remaining 13 studies did not provide details on funding. One included study was specific to children (under 18 years of age; Diaz 2018), and the remaining studies all included adult populations only.

Patient conditions across the included studies varied and we categorised them as: patients with suspected or confirmed COVID-19 (7 studies; Albutt 2020; Balakrishnan 2020; Choi 2020; Janz 2020; Peng 2020; Singh 2020; Ting 2020); patients with ARDS (7 studies; Mellor 1999; Jung 2012; Yang 2014; Luedike 2015; Yue 2015; Diaz 2018; Duggal 2020); patients with other influenza or viral pneumonia (5 studies; Cornejo 2011; Georges 2013; Guo 2014; Thomas 2014; Wang 2018); patients with severe respiratory failure (1 study; Peek 2009); and patients with mixed conditions (1 study; Phua 2016).

The designs of the 21 included studies ranged as follows: systematic review of standardised care measures in the ICU or emergency department setting (1 study; Phua 2016); RCT (1 study; Peek 2009); prospective controlled study (1 study; Yang 2014), before-and-after studies (7 studies; Georges 2013; Guo 2014; Luedike 2015; Yue 2015; Diaz 2018; Wang 2018; Duggal 2020); prospective observational cohort study (1 study; Jung 2012); retrospective observational cohort studies (two studies; Choi 2020; Janz 2020); case series/case report (three studies; Peng 2020; Singh 2020; Ting 2020); quality improvement analysis/descriptive reports (four studies; Mellor 1999; Cornejo 2011; Albutt 2020; Balakrishnan 2020); and audit (one study; Thomas 2014).

These summary characteristics of these 21 included studies are presented in he Characteristics of included studies tables, and in Appendix 4 in an aggregated format by patient condition.

Description of care bundles

The care bundles and included evidence-based practices described in the included studies were variable. Of the seven care bundles that were explicitly implemented for patients with confirmed or suspected COVID-19, one was based on a core team (the COBRA team) performing bundled procedures, involving arterial lines, central venous catheters and orogastric/nasogastric tubes (Albutt 2020), three involved intubation guidance, ventilation care or ventilator settings (Balakrishnan 2020; Janz 2020; Peng 2020), one was specific to pressure injury care (Singh 2020), and one was specific to eye care (Ting 2020). The remaining bundle consisted of mixed practices related to tracheostomy, enhanced personal protective equipment (PPE), temporary negative pressure ICU, rotating ear-nose-throat (ENT) surgeons and active monitoring for healthcare workers (Choi 2020).

Of the seven care bundles that were explicitly implemented for patients with ARDS, five described aspects related to ventilator settings or care, or respiratory support (Mellor 1999; Jung 2012; Luedike 2015; Yue 2015; Duggal 2020). Four care bundles included prone positioning (Mellor 1999; Jung 2012; Luedike 2015; Duggal 2020). Five care bundles included fluid restriction strategies (Mellor 1999; Luedike 2015; Yue 2015; Diaz 2018; Duggal 2020). Four care bundles involved vasoactive drugs (Mellor 1999; Jung 2012; Diaz 2018; Duggal 2020). Two included antibiotic therapy (Mellor 1999; Luedike 2015). Extracorporeal membrane oxygenation (ECMO) as part of rescue therapy was included in four care bundles (Mellor 1999; Jung 2012; Luedike 2015; Duggal 2020). Use of neuromuscular blocking agents or sedation plans was described in three care bundles (Luedike 2015; Yue 2015; Diaz 2018). Elements related to patient nutrition (e.g. early enteral feeds) were described in two care bundles (Luedike 2015; Diaz 2018), while inhaled nitric oxide

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therapy (Mellor 1999), and continuous blood purification treatment (Yue 2015), were each described in one care bundle. The care bundle in the Yang 2014 study is described as a ventilator bundle; however, the individual practices comprising the bundle were not described.

Five studies described care bundles for patients with another influenza or viral pneumonia, for example, avian flu H1N1 and community-acquired pneumonia (Cornejo 2011; Georges 2013; Thomas 2014; Guo 2014; Wang 2018). Elements of these bundles were more varied. Guo 2014 described the 6- and 12-hour severe sepsis bundle involving blood cultures, antibiotics within one hour, and various other intravenous fluid or medication therapies as might be required, for example, vasoactive drugs, packed red blood cells, low dosage corticosteroids, etc. Georges 2013, Thomas 2014 and Wang 2018 also included antibiotic therapy as part of their bundles, with Thomas 2014 additionally including blood and sputum cultures. Fluid restrictive treatment was described in two care bundles (Cornejo 2011; Wang 2018). Nutritional support and early enteral feeding comprised part of two care bundles (Cornejo 2011; Wang 2018). The following practices were each included in one care bundle; prone positioning (Cornejo 2011), ECMO as rescue therapy (Cornejo 2011), early exercise and mobilisation (Cornejo 2011), chest X-ray (Georges 2013), and isolation (Wang 2018).

Peek 2009 described a care bundle for patients with severe acute respiratory failure based on a series of practices including recommended ventilator settings, diuresis to dry weight, prone positioning and full nutrition. The included systematic review, which reported on standardised management measures within 24 hours in patients who are critically ill in ICU (and in the emergency department), included one study where a care bundle was described for patients in the ICU that had community-acquired pneumonia (Phua 2016). The care bundle consisted of antibiotic therapy, fluids and vasoactive agents.

Figure 2 delineates the discrete practices within the care bundles across the 21 studies and maps these by patient condition and study design. An Additional File describing the complete details of the care bundles in each of the 21 included studies has been prepared and provided to the WHO for completeness. This Additional File, titled 'Detailed descriptions of the care bundles', is available on the Open Science Framework platform (osf.io/mfc6z).

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Figure 2. Care bundle interventions mapped by patient condition and study design

		COVID-19 N = 7 studies		ARDS N = 7 studies		Influenza or viral pneumonia N = 5 studies		ARF N = 1 study	Mixed N = 1 study
Studies	**Care bundle component**								
Balakrishnan 2020; Peng 2020; Mellor 1999; Jung 2012; Luedike 2015; Duggal 2020;	Ventilator settings	O	Ca	CP BA	BA O	BA O	BA	RT	
Mellor 1999; Luedike 2015; Yue 2015; Diaz 2018; Duggal 2020; Cornejo 2011; Wang 2018; Peek 2009	Restrictive fluid management			BA BA O	BA BA	BA	O	RT	
Balakrishnan 2020; Luedike 2015; Yue 2015; Diaz 2018; Duggal 2020; Cornejo 2011; Wang 2018	Sedation	O	BA BA	BA BA	BA	O			
Peng 2020; Mellor 1999; Jung 2012; Luedike 2015; Duggal 2020; Cornejo 2011; Peek	Prone positioning	Ca		CP BA	BA O	O		RT	
Mellor 1999; Jung 2012; Diaz 2018; Duggal 2020; Georges 2013; Guo 2014; Phua 2016	Vasoactive drugs			CP BA	BA O	BA	BA		SR
Mellor 1999; Luedike 2015; Diaz 2018; Thomas 2013; Guo 2014; Phua 2016	Antibiotics			BA BA	O	BA	BA		SR
Balakrishnan 2020; Peng 2020; Janz 2020; Choi 2020	Intubation/respiratory support	CR O	CR Ca	BA		BA			
Mellor 1999; Jung 2012; Luedike 2015; Duggal 2020; Cornejo 2011; Peek 2009	ECMO as rescue therapy			CP BA	BA O	O		RT	
Singh 2020; Mellor 1999; Luedike 2015; Diaz 2018; Cornejo 2011; Wang 2018	Nutrition	Ca		BA O	BA	BA	O	RT	
Diaz 2018; Georges 2013; Guo 2014; Phua 2016	IV fluid therapy			BA		BA	BA		SR
Albutt 2020; Balakrishnan 2020; Choi 2020	Core team	CR O	O						
Luedike 2015; Guo 2014; Thomas 2014	Blood or sputum cultures			BA		BA	A		
Balakrishnan 2020; Choi 2020; Wang 2018	Isolation/enhanced PPE/enhanced infection contr	CR	O			BA			
Janz 2020; Georges 2013	Extubating	CR				BA			
Singh 2020; Cornejo 2011	Pressure ulcer prevention	Ca				O			
Thomas 2013	Chest X-ray					A			
Georges 2013	Blood transfusion guidance					BA	BA		
Georges 2013; Guo 2014	Corticosteroids					BA	BA		
Albutt 2020	Arterial lines/ other internal catheters	O							
Cornejo 2011	Mobilisation					O			
Ting 2020	Eye care	Ca							
Choi 2020	Temporary negative pressure ICU	CR							
Choi 2020	Active monitoring for healthcare workers	CR							

ARDS: acute respiratory distress syndrome; **ARF:** acute respiratory failure; **ECMO:** extracorporeal membrane oxygenation; **IV:** intravenous

A: audit
BA: before and after study
Ca: case report
CR/CP: cohort retrospective/cohort prospective
O: observational
RT: randomised controlled trial
SR: systematic review

Number and type of studies that report the review's prespecified outcomes

The prespecified outcomes of ICU-acquired weakness (muscle wasting, weight loss) and users' experience in adapting care bundles were not reported in any of the included studies. For the other prespecified outcomes, the numbers of studies that reported on these are as follows: death in ICU (14 studies); days of ventilation or ventilator-free days (nine studies); length of stay ICU in days (nine studies); death in hospital (five studies); length of stay in hospital in days (three studies); and adherence to the bundle (four studies).

Figure 3 maps the outcomes reported in each study by patient condition and study design. An Additional File that provides the numerical/statistical results as reported in the included studies has been prepared and submitted to the WHO. This Additional File, titled 'Outcome results', is available for view on the Open Science Framework platform (osf.io/mfc6z). These results have not undergone a formal synthesis, 'Risk of bias' assessment or GRADE assessments. A subsequent effectiveness review is required to explore in depth the point estimates across the included studies.

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Figure 3. Outcome results mapped by patient condition and study design

Studies	Pre-specified outcomes	COVID-19 N = 7 studies	ARDS N = 7 studies	Influenza or viral pneumonia N = 5 studies	ARF N = 1 study	Mixed N = 1 study
Peng 2020; Singh 2020; Diaz 2018; Duggal 2020; Jung 2018; Luedike 2015; Mellor 1999; Yang 2014; Yue 2015; Cornejo 2011; Wang 2018; Georges 2013; Thomas 2013; Phua 2016	Death in ICU	Ca, Ca	CP, CP, BA, BA, BA, O	BA, BA, O, A		SR
Janz 2020; Peng 2020; Singh 2020; Diaz 2018; Duggal 2020; Yang 2014; Yue 2015; Guo 2014; Georges 2013	Days on ventilation (or ventilator free days)	CR, Ca, Ca	BA, CP, BA, BA	BA, BA		
Peng 2020; Diaz 2018; Duggal 2020; Jung 2019; Yang 2014; Yue 2015; Cornejo 2011; Wang 2018; Georges 2013	Length of stay in ICU	Ca	CP, CP, BA, BA, BA	BA, O, BA		
Janz 2020; Duggal 2020; Mellor 1999; Guo 2014; Peek 2009	Death in hospital	CR	BA, O	BA	RT	
Duggal 2020; Cornejo 2011; Wang 2018	Length of stay in hospital		BA	BA, O		
Duggal 2020; Luedike 2015; Guo 2014; Thomas 2013	Adherence to the bundle		BA, BA	BA, A		

Study design key

Systematic review	SR	Randomised controlled trial	RT	Before and after study	BA	Audit	A
Cohort retrospective; Cohort prospective	CR; CP	Observational	O	Case report/case/series	Ca		

ARDS = acute respiratory distress syndrome

ARF = acute respiratory failure

Patients with confirmed or suspected COVID-19

Of the seven studies involving patients with confirmed or suspected COVID-19, four did not report on any of the review's prespecified outcomes (Albutt 2020; Balakrishnan 2020; Choi 2020; Ting 2020). This is mainly due to the study designs, where the majority are observational or descriptive quality improvement initiatives or analyses, reporting on clinical care experiences during COVID-19 rather than on collected patient outcome data. Of the three studies that did report outcome data, two report death in ICU (Peng 2020; Singh 2020), all three report days of ventilation (Janz 2020; Peng 2020; Singh 2020), one reports length of stay in ICU (Peng 2020), and one reports death in hospital (28-day mortality; Janz 2020). See Figure 3. The studies did not report the outcomes length of stay in hospital, ICU-acquired weakness, adherence and user experiences.

Patients with ARDS

Of the seven studies involving patients with ARDS, all reported on the outcome death in ICU (Mellor 1999; Jung 2012; Yang 2014; Luedike 2015; Yue 2015; Diaz 2018; Duggal 2020). Four reported on days of ventilation (Yang 2014; Yue 2015; Diaz 2018; Duggal 2020). Five reported on length of stay in ICU (Jung 2012; Yang 2014; Yue 2015; Diaz 2018; Duggal 2020). Three reported on death in hospital (Mellor 1999; Jung 2012; Duggal 2020). Only Duggal 2020 reported length of stay in hospital. Two studies reported adherence to elements of the bundles (Luedike 2015; Duggal 2020). None of the included studies reported on ICU-acquired muscle weakness or users' experience adapting care bundles (Figure 3).

Patients with another influenza or viral pneumonia

Of the five studies involving patients with another influenza or viral pneumonia, four reported death in ICU (Cornejo 2011; Georges 2013; Thomas 2014; Wang 2018), two reported days of ventilation (Georges 2013; Guo 2014), three reported length of stay in ICU (Cornejo 2011; Georges 2013; Wang 2018), one reported death in hospital (Guo 2014), two reported length of stay in hospital (Cornejo 2011; Wang 2018), and two reported adherence to the care bundle (Thomas 2014; Guo 2014). None of the five studies reported ICU-acquired muscle-wasting or users' experience of adapting the care bundle (Figure 3).

Patients with severe respiratory failure

Peek 2009 reports on a multicentre randomised trial in adult patients with severe but potentially reversible respiratory failure, defined as a Murray score above 3.0, or uncompensated hypercapnoea with a pH less than 7.20. The care bundle involved varied practices including ventilator-specific settings, prone positioning, full nutrition, diuresis and ECMO in non-responders within 12 hours. The bundle is compared to conventional management based on best practices at the study centre. The outcome of mortality is the only relevant outcome to this review reported in the study.

Mixed category

One study is included in this category. Phua 2016 reports a systematic review of varied standardised management measures implemented within 24 hours in patients in the ICU or emergency department settings. Although the review targeted

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studies involving populations specifically with community-acquired pneumonia, included studies also included patients with ARDS, sepsis and septic shock. The review refers to one study specific to care bundle use in ICU and reports the outcome mortality only. The referenced study is also included in this systematic review (Georges 2013).

DISCUSSION

This scoping review provides an overview of the type of available evidence and associated findings on the use of care bundles in the ICU for patients with SARS-CoV-2, ARDS, influenza or viral pneumonia, and severe respiratory failure. The included studies were mainly before and after studies exploring the effectiveness of care bundles for improving patient outcomes, followed by quality improvement/descriptive analytical reports or case series/case reports. Fourteen of the 21 studies included patients with suspected or confirmed COVID-19 or patients with ARDS. A further five studies included patients with another influenza type of viral pneumonia. Studies varied in size ranging from a case report based on one COVID-19 patient (Ting 2020), to a before and after study involving 450 patients with ARDS (Duggal 2020), and were mainly conducted in high-income countries. The care bundles described in this review, although varied, predominantly focused on the ventilation strategies of the ARDSnet guidelines, which have been adopted clinically as a suitable approach to caring for patients with COVID-19 who require mechanical ventilation. Furthermore, the care bundles explicit to patients with COVID-19 focused on procedural aspects of care, including intubation, tracheostomy and invasive arterial and central venous line placement, with emphasis on infection control and use of PPE for minimisation of transmission of the virus as common elements. Few of the studies explicit to patients with COVID-19 reported on our review's prespecified outcome measures. Furthermore, we extracted and reported on outcomes that the commissioner of this review, the WHO, deemed critical and important. Although we added two additional outcomes related to the scoping nature of the review, we did not seek or extract any additional outcomes that might have been reported in the included studies (e.g. outcomes related to sedation and delirium, pain, exercise/mobility, etc.). As such it is unclear if further gaps in the evidence exist for other outcomes as these have not been mapped as part of this review.

This scoping review did not identify any studies that investigated the use of many established care bundles such as those implemented to increase liberation from ICU (Marra 2017), and reduce central venous catheter-associated blood stream infection in the wider ICU patient population (Pronovost 2010). It is likely that these care bundles are being implemented for patients with COVID-19, but due to their universal nature, they have not been investigated in this patient cohort specifically. We did not identify any care bundles that target the long-term effects of COVID-19, many of which can last for months after ICU admission, and can have a significant impact on patient outcome as well as bearing a substantial social and economic cost (Hosey 2020).

In the scoping process we identified two studies that described bundled pharmacotherapy treatment, including anti-viral medication and traditional Chinese medicine for patients with COVID-19. As these bundles lacked evidence, they did not meet the criteria necessary to be considered a care bundle. We did not identify any studies that looked at care bundles that incorporated specific evidenced-based therapeutic interventions such as corticosteroids in patients with COVID-19 (The Recovery Collaborative Group 2020). Given the rapidly changing landscape of therapeutic interventions in COVID-19 treatment, care bundles including pharmacological therapies specifically for the treatment of COVID-19 are likely to remain controversial. It is clear from this scoping review that further investigation of the use of care bundles in patients with COVID-19 is required, with the use of a core outcome set to ensure that meaningful data are obtained. This should include research on the effect of established care bundles in this specific patient population as well as care bundles specifically developed for COVID-19.

There were some challenges to and limitations in our review. Given the scoping nature of this review we included studies with both COVID-19 and other viral pneumonias. It is possible, but unlikely, that a care bundle's effect on a non-COVID viral pneumonia would have significantly different results than on a SARS-CoV viral pneumonia. Furthermore, the timelines for completion of the review meant that we took some decisions to do the work rapidly while balancing usefulness and timeliness of the review with methodological rigour. While we are confident in our findings, they are in the context that one author screened and extracted all data. Nevertheless, a second author did verify 20% of all excluded material, and independently screened all papers included at the full-text screening stage, with few inconsistencies identified.

Implications for a subsequent effectiveness review

This review was commissioned by the WHO as a scoping review to identify the available evidence on the use of care bundles in the ICU for patients with COVID-19, ARDS, influenza or viral pneumonia, and severe respiratory failure. We mapped the reported outcome results to patient conditions and by study design. A formal synthesis of the results and a critical appraisal of the evidence is required to further explore effect estimates across the included studies.

AUTHORS' CONCLUSIONS

This scoping review identified 21 studies, and three ongoing studies on the use of care bundles in critically ill patients in the ICU with COVID-19, ARDS, influenza or viral pneumonia, severe acute respiratory failure, and mixed conditions. The data for patients with COVID-19 specifically are limited, and the care bundles described were varied. Research is required, rapidly, to further assess care bundle use and optimum components of these bundles in this patient cohort. None of the studies identified in this scoping review measured users' experience of adapting care bundles. For care bundles to be effectively implemented, the components of the bundle must be collectively and consistently applied. Data on the challenges, barriers and facilitators to care bundle use in the ICU are needed. A formal synthesis of the outcome data presented in this review and a critical appraisal of the evidence would be required in a subsequent effectiveness review. This subsequent review would further explore effect estimates across the included studies.

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WHO Working Group on the Clinical Characterisation and Management of COVID-19 infection. A minimal common outcome measure set for COVID-19 clinical research. *Lancet Infectious Diseases* 2020;**20**:e192-97.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Albutt 2020

Study characteristics	
Description of study	Study aim: "To share the design, creation, and preliminary outcomes of a streamlined multidisciplinary procedure team at our institution: the COVID-19 Bundled Response for Access (COBRA) team" Study design: observational (quality improvement) Dates study conducted: April 2020 (for 2 weeks) Setting: Massachusetts General Hospital ICU; in the first few weeks of the pandemic, several medical and surgical floors were converted into surge ICUs
Participants	Critically ill patients with COVID-19; n = 102; median age 60 years, 68.6% male, mainly white (37.3%) or Hispanic (41.2%) and median BMI of 31.2
Notes	Funding source: none reported

Balakrishnan 2020

Study characteristics	

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Balakrishnan 2020 *(Continued)*

Description of study	Study aim: "To describe a step-by-step approach to endotracheal intubation of critically ill patients with suspected or confirmed COVID-19 and other airborne diseases to limit the risk of exposure to healthcare providers" Study design: descriptive (quality improvement) Dates study conducted: not reported Setting: Department of Emergency Medicine, Kasturba Medical College, Manipal, India
Participants	Critically ill patients with suspected or confirmed COVID-19 and other airborne diseases (number not reported)
Notes	Funding source: unfunded

Choi 2020

Study characteristics	
Description of study	Study aim: "To describe our experience and protocol for surgical tracheostomy in patients with COVID-19" Study design: descriptive (quality improvement analysis) Dates study conducted: May-July 2015 (MERS outbreak); March 2020 (COVID-19 outbreak) Setting: not described (Republic of Korea)
Participants	8 patients with MERS and one with COVID-19 who had undergone surgical tracheostomy; n = 9
Notes	Funding source: none reported

Cornejo 2011

Study characteristics	
Description of study	Study aim: "To report the experience of a critical care team in assessing a strict multifaceted management protocol, incorporating evidence-based strategies in the form of ventilatory and non-ventilatory strategies, to treat the most severely ill subset of patients with influenza A(H1N1) virus infection" Study design: observational (quality improvement) Dates study conducted: 13 June-27 August 2009 Setting: a critical care service, which includes 55 beds, 12 in ICU and 43 in intermediate care units in Hospital Clínico Universidad de Chile, Santiago
Participants	All influenza patients requiring MV were transferred to ICU for management and isolation; n = 19 required MV and were the study cohort; mean age 41 ± 13 years, 10 participants were female; 15 participants had pre-existing medical conditions, and in 4 participants, these were severe comorbidities
Notes	Funding source: partially funded by Research Grant Fondecyt N°. 11070156, Chilean government

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Diaz 2018

Study characteristics	
Description of study	Study aim: "To implement a bundle strategy to prevent FO in children with sepsis and PARDS and to compare the outcomes with a historical cohort" Study design: before and after Dates study conducted: June-December 2014 (historical cohort); January-December 2016 (study cohort) Setting: PICU at Hospital Padre Hurtado, Chile; 12-bed general medical and surgical PICU
Participants	All patients < 24 months who received MV and fulfilled the PARDS and sepsis criteria; n = 76 (37 intervention, 39 control), 54% vs 64% male, age range 2-11 vs 1-7; 38% vs 49% had comorbidity
Notes	Funding source: partially funded by Fondo Nacional de Desarrollo Científicoy Tecnológico

Duggal 2020

Study characteristics	
Description of study	Study aim: "To study the impact of an evidence-based ARDS management on outcomes" Study design: before and after Dates study conducted: January 2012-May 2014 (pre-intervention); June 2015-June 2017 (intervention) Setting: a 64-bed closed medical ICU at Cleveland Clinic main campus hospital (Cleveland, Ohio, USA)
Participants	Patients with a diagnosis of ARDS based on the Berlin definition; n = 450 (118 intervention, 332 control). Intervention group participants had significantly higher severity of illness at the time of diagnosis of ARDS
Notes	Funding source: none reported

Georges 2013

Study characteristics	
Description of study	Study aim: "To assess the prognosis of patients admitted to the ICU for CAP after implementation of new care processes" Study design: before and after Dates study conducted: 1995-2000 (control); 2005-2010 (intervention) Setting: 16-bed multidisciplinary ICU in an urban teaching hospital; Toutcoing Hospital, France
Participants	All consecutive patients ≥ 18 years of age with severe CAP; n = 317 (142 intervention, 175 control); mean ages 64.2 vs 65.7 years, male 65.1% vs 75.7%
Notes	Funding source: none reported

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Guo 2014

Study characteristics	
Description of study	Study aim: "To determine compliance with severe sepsis bundles and to report its effect on outcomes in patients with severe CAP in a limited resources country" Study design: before and after Dates study conducted: 1 November 2004-31 October 2006 (control); 1 November 2006-July 2008 (intervention) Setting: Affiliated Futian Hospital, Guangdong Medical College, Shenzhen, Guangdong, China
Participants	Adult patients who met criteria for severe CAP with severe sepsis or septic shock presenting to the respiratory ICU; n = 212 (106 intervention, 106 controls), mean ages 62.8 and 64.0 years, male in each group 77.4% and 66.1%
Notes	Funding source: the non-profit foundation of Ying-Dong Huo in Hongkong

Janz 2020

Study characteristics	
Description of study	Study aim: "To assess if evidence-based pilot protocol that guided the management of the patient with ARF and ARDS would be associated with increased ventilator-free days in critically ill adults with COVID-19" Study design: retrospective cohort Dates study conducted: 9 March 2020 to 14 April 2020 Setting: 4 hospitals, New Orleans, USA
Participants	Critically ill adults who were admitted to any ICU in the network of hospitals and had a positive nasopharyngeal swab for SARS-CoV-2; n = 147 (54 intervention, 93 control); 93% were African Americans
Notes	Funding source: data collection used the REDCap tool developed and maintained with grant support (UL1 TR000445 from NCATS/NIH)

Jung 2012

Study characteristics	
Description of study	Study aim: "To evaluate an evidence based ARDS treatment algorithm, including rescue strategies" Study design: prospective cohort Dates study conducted: July 2005-June 2011 Setting: not described
Participants	Patients with ARDS; n = 240
Notes	Funding source: none reported

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Luedike 2015

Study characteristics	
Description of study	Study aim: "To present a retrospective analysis of the impact of implementing an ARDS SOP in our level-III maximum care unit after 1 year" Study design: before and after Dates study conducted: 2011-2014 Setting: an academic, interdisciplinary ICU of the University Hospital of the Heinrich-Heine University, Düsseldorf
Participants	Severe ARDS in patients > 18 years; n = 59; median age 51.3 ± 15.7; 73% male
Notes	Funding source: PL & MT funded by the Research Committee of the Medical Faculty of the University of Duesseldorf. TR is a Heisenberg professor funded by the DFG (Ra969/7-2)

Mellor 1999

Study characteristics	
Description of study	Study aim: "To evaluate the effect of a combined therapeutic approach on survival of patients with ARDS when treated according to a strict algorithm" Study design: observational (quality improvement) Dates study conducted: not described Setting: not described
Participants	Patients with ARDS as defined by the American-European Consensus Conference on ARDS and a lung injury score of > 2.5; n = 84, age range 12-73 years including 58 referrals for ECMO
Notes	Funding source: none reported

Peek 2009

Study characteristics	
Description of study	Study aim: "To delineate the safety, clinical efficacy, and cost-effectiveness of ECMO compared with conventional ventilation support" Study design: RCT (multicentre) Dates study conducted: 1 July 2000-31 December 2007 Setting: not described (UK, multiple centres)
Participants	Adult patients, 18-65 years, with severe, but potentially reversible respiratory failure; n = 177 (90 intervention and 87 control
Notes	Funding source: NIHR-HTA Programme (UK)

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Peng 2020

Study characteristics	
Description of study	Study aim: "To report the successful management of seven critically ill patients diagnosed with COVID-19 who suffered ARF" Study design: case series Dates study conducted: 20 January-6 February 2020 Setting: ICU of the Third People's Hospital of Shenzhen, China
Participants	Critically ill patients admitted to the ICU and treated for COVID-19; n = 7, age range 36-71 years, 4/7 female, 3/7 had an underlying disease, BMI range 21-28
Notes	Funding source: none reported

Phua 2016

Study characteristics	
Description of study	Study aim: "To review the impact of management measures implemented within the first 24 hours and carried out in the emergency department and in the ICU" Study design: systematic review Dates study conducted: electronic search of PubMed 1981-June 2016 Setting: not applicable
Participants	Not applicable
Notes	Funding source: unfunded

Singh 2020

Study characteristics	
Description of study	Study aim: "To describe four cases of patients with COVID-19 who developed skin or mucosal injuries within several days of being admitted to our ICU" Study design: case report Dates study conducted: March 2020 Setting: 48-bed ICU centrally located within a metropolitan city that serves an underserved community; Regional Medical Center, San Jose, California, USA
Participants	Patients admitted to ICU at a high risk for developing pressure injuries; n = 4 patients with COVID-19, age range 44-66 years, 2/4 male, all 4 had hypertension
Notes	Funding source: none reported

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Thomas 2014

Study characteristics	
Description of study	Study aim: "To describe the concordance of a busy, inner city ICU with BTS [British Thoracic Society] guidelines and the consequent outcomes for involved patients" Study design: audit Dates study conducted: 1 January 2012-23 September 2012 Setting: ICU, Queen Elizabeth Hospital Birmingham, UK
Participants	All patients with diagnosis of pneumonia admitted to ICU; n = 37 with a primary diagnosis of CAP, mean age 64 years, 59% male
Notes	Funding source: none reported

Ting 2020

Study characteristics	
Description of study	Study aim: "To provide some practical and important practice points with an aim to improve the eye-care for critically ill patients" Study design: correspondence based on COVID-19 case Dates study conducted: April 2020 (case) Setting: Department of Ophthalmology, Queen's Medical Centre, Nottingham, UK
Participants	Case patient with COVID-19 in ICU, ventilated for several days, developed an exposure keratopathy with corneal abrasion, which was reported as "white cornea with presumed infection"
Notes	Funding source: none reported

Wang 2018

Study characteristics	
Description of study	Study aim: "To describe a bundle treatment plan in the early stage for severe human infection by avian influenza H7N9, and explore its clinical efficacy and application value" Study design: before and after Dates study conducted: 29 December 2016-5 March 2017 (control); 6 March 2017-7 June 2017 (intervention) Setting: Department of ICU, the People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture, Kaili 556000, Guizhou, China
Participants	Patients with severe human infection by avian influenza H7N9 in Guizhou; n = 15 (9 treatment group, 6 control group)
Notes	Funding source:

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Yang 2014

Study characteristics	
Description of study	Study aim: "To investigate the effect of ventilator bundle on prognosis of patients with ARDS" Study design: prospective controlled study Dates study conducted: January 2013-December 2013 Setting: Department of Critical Care Medicine of the Second Hospital of Lanzhou University, China
Participants	Patients with ARDS; patients who received treatment of invasive MV; n = 54, (29 bundle-dependent, 25 non-dependent)
Notes	Funding source: none reported

Yue 2015

Study characteristics	
Description of study	Study aim: "To investigate the efficacy of bundle treatment on patients with moderate or severe ARDS" Study design: before and after Dates study conducted: January 2010-August 2012 (matched control); September 2012-May 2014 (intervention) Setting: Department of Critical Care Medicine of Taian Central Hospital and Handan Central Hospital, China
Participants	Patients with moderate or severe ARDS according to the new Berlin standard of definition, age from 18 to 65 years; n = 73 (33 intervention and 40 control)
Notes	Funding source: none reported

ARF: acute respiratory failure; **ARDS:** acute respiratory distress syndrome; **BMI:** body mass index; **BTS:** British Thoracic Society; **CAP:** community-acquired pneumonia; **ECMO:** extracorporeal membrane oxygenation; **FO:** fluid overload; **ICU:** intensive care unit; **MERS:** Middle East respiratory syndrome; **MV:** mechanical ventilation; **PARDS:** paediatric acute respiratory distress syndrome; **PICU:** paediatric intensive care unit; **RCT:** randomised controlled trial; **SOP:** standard operating procedure

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Achen 2013	Not patients with COVID-19, ARDS, viral pneumonia or pneumonitis
Afessa 2007	Not patients with COVID-19 ARDS, viral pneumonia, pneumonitis
Aissaoui 2020	Letter to the Editor
Amiel 2020	Not in English (French); no English language abstract to assess eligibility
Andrejak 2020	Narrative literature review
Arnold-Day 2019	Not patients with COVID-19, a related condition (i.e. ARDS, viral pneumonia, pneumonitis), or both

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Study	Reason for exclusion
Aydon 2014	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Burja 2018	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Cannon 2017	Narrative literature review
Carrillo-Esper 2011	Abstract - unclear if eligible; full-text paper in Spanish
Carrillo-Esper 2011a	Duplicate record
Chang 2015	Not an ICU setting
Chang 2016	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Chao 2020	Not a care bundle (as per IHI definition)
Chen 2020	Not in English; unable to access to assess eligibility
Chiche 2008	Editorial
ChiCTR-INR-16009510	Not in English (Chinese); unable to access the registry to assess eligibility
ChiCTR-PNRC-09000419	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Christofi 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Costello 2007	Editorial
CTRI/2017/02/007904	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
CTRI/2017/08/009538	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
CTRI/2018/03/012701	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
CTRI/2019/03/018270	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
CTRI/2020/04/024748	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Daniel 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
De Oliveira Paes 2018	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Devlin 2020	Narrative literature review
Dreyfuss 2002	Narrative literature review
Dries 2016	Narrative literature review
Dubernet 2020	Not an ICU setting
Engelman 2005	Not in English (German); no English language abstract to assess eligibility
Eom 2014	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Ervin 2020	Not a care bundle (as per IHI definition)

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Study	Reason for exclusion
Evodkimov 2010	Abstract - unclear if eligible (full text paper in Russian)
Eyre 2020	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Ferreira 2016	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Gale 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
George 2008	Narrative literature review
Goodwin 2018	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Haisbeder 2010	Narrative literature review
Hifumi 2020	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
IRCT20141209020258N116	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Junma 2018	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Kaisers 2001	Not a care bundle (as per IHI definition)
Kaisers 2007	Editorial
Kampmeier 2020	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Kane 2004	Narrative literature review
Keyt 2014	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Klompas 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Kneyber 2014	Narrative literature review
Kolleff 2012	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Kushimoto 2019	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Lapinsky 2003	Narrative literature review
Lepak 2020	Not an ICU setting
Lewandowski 1997	Not a care bundle (as per IHI definition)
Marini 2007	Narrative literature review
Marraro 2017	Narrative literature review
Maurer 2020	Not a care bundle (as per IHI definition)
Morau 2020	Narrative literature review
Mosher 2009	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Murthy 2020	Narrative literature review

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Study	Reason for exclusion
Namendys-Silva 2020	Not a care bundle (as per IHI definition)
National Health Commission 2020	Not a care bundle (as per IHI definition)
NCT01966861	Not a care bundle (as per IHI definition)
NCT02060045	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
NCT02837497	Not a care bundle (as per IHI definition)
NCT03361085	Not an ICU setting
NCT03763695	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
NCT04097899	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Nielsen 2009	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Noppens 2012	Narrative literature review
Oba 2008	Letter to the Editor
Parhar 2020a	Duplicate record
Pena-Lopez 2018	Narrative literature review
Peng 2020a	Not a care bundle (as per IHI definition)
Priebe 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Puthucheary 2017	Narrative literature review
Rello 2013	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Rhodes 2015	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Rice 2020	Narrative literature review
Roche-Campo 2011	Narrative literature review
Ruffell 2004	Narrative literature review
Salluh 2020	Narrative literature review
Shiu 2019	Not a care bundle (as per IHI definition)
Singleton 2006	Narrative literature review
Sinha 2020	Not a care bundle (as per IHI definition)
Sivaloganathan 2020	Not a care bundle (as per IHI definition)
Smith 2013	Not patients with COVID-19, a related condition (i.e. ARDS, viral pneumonia, pneumonitis), or both

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Study	Reason for exclusion
Su 2017	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Sun 2003	Not an ICU setting
Tinti 2013	Narrative literature review
Van der Jagt 2012	Not a care bundle (as per IHI definition)
Verder 2007	Narrative literature review
Veronese 2020	Not a care bundle (as per IHI definition)
Vincent 2009	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Vitacca 2020	Not an ICU setting
Wang 2017	Duplicate record
Wang 2018a	Duplicate record
Wang 2018b	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Westafer 2020	Narrative literature review
Wip 2009	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Wong 2017	Narrative literature review
Xu 2018	Abstract - unclear if eligible
Yang 2014a	Duplicate record
Yue 2015a	Duplicate record
Zamora Gomez 2017	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Zhang 2012	Not patients with COVID-19, ARDS, viral pneumonia, pneumonitis
Zhang 2012a	Duplicate record

ARDS: acute respiratory distress syndrome; **ICU:** intensive care unit; **IHI:** Institute for Healthcare

Characteristics of ongoing studies *[ordered by study ID]*

NCT03504176

Study name	Pediatric acute respiratory distress syndrome bundle vs. standard care; a before-and-after study
Starting date	6 April 2018 (estimated completion date January 2021)
Contact information	Dr Judith Wong Ju-Ming, KK Women's and Children's Hospital, Singapore
Notes	Study design: before and after (n = 134)

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NCT03504176 *(Continued)*

	Aim: "To determine if implementing a ventilation bundle comprising PALICC recommendations lowers PARDS and pediatric intensive care unit (PICU) mortality rates" Bundle treatment: a PARDS ventilation bundle compliant with PALICC recommendations. The bundle contains a daily checklist for ventilation targets and reference tables listing targeted tidal volumes and end expiratory pressure-fraction of inspired oxygen titration. We will recruit MV patients who meet PARDS criteria. After a 1-month implementation period, we will collect patient data over the subsequent 18 months, and compare them with the corresponding data in the 24 months prior to the implementation. The primary outcome is PARDS mortality, defined as number of deaths out of PARDS cases. Secondary outcomes are feasibility of ventilation bundle implementation, ventilator (VFD) and intensive care unit (IFD) free days and PICU mortality (number of deaths out of PICU admissions) Funding: none reported

NCT04070053

Study name	Treatment of hypoxemic respiratory failure and ARDS with protection, paralysis, and proning (TheraPPP) Pathway (TheraPPP)
Starting date	23 August 2019 (estimated completion date 30 September 2020)
Contact information	Ken Parhar, Foothills Medical Centre, Calgary; ken.parhar@ahs.ca
Notes	Study design: before and after quasi-experimental design (n = 1250) Aim: "To test the feasibility and acceptability of the TheraPPP Pathway. To assess feasibility, the investigators will test the ability to measure adherence to the pathway as well as patient and economic outcomes. To assess perceptions about the acceptability of the TheraPPP Pathway, the investigators will conduct a survey to clinicians who used the Pathway. Patient data will be collected for two years and one month: one year immediately prior to implementation as well as one month during plus one year following implementation." Bundle treatment: TheraPPP Steps 1. All mechanically ventilated patients will have a height measured and documented 2. Screening for HRF 3. Initiate LPV 4. Paralysis 5. Prone positioning Funding: MSI Foundation

NCT04459819

Study name	Respiratory physiotherapy in severe COVID-19 patients (FTR-COVID)
Starting date	1 March 2020 (estimated completion date listed as 12 May 2020)
Contact information	Emilia Privitera, Ospedale Maggiore Policlinico; emilia.privitera@policlinico.mi.it
Notes	Study design: observational (case only) (n = 80) Aim: "To describe the bundle and the timing of respiratory physiotherapy used with severe COVID-19 patients from ICU to hospital discharge. Functional condition of patients at discharge will be assessed and described"

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NCT04459819 *(Continued)*	Bundle treatment: respiratory physiotherapy consisting of early mobilisation (passive and active mobilisation, muscle-strengthening exercises, mobilisation out of bed, standing, walking, ADL), patient's positioning, non-invasive MV/CPAP, tracheostomy management, invasive mechanical ventilation weaning, airway clearance and oxygen titration Funding: Fondazione IRCCS cA' Granda, Ospedale Maggiore Policlinico

ADL: activities of daily living; **CPAP:** continuous positive airway pressure; **HRF:** hypoxic respiratory failure; **ICU:** intensive care unit; **LPV:** lung-protective ventilation; **MV:** mechanical ventilation; **PALLIC:** Pediatric Acute Lung Injury Consensus Conference; **PARDS:** paediatric acute respiratory distress syndrome; **PICU:** paediatric intensive care unit

APPENDICES

Appendix 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Title			
Title	1	Identify the report as a scoping review.	Title page
Abstract			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	3
Methods			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	3, Appendix 2
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	3
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify	4

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(Continued)

		additional sources), as well as the date the most recent search was executed.	
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 3
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	4
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	5
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	4
Results			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	5
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	6
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	5
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	7-8, Figures 2, 3
Discussion			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	9
Limitations	20	Discuss the limitations of the scoping review process.	9
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	9

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(Continued)

Funding			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	NA

Appendix 2. Review protocol

Care bundles for improving outcomes in patients with COVID-19 in intensive care – a rapid scoping review (protocol)

Team

Smith V, Devane D, Nichol A, Roche D.

Contact

Valerie Smith, School of Nursing and Midwifery, Trinity College Dublin, Ireland; smithv1@tcd.ie

Date protocol completed

[dd/10/2020]

IMPORTANT: This protocol template is designed for rapid reviews of interventions and intended for questions that have been undergone topic refinement to address urgent questions arising from the COVID-19 pandemic. All sections should be completed, and no inclusion/exclusion decisions made until the process is finalised. If you have not already done so, please review the information about the rapid review process and available resources for author teams on the website which are being updated regularly. The template was developed to maximise quality and efficiency in the review process and may be adapted or improved as reviews are published. It is primarily aimed at questions about effectiveness (intervention reviews) and will require adaptation for other types of review (e.g. diagnosis, prognosis or reviews that include qualitative evidence). See the 'Links to additional guidance' section on the resources for author teams webpage for more details. Th

e structure and methods are based on a template used by Cochrane Response and have been adapted in line with preliminary recommendations made by the Cochrane Rapid Reviews Method Group (RRMG March 2020). Recommended approaches from the Cochrane RRMG are indicated throughout the protocol by the prespecified ticked boxes but may be amended and tailored to the review question (if you deviate from the recommendations, please specify why). If you have any questions about Cochrane COVID-19 Rapid Reviews, email covidrapidreviews@cochrane.org

1. Background

1.1. Description of the condition under consideration

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), was declared a Public Health Emergency of Concern in January 2020 and a pandemic by the World Health Organisation (WHO) in March 2020. The virus has since spread rapidly across the globe, and, as of 12th October 2020, around 37.3 million cases have been confirmed with almost 1.1 million associated deaths. Disease manifestation is variable, with some infected people remaining asymptomatic, and others suffering mild flu-like symptoms. For others however, infection can cause serious illness, with organ dysfunction requiring admission to intensive care units (ICU) and frequently, ventilatory support for acute respiratory failure. Many of these patients develop Acute Respiratory Distress Syndrome, as defined using the Berlin definition (The ARDS Definition Task Force, 2012). A recent systematic review and meta-analysis identified a global ICU admission rate of 26% and a prevalence of ICU mortality of 31%, based on pooled data from 26 studies of patients with COVID-19 (Abate 2020). Evaluating ICU care, and what is effective in improving outcomes for these patients is critical. This rapid scoping review will identify and describe the available evidence on use of care bundles in the ICU for patients with SARS-COV-2.

1.2. Description of the intervention

The concept of care bundles was introduced by the Institute for Health Improvement (IHI) in 2001 and is defined as;

"A small set of evidence-based interventions for a defined patient segment/population and care setting that, when implemented together, will result in significantly better outcomes than when implemented individually" (Resar *et al*. 2012)

Care bundles are a way of re-organising and restructuring care processes by introducing a package of evidence-based practices aimed at reducing variability in how care is provided and delivered. Care bundles may help improve the teamwork required to improve the reliability of care (Resar *et al.* 2005). The most common implementation strategies used for care bundles include, education sessions,

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reminders and audit and feedback. A systematic review of implementation strategies, however, was unable to determine the most effective implementation strategy (Borgert *et al*. 2015)

1.3. How the intervention might work

Previous systematic reviews have suggested that care bundles are effective in managing a range of conditions including ventilator associated pneumonia (Resar *et al.* 2005), sepsis, pressure ulcers and central line associated blood stream infections (Lavallee *et al*. 2017). It is important to note that a care bundle does not constitute comprehensive care; rather, a care bundle is an intervention where compliance with a core set of accepted care interventions in a particular clinical setting are measured, incorporating the reorganisation of infrastructure, communication and team dynamics. The goal of a care bundle intervention is to improve overall patient care and patient outcomes (Resar *et al.* 2012). The COVID-19 pandemic has required restructuring of care processes in relation to isolation precautions and personal protective equipment (PPE) as well as the increased frequency of prone positioning of ventilated and non-ventilated patients in the ICU. Care bundles may have a role in reducing variability of care and ensuring that patients with COVID-19 who require treatment in the ICU receive the same package of evidence-based interventions with the goal of improving outcomes.

2. Objectives of the review

To identify and describe the available evidence (scope of literature) on use of care bundles in patients with COVID-19, related conditions (e.g. ARDS, viral pneumonia), or both in the ICU.

In carrying out this rapid scoping review, we will draw on methodological guidance from The *Joanna Briggs Institute (JBI) Manual for Evidence Synthesis, Chapter 11: Scoping reviews* (Godfrey *et al.* 2020) and *Cochrane Rapid Reviews Methods Group offers evidence-informed guidance to conduct rapid reviews* (Garritty *et al.* 2020). The review will be reported using the PRISMA for Scoping Reviews extension (Tricco *et al.* 2018) which will be completed as part of the final report.

3. Methods

3.1. Criteria for considering studies for this review

Study and source eligibility	
Study design	As this is a rapid scoping review which seeks to identify the scope and type of available evidence on the use of care bundles, studies of all designs will be included; o RCTs o Quasi-RCTs o Cluster- RCTs o Prospective cohort studies o Retrospective cohort studies o Controlled before-and-after studies o Case-control studies o Cross-sectional studies o Case series o Systematic reviews
	Minimum duration: We will consider studies of any duration and follow-up periods.

'PICO' eligibility	
Population	Patients with SARS-CoV-2 infection and related conditions (e.g. ARDS and viral pneumonia) who are critically ill in ICU, with or without invasive ventilation. Populations of child (defined <18 years) and adult patients (>18 years) will be included and categorised accordingly.

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Intervention(s) Exposure	Care bundle - based on IHI definition of at least three (or more) evidence-informed practices, which are delivered collectively and consistently with the aim of improving patient outcomes.
Comparator(s)	No care bundle (if applicable)
Outcome(s)	Critical · Death in ICU (within 30, 60, 90 days, and longer if data available) (listed as one of three proposed minimal core outcomes by the WHO Working Group in the Clinical Characterisation and Management of COVID-19 infections (WHO, 2020); Accessible also via the COMET database; https://www.comet-initiative.org/Studies/Details/1538) · Days of ventilation (or ventilator free days) · Length of stay (LOS) in ICU (in days) Important · LOS in hospital (in days) · Death in hospital (within 30 days, within 90 days, and longer if data available) · ICU-acquired weakness (muscle wasting, weight loss) Additional 'scoping' outcomes · Rates of adherence to all components of the care bundle · User experiences in adapting care bundles

3.2. Search methods for identification of studies

Search methods			
Expertise	The searches will be developed and conducted by an information specialist from Cochrane Anaesthesia and Cochrane Emergency and Critical Care Group [JV], reviewed by content experts [AN, DR] and independently peer reviewed [RF].		
Electronic databases	Database ☒ MEDLINE ☒ CENTRAL ☒ EMBASE COVID research registers ☒ covid-19.cochrane.org ☒ Clinical Trial Registry – ICTRP platform Note: both CENTRAL and the Cochrane COVID-19 Study Register include references from ClinicalTrials.gov	From: 2000 (date care bundles were introduced)	To: present

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(Continued)

Other searches	☒ Systematic review references ☒ Reference lists of included studies ☐ Grey literature (opengrey.eu, greylit.org) ☐ Citation tracking ☐ Data from the pharmaceutical industry ☐ Data from Governments/ intergovernmental agencies ☐ Citation tracking ☐ Contact experts for references ☐ Other	As per recent interim guidance on RRs (Garrity *et al.* 2020) the reference lists of papers selected for full text review will be examined for any additional potentially relevant references by one reviewer [VS] and eligibility confirmed by a second reviewer [DR]. Reference lists of systematic review references will also be screened. Grey literature searching will not be included (Garrity *et al.* 2020).
Approach to ongoing and unpublished studies	☒ Include ongoing studies ☐ Unpublished studies ☒ Studies in press ☐ Exclude all studies that are ongoing, unpublished, or in press	MEDLINE and EMBASE include 'ahead of print' references to journal articles; ongoing studies will be identified from the ICTRP platform; the Cochrane COVID-19 Study Register also includes preprints.

Methods for screening search results

Expertise	Screening will be performed by VS (methodologist) and DR (topic expert) in Covidence		
Screening methods	Dual - second reviewer checks all excluded records	*Abstract*	*Full text*
	Dual - second reviewer checks 20% of excluded records	☐	☐
	Dual - independent screen and cross check	☒	☐
	A single reviewer will screen all abstracts [VS]; a second reviewer will screen 20% of included and excluded abstracts [DR]; if agreement is <80%, the second reviewer will dual screen all abstracts. Two reviewers [VS and DR] will screen all included full text articles.	☐	☒
Discrepancy resolution	☒ Consensus and/or third reviewer (AN) ☐Other		
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies.		
Inclusion of abstracts and conference proceedings	☐ Exclude all ☒ Include if clearly eligible and have usable data ☐ Include if clearly eligible regardless of usable data ☐ Include if eligibility is unclear and add to section in report		
Inclusion of non-English	☒ Include abstracts and full texts (where at least the abstract is in English); we will classify and report on the numbers/extend of non-English language full-text publications		

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(Continued)

language studies	☐ Include full texts only ☐ Exclude
	☒ All potentially relevant abstracts will progress to full text screen ☐ Listed as non-English language and not assessed further

3.3. Data collection and analysis

Data extraction	
Expertise	Data extraction will be performed by VS (methodologist) in consultation with and checked for accuracy by DR (topic expert).
Software	Data will be extracted using purposively developed pilot-tested data extraction forms in Microsoft Word/ Excel.
Data to be extracted	1. Record details which will include year, authors, title, journal and funding source 2. Study design which will include study methods, follow-up times location of study/description of setting, study groups and sample sizes 3. Participant characteristics which will include age, gender, invasive/non-invasive ventilation and time in ICU 4. Intervention characteristics which will include description of care bundle, application, compliance to care bundle and duration of intervention 5. Comparator characteristics (where relevant) which will include a description of standard care in the study setting 6. Outcomes assessed and the measurement tool used (where relevant) 7. Numerical data for outcomes of interest 8. Confounding factors (NRS) controlled for in each relevant analysis presented
Data extraction methods	☐ Single - no second reviewer ☐ Dual - second reviewer checks all data ☒ Dual - second reviewer checks 20% of data (items 2-8 inclusive) ☐ Dual - independent screen and cross check A second reviewer will check 20% of data; if there is <80% agreement in accuracy of extracted data, a second reviewer will check all data.
Risk of bias tool	☒ No risk of bias assessment – N/A as this is a scoping review ☐ Cochrane RCT risk of bias tool ☐ ROBINS-I tool for non-randomised studies ☐ Adapted-hybrid of the RCT-ROBINS-I tools

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(Continued)

	☐ Newcastle-Ottawa Scale (cohort and case-control studies) ☐ Another tool	
Method of risk of bias assessment	☐ Single - no second reviewer ☐ Dual - second reviewer checks all judgements ☐ Dual - second reviewer checks ☐ Dual - independent screen and cross check	☐ Results going into the SoF tables ☐ Other
Discrepancy resolution	☐ Consensus and/or third reviewer ☐ Other	
Contacting study authors	☐ Authors will be contacted for missing information and data ☐ Authors will be contacted for missing data only ☒ Authors will not be contacted	
Data management		
Software	Microsoft Word (data extraction forms) and Microsoft Excel (developing summary tables of included studies).	
Resolving conflicts between sources	If there is a conflict between data reported across multiple sources for a single study (e.g. between an abstract and full study record) we will use the data from the main study report.	

Data synthesis	
Measures of treatment effect	Not applicable as this is a scoping review; summary result details in evidence tables will be presented. ☐ Continuous outcome: mean difference and 95% CIs ☐ Continuous outcome: standardised mean difference and 95% CIs ☐ Dichotomous outcome: risk ratio / relative risk (RR) and 95% CIs ☐ Dichotomous outcome: odds ratio (OR) and 95% CIs ☐ Dichotomous outcome: risk difference (absolute risk reduction) ☐ Peto odds ratio method ☐ Other (please specify)
Decision rules for extraction of quantitative data	All data will be extracted from the study records as reported/presented.
Data standardisation	Not applicable
Unit of analysis issues	Not applicable
Assessment of heterogeneity	Not applicable

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Assessment of reporting biases	Not applicable
Preparation for synthesis	The description of and results from the included studies will be presented in summary tables. These will be developed to account for variation in study designs (if relevant) and to present a summary of the results; ☒ Table to compare PICO elements / study design features ☒ Table of extracted numerical data for presenting the results ☐ Conversion of numerical data for meta-analysis (as needed)
Data synthesis	☐ Forest plots ☐ Qualitative synthesis ☒ Synthesis without meta-analysis – Summary tables of evidence from included studies, charted according to key groupings with descriptive summary provided as text. ☐ Network meta-analysis
Model	Not applicable
Synthesis without meta-analysis	☐ Alternative statistical synthesis ☐ Visual display of data e.g. forest plot without (pooling / other) ☒ Tabulation of data by comparison ☒ Summary of the evidence
Strategies for dealing with sparse data	Not applicable
Subgroup analyses	Data from sub-groups analyses will be reported as presented in the study record.
Sensitivity analysis	Not applicable as this is a scoping review
GRADE approach	☐ GRADE will not be applied as this is a scoping review.

4. Acknowledgements

We acknowledge the support of Janne Vendt, Cochrane Information Specialist, for developing the search strategy, Rachell Marshall and Helen Wakeford, Senior Editorial Officers, Cochrane Central Executive, and Robin Featherstone for peer review of the search strategy.

5. Funding sources

Not funded

6. Declarations of Interest

VS, DD, AN, and DR independently declare that they have no conflict of interest.

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8. Appendices

8.1. Search strategies

(revised following peer review – final version as per Appendix 3)

8.2. Data extraction form

Data Extraction Form: Rapid Scoping Review

Review Title: Care bundles for improving outcomes in patients with COVID-19 in intensive care – a rapid scoping review (Protocol)

Person extracting data
Date of data extraction
Study details
Reference
Aim of study
Dates study conducted
Study design
Description of study setting
Description of study population
Description of care bundle (number (n) and type of interventions included in bundle, etc.)
Compliance to the care bundle (% rate or other measure
Comparator (if applicable; n comparators; description of comparator, etc.)
Method(s) of data capture

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Method(s) of data analysis
Results on review's prespecified outcomes (as reported in the study)
If applicable - results adjusted for confounders (yes/no); if yes, list confounders
Additional comments (if relevant)

Appendix 3. Search strategy

Ovid MEDLINE(R) ALL <1946 to 26 October 2020>

1 exp coronavirus/ (38803)

2 exp Coronavirus Infections/ (41916)

3 (coronavirus* or corona virus* or Covid or Covid19 or Covid2019 or SARS-CoV* or SARSCov* or ncov* or 2019nCoV or new CoV* or novel CoV*).ti,ab,kf. (79267)

4 covid-19.rs. (31740)

5 severe acute respiratory syndrome coronavirus 2.os. (26892)

6 1 or 2 or 3 or 4 or 5 (87402)

7 6 and (201912* or 2020*).dt,ez,dp. (69076)

8 Respiratory Distress Syndrome, Adult/ (19932)

9 exp Severe Acute Respiratory Syndrome/ (5232)

10 (ards or ardss or sars or mers or respiratory distress syndrome*).ti,ab,kf. (64916)

11 ((acute or adult) adj3 respiratory adj3 (distress or syndrome*)).ti,ab,kf. (33292)

12 (((pulmonary* or lung* or alveol*) adj3 (dysfunction* or edema* or oedema* or collapse* or injur* or failure*)) or ((stiff or shock) adj3 lung*)).ti,ab,kf. (69951)

13 Acute Lung Injury/ (6360)

14 Acute Chest Syndrome/ (279)

15 (acute adj chest adj syndrome*).ti,ab,kf. (1072)

16 Pneumonia, Viral/ (37193)

17 (pneumonitis or (pneumon* adj3 (viral or virus))).ti,ab,kf. (17860)

18 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (200498)

19 Patient Care Bundles/ (886)

20 Critical Pathways/ (6930)

21 Clinical Protocols/ (28350)

22 Critical Care/mt (13720)

23 Critical Care Nursing/mt (393)

24 Intensive Care Units/mt (17)

25 ((ICU or PICO or care or evidence or treatment or clinical or critical) adj3 (package* or checklist* or check list* or algorithm* or bundl* or map* or path or paths or pathway* or protocol*)).ti,ab,kf. (96902)

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26 19 or 20 or 21 or 22 or 23 or 24 or 25 (138697)

27 18 and 26 (2601)

28 (2000* or 2001* or 2002* or 2003* or 2004* or 2005* or 2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 2020*).dt,ez,dp,ed. (20314566)

29 27 and 28 (2297)

30 exp animals/ not humans.sh. (4749020)

31 29 not 30 (2217)

Embase via OVID Sp <1974 to 26 October 2020>

1 exp coronaviridae infection/ (22148)

2 exp coronavirinae/ (20631)

3 (coronavirus* or corona virus* or Covid or Covid19 or Covid2019 or SARS-CoV* or SARSCov* or ncov* or 2019nCoV or new CoV* or novel CoV*).ti,ab,kw. (78056)

4 1 or 2 or 3 (88837)

5 4 and (201912* or 2020*).dc,dp. (66661)

6 adult respiratory distress syndrome/ (39674)

7 severe acute respiratory syndrome/ (9521)

8 (ards or ardss or sars or mers or respiratory distress syndrome*).ti,ab,kw. (81001)

9 ((acute or adult) adj3 respiratory adj3 (distress or syndrome*)).ti,ab,kw. (42467)

10 (((pulmonary* or lung* or alveol*) adj3 (dysfunction* or edema* or oedema* or collapse* or injur* or failure*)) or ((stiff or shock) adj3 lung*)).ti,ab,kw. (101692)

11 exp acute lung injury/ (15627)

12 acute chest syndrome/ (2364)

13 (acute adj chest adj syndrome*).ti,ab,kw. (2188)

14 exp virus pneumonia/ (25392)

15 (pneumonitis or (pneumon* adj3 (viral or virus))).ti,ab,kw. (27823)

16 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (261931)

17 care bundle/ (1373)

18 clinical pathway/ (8603)

19 clinical protocol/ (100892)

20 critical illness/dm (248)

21 ((ICU or PICO or care or evidence or treatment or clinical or critical) adj3 (package* or checklist* or check list* or algorithm* or bundl* or map* or path or paths or pathway* or protocol*)).ti,ab,kw. (149647)

22 17 or 18 or 19 or 20 or 21 (239946)

23 16 and 22 (2996)

24 (2000* or 2001* or 2002* or 2003* or 2004* or 2005* or 2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 2020*).dc,dp. (23808570)

25 23 and 24 (2737)

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26 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti,ab.) (6058022)

27 25 not 26 (2567)

CENTRAL via the Cochrane Library

2020; issue 10 of 12, searched October 2020 (cochranelibrary.com/advanced-search/search-manager?search=4086252)

#1 MeSH descriptor: [Coronavirus] explode all trees 72

#2 MeSH descriptor: [Coronavirus Infections] explode all trees 395

#3 (coronavirus* or (corona near virus*) or Covid or Covid19 or Covid2019 or SARS-CoV* or (SARS next CoV*) or SARSCov* or ncov* or 2019nCoV or (new next CoV*) or (novel next CoV*)):ti,ab,kw 1761

#4 #1 or #2 or #3 with Cochrane Library publication date in The last year 1671

#5 MeSH descriptor: [Respiratory Distress Syndrome, Adult] explode all trees 1359

#6 MeSH descriptor: [Severe Acute Respiratory Syndrome] explode all trees 235

#7 MeSH descriptor: [Acute Lung Injury] explode all trees 477

#8 MeSH descriptor: [Acute Chest Syndrome] explode all trees 37

#9 MeSH descriptor: [Pneumonia, Viral] explode all trees 147

#10 (ards or ardss or sars or mers or (respiratory near distress near syndrome*)):ti,ab,kw 6135

#11 ((acute or adult) near respiratory near (distress or syndrome*)):ti,ab,kw 3373

#12 (((pulmonary* or lung* or alveol*) near (dysfunction* or edema* or oedema* or collapse* or injur* or failure*)) or ((stiff or shock) near lung*)):ti,ab,kw 7758

#13 (acute near chest near syndrome*):ti,ab,kw 259

#14 (pneumonitis or (pneumon* near (viral or virus))):ti,ab,kw 1651

#15 #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 15052

#16 MeSH descriptor: [Patient Care Bundles] explode all trees 27

#17 MeSH descriptor: [Critical Pathways] explode all trees 193

#18 MeSH descriptor: [Clinical Protocols] explode all trees 18389

#19 MeSH descriptor: [Critical Care] explode all trees and with qualifier(s): [methods - MT] 825

#20 MeSH descriptor: [Critical Care Nursing] explode all trees and with qualifier(s): [methods - MT] 19

#21 ((ICU or PICO or care or evidence or treatment or clinical or critical) near (package* or checklist* or (check next list*) or algorithm* or bundl* or map* or path or paths or pathway* or protocol*)):ti,ab,kw 34927

#22 #16 or #17 or #18 or #19 or #20 or #21 49005

#23 #15 and #22 843

#24 #23 with Cochrane Library publication date Between Jan 2000 and Dec 2020 777

Trials 768 / reviews 9

Cochrane COVID-19 Study Register

covid-19.cochrane.org

bundl* or pathway* or "care protocol" or "care package" or "care algorithm" or "care protocols" or "care packages" or "care algorithms" or "treatment protocol" or "treatment package" or "treatment algorithm" or "treatment protocols" or "treatment packages" or "treatment algorithms" or "clinical protocol" or "clinical package" or "clinical algorithm" or "clinical protocols" or "clinical packages" or "clinical

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algorithms" or "critical protocol" or "critical package" or "critical algorithm" or "critical protocols" or "critical packages" or "critical algorithms"
594 matching studies

WHO International Clinical Trials Registry Platform

Standard search

bundl* AND respiratory 15

bundl* AND pneumon* 19

pathway* AND respiratory 30

pathway* AND pneumon* 11

care protocol* AND respiratory 13

care protocol* AND pneumon* 5

treatment protocol* AND respiratory 13

treatment protocol* AND pneumon* 14

Appendix 4. Summary characteristics of included studies in aggregated form by patient condition

Author/year	Study aim	Study design	Dates of study	Study setting	Study population	Funding
Participants with confirmed or suspected COVID-19						
Albutt 2020	"To share the design, creation, and preliminary outcomes of a streamlined multidisciplinary procedure team at our institution: the COVID-19 Bundled Response for Access (COBRA) team"	Observational (quality improvement)	April 2020 for 2 weeks	Massachusetts General Hospital, ICU; in the first few weeks of the pandemic, several medical and surgical floors were converted into surge ICUs	Critically ill patients with COVID-19; n = 102; median age 60 years, 68.6% male, mainly white (37.3%) or Hispanic (41.2%) and median BMI of 31.2	NR
Balakrishnan 2020	"To describe a step-by-step approach to endotracheal intubation of critically ill patients with suspected or confirmed COVID-19 and other airborne diseases with the goal of limiting the risk of exposure to healthcare providers"	Observational (quality improvement)	NR	Department of Emergency Medicine, Kasturba Medical College, Manipal, India	Critically ill patients with suspected or confirmed COVID-19 and other airborne diseases; n = NR	No sources of funding to declare
Choi 2020	"To describe our experience and protocol for surgical tracheostomy in patients with COVID-19 in our hospital"	Retrospective cohort	May-July 2015 (MERS outbreak); March 2020 (COVID-19 outbreak)	Not described (Republic of Korea)	Patients with MERS and one with COVID-19 who had undergone surgical tracheostomy; n = 9	NR

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Janz 2020	"To assess if evidence-based pilot protocol that provided guidance on the management of the patient with ARF and ARDS would be associated with increased ventilator-free days in critically ill adults with COVID-19"	Retrospective cohort	9 March 2020-14 April 2020	4 hospitals, New Orleans, USA	Critically ill adults who were admitted to any ICU in the network of hospitals and had a positive nasopharyngeal swab for SARS-CoV-2; n = 147 (54 intervention *vs* 93 control); 93% were African Americans	Data collection used the Research Electronic Data Capture (REDCap) tool developed and maintained with Vanderbilt Institute for Clinical and Translational Research grant support (UL1 TR000445 from NCATS/NIH)
Peng 2020	"To report the successful management of 7 critically ill patients diagnosed with COVID-19 who suffered acute respiratory failure"	Case series	20 January-6 February 2020	ICU of the Third People's Hospital of Shenzhen, China	Critically ill patients admitted to the ICU and treated for COVID-19; n = 7, age range 36-71 years, 4/7 female, 3/7 had underlying disease, BMI range 21-28	NR
Singh 2020	"To describe 4 case reports of patients who developed skin or mucosal injuries within several days of being admitted to our ICU"	Case series	March 2020	260-bed hospital (48-bed ICU) centrally located within a metropolitan city that serves an underserved community; Regional Medical Center San Jose, California, USA	Patients admitted to ICU at a high risk for developing pressure injuries; n = 4 patients with COVID-19, age range 44-66 years, 2/4 male, all 4 had hypertension	NR
Ting 2020	"To provide some practical and important practice points with an aim to improve the eyecare for critically ill patients"	Case report	April 2020 (case)	Department of Ophthalmology, Queen's Medical Centre, Nottingham, UK	Case patient: a patient with COVID-19 in ICU, ventilated for several days, developed an exposure keratopathy with corneal abrasion, which was reported as "white cornea with presumed infection".	NR
Participants with ARDS						
Diaz 2018	"To implement a bundle strategy to prevent FO in children with sepsis and PARDS and to compare	Before and after	January-December 2016 (study co-	Pediatric ICU (PICU) at Hospital Padre Hurtado,	All patients < 24 months who received MV and fulfilled the paediatric ARDS and sepsis criteria; n =	Partially funded by Fondo Nacional de

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(Continued)

	the outcomes with a historical cohort"		hort); June to December 2014 (historical cohort)	Chile; 12-bed general medical and surgical PICU	37 (intervention) vs n = 39 (control); 54% vs 64% male, age range 2-11 vs 1-7; 38% vs 49% had comorbidity	Desarrollo Científicoy Tecnológico
Duggal 2020	"To study the impact of an evidence-based ARDS management on outcomes"	Before and after	2012-2017; pre-intervention period January 2012-May 2014; intervention period June 2015-June 2017	A 64-bed closed medical ICU at Cleveland Clinic main campus hospital (Cleveland, Ohio, USA)	All patients with a diagnosis of ARDS based on the Berlin definition from 2012-2017; n = 118 (before cohort) vs n = 332 (after cohort). Participants in the after group had higher severity of illness at the time of diagnosis of ARDS	NR
Jung 2012	'To evaluate an evidence based ARDS treatment algorithm, including rescue strategies"	Prospective cohort	6 years; July 2005-June 2011	Not described	Patients with ARDS; n = 240	NR
Luedike 2015	"To present a retrospective analysis on the influences of the implementation of the ARDS SOP in the clinical routine in our level-III maximum care unit after 1 year"	Before and after	2011-2014	An academic, interdisciplinary ICU of the University Hospital of the Heinrich-Heine University Düsseldorf	Severe ARDS in patients > 18 years between 2011 and 2014; n = 59; median age 51.3 ± 15.7; 73% male	PL and MT are funded by the Research Committee of the Medical Faculty of the University of Duesseldorf. TR is a Heisenberg professor funded by the DFG (Ra969/7-2)
Mellor 1999	"To evaluate the effect of a combined therapeutic approach on survival of patients with ARDS when treated according to a strict algorithm"	Observational (quality improvement)	NR	Not described	Patients with ARDS as defined by the American-European Consensus Conference on ARDS and a lung injury score of > 2.5; n = 84, age range 12-73 years including 58 referrals for ECMO	NR
Yang 2014	"To investigate the effect of ventilator bundle (VB) on prognosis of patients with ARDS"	Prospective controlled study	January 2013-December 2013	Department of Critical Care Medicine of the Second Hospital of Lanzhou University, China	Patients with ARDS who received treatment of invasive MV; n = 54, subdivided by completely bundle-dependent n = 29 and non-dependent n = 25	NR
Yue 2015	"To investigate the efficacy of bundle treatment on patients with moder-	Before and after	Sep 2012-May 2014 (interven-			

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(Continued)

	ate or severe acute respiratory distress syndrome (ARDS)"		tion); Jan 2010-Aug 2012 (control)			
Participants with influenza or viral pneumonia						
Cornejo 2011	"To report the experience of a critical care team in assessing a strict multifaceted management protocol, incorporating evidence-based strategies in the form of ventilatory and non-ventilatory strategies, to treat the most severely ill subset of patients with influenza A(H1N1) virus"	Observational	13 June-27 August 2009	A critical care service, which includes 55 beds, 12 in ICU and 43 in intermediate care units in Hospital Clínico Universidad de Chile, Santiago	All influenza patients requiring MV transferred to ICU for management and isolation; n = 19 required MV and were the study cohort; mean age was 41 ± 13 years, 10 participants were female; 15 participants had pre-existing medical conditions, and in 4 participants, these were severe comorbidities	Partially funded by Research Grant Fondecyt N°. 11070156, Chilean government
Georges 2013	"To assess the prognosis of patients admitted to the ICU for community acquired pneumonia (CAP) after implementation of new processes of care"	Before and after	1995-2000 (control); 2005-2010 (intervention)	16-bed multidisciplinary ICU in an urban teaching hospital (Toutcoing Hospital, France)	All consecutive patients ≥ 18 years of age with severe CAP; n = 317 (142 intervention vs 175 control); mean ages 64.2 vs 65.7 years, male 65.1% vs 75.7%	NR
Guo 2014	"To determine compliance with severe sepsis bundles and to report its effect on outcomes in patients with severe CAP in a limited resources country"	Before and after	1 November 2004-31 October 2006 (control); 1 November 2006-July 2008 (intervention)	Affiliated Futian Hospital, Guangdong Medical College, Shenzhen, Guangdong, China	Adult patients who met criteria for severe CAP with severe sepsis or septic shock presenting to the respiratory ICU; n = 212 (106 intervention, 106 controls), mean ages 62.8 and 64.0 years, male in each group 77.4% and 66.1%	The nonprofit foundation of Ying-Dong Huo in Hongkong
Thomas 2014	"To describe the concordance of a busy, inner city ICU with BTS guidelines and the consequent outcomes for the patients involved"	Audit	1 January 2012- 23 September 2012	ICU, Queen Elizabeth Hospital Birmingham, UK	All patients with an admission diagnosis of CAP admitted to ICU; n = 37, mean age 64 years, 59% male	NR
Wang 2018	"To design bundle treatment plan in the early stage for severe human infection by avian influenza H7N9, and explore its clinical efficacy and application value"	Before and after	6 March 2017-7 June 2017 (bundle group); 29 December 2016-5 March 2017 (control group)	Department of ICU, the People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture, Guizhou, China	Patients with severe human infection by avian influenza H7N9 in Guizhou; n = 15 (n = 9 treatment group vs n = 6 control group)	NR

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(Continued)

Participants with acute respiratory failure						
Peek 2009	"To delineate the safety, clinical efficacy, and cost-effectiveness of ECMO compared with conventional ventilation support"	RCT	1 July 2000-31 December 2007	UK (multicentre)	Adult patients, 18-65 years, with severe, but potentially reversible respiratory failure, defined as a Murray score > 3.0, or uncompensated hypercapnoea with a pH < 7.20; n = 177 (90 intervention; 87 control)	NIHR HTA Programme (UK)
Participants with mixed conditions						
Phua 2016	"To review the impact of management measures implemented within the first 24 hours and carried out both in the ED and in the ICU"	Systematic review	Electronic search of PubMed 1981–June 2016	NA	NA	States the work is unfunded

ARF: acute respiratory failure; **ARDS:** acute respiratory distress syndrome; **BMI:** body mass index; **BTS:** British Thoracic Society; **CAP:** community-acquired pneumonia; **ECMO:** extracorporeal membrane oxygenation; **FO:** fluid overload; **ICU:** intensive care unit; **MERS:** Middle East respiratory syndrome; **MV:** mechanical ventilation; **PARDS:** paediatric acute respiratory distress syndrome; **PICU:** paediatric intensive care unit; **RCT:** randomised controlled trial; **SOP:** standard operating procedure

HISTORY

Review first published: Issue 12, 2020

CONTRIBUTIONS OF AUTHORS

VS screened and selected studies for inclusion, extracted the data, drafted the review and approved the final version prior to submission.

DD provided methodological advice, provided intellectual content to the review and approved the final version prior to submission.

AN provided topic advice, provided intellectual content to the review and approved the final version prior to submission.

DR screened 20% of excluded/included studies, reviewed 20% of the extracted data for accuracy, provided intellectual content to the review and approved the final version prior to submission.

DECLARATIONS OF INTEREST

VS: none to declare; DD: none to declare; AN is a REMAP-CAP (COVID-19 Adaptive Platform Trial) Investigator, funded by the Health Research Board of Ireland; DR is enrolled in the College of Anaesthesiologists of Ireland specialist training program

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Internal sources

- Cochrane Central Editorial Service, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We had indicated in our protocol that we would limit the search from 2000 onwards, around the time care bundles were implemented in practice. As the search was implemented covering all dates, to ensure high sensitivity, we searched all retrieved records irrespective of year.

INDEX TERMS

Medical Subject Headings (MeSH)

COVID-19 [complications] [epidemiology] [*therapy]; *Critical Care; Influenza, Human [therapy]; Intensive Care Units; Pandemics; Patient Care Bundles [*methods]; Pneumonia, Viral [therapy]; Respiratory Distress Syndrome [therapy]; Respiratory Insufficiency [therapy]; *SARS-CoV-2; Treatment Outcome

MeSH check words

Humans

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