Screening and Treatment for Post-intensive Care Syndrome after Discharge of Patients with COVID-19

Post-intensive Care Syndrome (PICS) is a nonspecific syndrome involving the physical, mental, and emotional stress associated with critical illness and its treatment in intensive care units (ICUs). Cardinal features of PICS in patients include neuromuscular weakness, cognitive impairment, and anxiety, depression, or post-traumatic stress syndrome (PTSD). These symptoms can manifest days, weeks, or months after discharge. Risk factors for PICS are longer ICU stay, mechanical ventilation and sedation, delirium episodes, and insufficient communication and psychosocial support. Insufficient recognition of these risk factors, some of which are modifiable, and their effects after discharge remain a barrier to effective PICS management. In the COVID-19 pandemic, patients who require substantially long periods of mechanical ventilation and ICU stay are at high risk of developing PICS. Sufficient screening for PICS to effectively treat and manage the syndrome is needed, although increased diagnosis and treatment could also create a capacity challenge for rehabilitation facilities in regions with many survivors of COVID-19.

No published studies provide data to assess PICS diagnosis and treatment in ICU patients who survived COVID-19. Our assessment of systematic reviews with meta-analyses of studies on PICS and patients treated in ICUs for any reason show that physical therapy and ICU diaries improve patient quality of life (QOL) after ICU discharge. ICU diaries also reduce postdischarge anxiety and depression risks. However, data are inconclusive on the effectiveness of physical rehabilitation and specialized post-ICU follow-up services because findings were too inconsistent across studies. Too few studies of other diagnostic or prevention strategies are available to draw conclusions. Large, multicenter studies are needed on PICS in ICU patients with COVID-19 to address evidence limitations and gaps. An evidence-based guideline recommends dedicated follow-up for patients discharged from ICUs. Two guidelines based on expert consensus emphasize the role of dedicated follow-up and family and caregiver education to prevent PICS.

Evidence limitations: For several interventions and outcomes of interest, pooled confidence intervals reported in meta-analyses were too wide to support conclusions. Reported findings may not generalize to all intervention protocols and patient groups because of variability in methods and patient demographics across included studies. Individual clinical studies we reviewed in addition to the SRs need independent validation and are at high risk of bias from lack of randomization, controls, or independent validation. Only one clinical study reported on prognostic or diagnostic interventions intended to identify patients with PICS.
Executive Summary

Findings

We assessed 4 systematic reviews (SRs) and 6 clinical studies not included in the SRs.

- **ICU follow-up services**: A meta-analysis of 5 studies (Schofield-Robinson et al. 2018) found that dedicated follow-up programs provided no QOL benefit after 1 year and did not reduce mortality or PTSD risks after ICU discharge; however, data are of unclear significance because confidence intervals (CIs) were wide.

- **Physical therapy**: A meta-analysis of 7 studies (Geense et al. 2019) found that rehabilitation before and after discharge improved Short Form-36 (SF-36) mental scores by a mean 2.62 points (95% CI, 0.92 to 4.32), but not physical scores; however, CIs were wide. An SR of 10 studies (Taito et al. 2019) reported no mortality benefits (relative risk [RR] 1.05, 95% CI 0.66 to 1.66) of physical therapy in patients who received mechanical ventilation. One sham-controlled RCT reported no benefits with leg neurostimulation in hospitalized patients.

- **ICU diaries**: A meta-analysis of 12 studies (Barreto et al. 2019) found that diary use reduced the risk of depression (RR 0.41, 95% CI 0.23 to 0.75) and improved SF-36 QOL scores by a mean 10.3 points (95% CI 0.79 to 19.8) in patients discharged from ICUs, but not in their relatives.

- **Other preventive interventions**: Geense et al. found too few studies to draw conclusions about psychosocial interventions. A before-and-after study (Daniels et al. 2018) reported no QOL benefits with a PICS education program for patients and relatives. A prospective case series (Venni et al. 2018) reported near-normal SF-36 scores and 18% PICS prevalence after 6 months in patients discharged from an ICU that adopted sedation and ventilation reduction, early mobilization, and delirium surveillance protocols. A prospective case series (Stollings et al. 2018) reported that post-ICU pharmacotherapy review resulted in actionable findings in up to 32% of cases.

- **Prognosis**: A prospective cohort study (Milton et al. 2017) reported that discharge Hospital Anxiety and Depression Scale (HADS) and the Post-Traumatic Stress Symptoms Checklist-10 (PTSS-10) scores predicted 3-month morbidity with moderate accuracy (area under receiver operating characteristic curve: HADS-anxiety, 0.75; HADS-depression, 0.80, PTSS-10, 0.90).

Evidence

Search dates: January 1, 2015, to April 23, 2020. We reviewed full text of 4 SRs, full text of 5 clinical studies (not in the SRs), and the abstract of 1 clinical study reporting on a total of 8,856 patients.

- We identified no studies specific to COVID-19 and therefore included studies of interventions for PICS in patients treated for any reason in ICUs. We reviewed full-text articles available through open access or our library subscriptions and abstracts of other studies. We included SRs and clinical studies with n >10. Please see full text for additional details about the included SRs.

- 4 SRs (>15% overlap of included patients): 1 SR (Geense et al. 2019, n = 5,165) included physical and psychosocial therapies, dedicated follow-up services, and ICU diaries and reported on physical function and QOL. 1 SR (Taito et al. 2019, n = 1,110) reported more detailed results of studies in the Geense SR by focusing on physical therapy in patients who received mechanical ventilation and reported on mortality. 2 SRs reported more detailed results of studies in the Geense et al. SR by focusing on ICU diaries (Barreto et al. 2019, n = 2,812) and follow-up (Schofield-Robinson et al. 2018, n = 1,707), respectively, and reporting on morbidity and QOL.

- 1 RCT (Wu et al. 2019, n = 66) compared physical therapy conducted by a dedicated team or by usual staff in patients discharged from ICUs to general wards and reported on stay length and QOL at 1-year follow-up.

- 1 sham-controlled RCT (Patsaki et al. 2017, n = 128) reported on physical function at discharge in patients who received muscle neurostimulation in addition to physical therapy after transfer from an ICU to a general ward.

- 1 pre-post study (Daniels et al. 2018, n = 196) compared QOL at 6-month follow-up in ICU patients before and after adoption of a PICS education program for patients and caregivers.

- 1 case series (Venni et al. 2018, n = 159) reported on QOL and PICS incidence in discharged ICU patients after the ICU implemented sedation and ventilation reduction protocols, early mobilization, and delirium surveillance.

- 1 case series (Stollings et al. 2018, n = 56) reported on pharmacotherapy changes in recently discharged ICU patients whose treatment was reviewed by a dedicated ICU recovery pharmacist.
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- 1 diagnostic cohort study (Milton et al. 2017, n = 82) reported on the prognostic accuracy of discharge scores (HADS and PTSS-10) to predict 3-month anxiety and PTSD, respectively.

- **Evidence limitations.** Meta-analyses of studies on ICU diaries and physical rehabilitation is conclusive for short-term QOL, but pooled CIs are too wide for other outcomes. Findings may also not generalize to all patient groups because of study heterogeneity. SRs found evidence inconclusive on other interventions. Many of the reviewed clinical studies are at high risk of bias from lack of randomization, controls, or independent validation. A single study reported on prognostic or diagnostic interventions.

Guidelines, Position, and Consensus Statements

Searched PubMed, EMBASE, and ECRI Guidelines Trust® (EGT) for relevant documents published January 1, 2015, to April 23, 2020. We identified 4 documents.

Guidelines Supported by Systematic Reviews

- We sought guidelines supported by published SRs or included in EGT, a public online repository of guidelines supported by SRs and developed by nationally and internationally recognized medical organizations and specialty societies. These guidelines must meet certain U.S. National Academy of Medicine criteria. We found 2 relevant guidelines supported by SRs, as follows:
  - Argentine Society for Intensive Care. Follow-Up Program after Intensive Care Unit Discharge, 2019. The document recommends ICU follow-up programs and rehabilitation referral for improving physical function, mental health, and QOL in patients at high PICS risk and lists validated instruments for outcome assessment. The SR found insufficient evidence on key questions. Recommendations are based on expert consensus.
  - Scottish Intercollegiate Guidelines Network. Risk Reduction and Management of Delirium, 2019. The guideline recommends that “in patients who have experienced delirium in ICU, consideration should be given to follow up for psychological sequelae including cognitive impairment.”

Other Documents

- European Academy of Rehabilitation Medicine. Covid-19 and Post Intensive Care Syndrome: A Call for Action. 2020. This document raises awareness that a spike in PICS incidence is expected as consequence of the 2019-20 COVID-19 pandemic and calls on governments, healthcare providers, medical societies, and medical societies to take steps to ensure that appropriate screening, prevention, and treatment options are in place for at-risk ICU survivors.
- Nurses Improving Care for Healthsystem Elders (NICHE). NICHE Recommended Care Of the Critically Ill Older Adult, 2015. This document recommends caregiver role training to reduce stress and prevent PICS in relatives who are in caregivers for elderly patients discharged from critical care.
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Background

Post-intensive Care Syndrome

PICS is a condition characterized by a health decline that presents within weeks or months of ICU discharge and is not directly related to the initial disease or injury (or to a new one), but rather to the physical, emotional, and mental stress associated with critical illness and critical care. Despite occurring in up to 80% of ICU survivors, PICS did not become recognized as an independent clinical entity until circa 2010. PICS manifestations may vary in nature and severity, but cardinal features include neuromuscular weakness (reduced grip, difficulty walking, fatigue), cognitive deficits (memory, thinking, and concentration difficulties), and psychological morbidity (anxiety, depression, and PTSD). Psychological features of PICS are also common in close relatives and caregivers of ICU survivors and are often referred to as PICS-Family (PICS-F). (For more information, see the review Post-intensive Care Syndrome: an Overview and the Cleveland Clinic article Post-Intensive Care Syndrome [PICS].)

The etiology of PICS is unclear, but major risk factors include patient characteristics, underlying disease, and ICU-related factors. Long-term disability and mortality are higher among ICU survivors who are older, frail, or have serious physical and mental comorbidities. PICS is also more common in survivors of certain severe, life-threatening conditions, such as sepsis and acute respiratory failure. ICU length of stay is a major PICS risk factor. High physical, mental, and emotional stress are inherent to critical illness, and critical care often involves aggressive treatments and difficult decisions that add to stress. The necessary presence of life-support systems, alarms, and nighttime disruptions also contribute to stress in contemporary ICUs. Nevertheless, some PICS risk factors associated with critical care are particularly significant because they may be amenable to modification to reduce PICS risks:

- **Delirium**: Underlying disease, ICU stressors, and the psychotropic medications trigger delirium episodes in 20% to 80% of ICU patients. The number and duration of inpatient delirium episodes are predictors for anxiety, depression, PTSD, and long-term cognitive dysfunction among ICU survivors. Elderly patients and patients with neuropsychiatric comorbidities are at higher risk of delirium in the ICU. (See Delirium in the Intensive Care Unit.)

- **Immobilization**: Muscle deconditioning from prolonged immobility is the proposed main driver of neuromuscular impairment onset in ICU patients, although histopathologic changes resulting from inflammation and hypoxia may also contribute. Neuromuscular weakness improves over several months in many patients but may last for years in others. (See also The Impact of Extended Bed Rest on the Musculoskeletal System in the Critical Care Environment.)

- **Mechanical ventilation**: Patients who require mechanical ventilation typically have severe illness and remain longer in the ICU. Mechanical ventilation typically involves sedation and prolonged immobility. Forced breathing can also injure chest and abdomen muscles. Even with mechanical ventilation, patients with respiratory failure may not achieve optimal oxygenation, resulting in subacute neural damage leading to cognitive impairment. Mechanical ventilation is also a PICS-F risk factor because relatives may perceive it as a portent of poor outcomes. (See Post-intensive Care Syndrome: its Pathophysiology, Prevention, and Future Directions.)

- **Pharmacotherapy**: Several sedatives (e.g., benzodiazepines) and analgesics (e.g., opioids) often used in critical care have psychotropic effects that may contribute to delirium episodes and onset of anxiety, depression, and PTSD. Neurotropic effects of medication may also contribute to long-term cognitive and neuromuscular impairment. (See also Sedation in the Intensive Care Setting.)

Physical and mental disability associated with PICS represent a significant societal burden. Up to 50% of ICU survivors are unable to fully resume previous work after a year. Furthermore, ICU survivors are at higher risk of rehospitalization and have lower QOL and mortality than the general population. Thus, effective diagnosis, prevention, and treatment of PICS remains an important clinical goal. (For more information, see the Society of Critical Care Medicine article Post-intensive Care Syndrome and the UptoDate article Post-Intensive Care Syndrome [PICS] [available with subscription only].)
PICS Diagnosis and Management

PICS diagnosis is a clinical diagnosis, based on symptoms and patient history. No specific tests are available for PICS, but clinicians may use several validated clinical evaluation instruments to assess and monitor physical function (e.g., Medical Research Council Scoring System for Muscle Strength, six-minute walking test), cognitive function (Montreal Cognitive Assessment, Mini-Mental State Examination), and mental status (e.g., Beck Depression Inventory II, Beck’s Anxiety Scale, PTSD Symptom Scale Interview). However, insufficient recognition of PICS remains a barrier to diagnosis.

PICS treatment consists of physical therapy, psychosocial interventions, and pharmacotherapy to achieve physical and cognitive rehabilitation and to reduce anxiety, depression, and PTSD symptoms. Physical rehabilitation may consist of exercise, device-assisted therapy (e.g., neurostimulation), and use of orthoses. Cognitive rehabilitation may involve occupational therapy and pharmacotherapy with anti-Alzheimer drugs (e.g., donepezil, memantine). Anxiety, depression, and PTSD management may involve psychotherapy and pharmacotherapy with anxiolytics and antidepressants. (For more information, see the UptoDate article Post-Intensive Care Syndrome [PICS].)

Many ongoing efforts to improve PICS-related outcomes focus on prevention, and explored strategies largely involve risk factors associated with ICU practices. Key risk reduction strategies include:

- Reducing mechanical ventilation use and duration by considering early ventilator weaning and use of noninvasive ventilation modes
- Reducing opioid analgesia and sedation reduction by reviewing pharmacotherapy on an ongoing basis and considering alternative drugs and treatments
- Reducing delirium episodes by eliminating or minimizing potential triggers and implementing structured recognition and management protocols
- Achieving mobilization and initiating physical and occupational rehabilitation as soon as possible in ICU patients
- Recognizing psychological and emotional stress and patient and family needs, and promote access to support measures, such as education materials, ICU diaries, and peer groups.
- Providing dedicated, proactive follow-up of patients discharged from ICUs with special attention to PICS recognition and management

Because of PICS’s multifactorial etiology, medical experts and professional societies argue that optimal PICS outcomes are more likely with multicomponent programs, such as the ABCDE bundle (Airway management, Breathing trials, Choice of anesthesia, Delirium assessment, and Early mobilization) and that their implementation should involve a multidisciplinary team, including ICU providers, primary physicians, physical and occupational therapists, mental health specialists, and social workers, as needed. (For additional information, see reviews Post-intensive Care Syndrome: Its Pathophysiology, Prevention, and Future Directions and Post-intensive Care Syndrome: an Overview.)

PICS in Patients with COVID-19

COVID-19 emerged in December of 2019; therefore, at the time of this report, no patients have been in recovery for longer than 4 months. Nevertheless, high PICS incidence is expected among survivors because patients with COVID-19 who become critically ill often require mechanical ventilation and require it for long periods, remain in the ICU for two to three weeks, and are exposed to higher stress levels because of the necessary isolation from relatives. The strain imposed by high patient volumes, additional safety measures, and equipment and staff shortages are also likely to disrupt PICS prevention practices in ICUs during the ongoing COVID-19 outbreak. Several experts have voiced concern that healthcare systems may not be sufficiently prepared to manage the increased PICS incidence that may result from the COVID-19 outbreak. In a poll of 100 ECRI members during a webinar conducted on May 1, 2020, two-thirds of respondents reported having no PICS prevention or ICU follow-up strategies in place to screen for PICS. (For more information, see Stress and Psychological Distress among SARS Survivors 1 Year after the Outbreak and the articles For Survivors of Severe COVID-19, Beating the Virus Is Just the Beginning and Covid-19 and Post Intensive Care Syndrome: A Call for Action.)
Guidelines, Position and Consensus Statements

Searches of PubMed, EMBASE, EGT, and other web-based resources identified three relevant guidelines and documents published between January 1, 2015, and April 23, 2020. We sought guidelines that are clearly supported by published systematic reviews (SRs) or included in EGT. EGT is a publicly available online repository of guidelines supported by SRs and developed by nationally and internationally recognized medical organizations and specialty societies. These guidelines must meet certain U.S. National Academy of Medicine criteria. We found two relevant guidelines supported by SRs and one other document.

Guidelines Supported by Systematic Review

- Argentine Society of Intensive Care. Follow-Up Program after Intensive Care Unit Discharge. 2019. This guideline conducted an SR but found insufficient evidence to support any conclusions to relevant key questions. In the absence of evidence, the guideline recommends the following based on expert consensus:

  Based on the trials included, it is not possible to establish a recommendation about the population to be included in the follow-up... Here the recommendation from our expert panel's: the patient should meet at least 2 of the aforementioned criteria [APACHE score >14, frailty, mechanical ventilation for >7 days, ICU stay for >10 days, non-ambulatory patient at discharge, and attending physician recommendation] to be included in the program.

  Our expert panel’s recommendation is this: the patient can be given an appointment within a month after hospital discharge and, depending on the alterations observed it will be the subsequent frequency including an appointment one year after discharge.

  Our expert panel’s recommendation is this: the management of the PICS should be conducted via a multidisciplinary team led by a physician, preferably one trained in the critical area, and one kinesiologist. Ideally, a psychologist and a nutritionist could join the team.

  Experts' recommendation: we consider that follow-up programs are useful for the assessment of survival, but data are insufficient to evaluate their impact.

  Experts' recommendation: follow-up programs are recommended for assessing and rehabilitating physical function at ICU discharge. Patients showing a significant reduction of their physical function as evidenced by their dependence on any of the ADA [activities of daily living], evaluated by the KI [Katz Index], or by their impossibility to walk by 6MWT [6-minute walking test], should be referred to motor rehabilitation.

  Experts' recommendation: follow-up programs are recommended for assessing and rehabilitating mental function at ICU discharge. In patients showing depression confirmed through the HADS > 7 or BDI-II [Beck Depression Inventory II] > 14---20, or anxiety confirmed by BAI [Beck's Anxiety Index] with scores over 11 or PTSD confirmed by the IES-R [Impact of Event Scale-revised] scale with scores over 24, referral to the area of psychiatry should be indicated.

  Experts' recommendation: follow-up programs are recommended to assess and treat pain at ICU discharge. Patients showing pain after answering question number 4 from the Euroqol EQ-5D-3L [European QOL 5-dimensional 3-level questionnaire] score on quality of life (see assessment of quality of life) should be referred to the corresponding specialist.

  Experts' recommendation: follow-up programs are recommended to assess and rehabilitate cognitive function at ICU discharge. Patients showing cognitive deficiencies assessed by the MOCA [Montreal Cognitive Assessment] test with values under 17 points should be referred to a specialist in cognitive therapy for their rehabilitation.

  Experts' recommendation: follow-up programs are recommended to assess and rehabilitate quality of life at ICU discharge. The assessment can be conducted with either questionnaire, the EQ-5D 3L or the SF-36.
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Experts' recommendation: follow-up programs are recommended to assess the nutritional condition at ICU discharge. Patients showing values ≥2 should be referred to the specialist for follow-up purposes (for further details, see supplementary data). In addition, feeding through nasogastric tube or the ostomy bag is an indication for follow-up for the nutrition team.

Experts' recommendation: a minimum duration of one year of follow-up is recommended after ICU discharge.

— Scottish Intercollegiate Guidelines Network. Risk Reduction and Management of Delirium. 2019. The guideline recommends that “in patients who have experienced delirium in ICU consideration should be given to follow up for psychological sequelae including cognitive impairment.”

Other Documents

Although we are currently overwhelmed by the astonishing speed of infection of the Covid-19 pandemic, and the daily onslaught of new, and ever-worsening predictions, it is vital that we begin to prepare for the aftershocks of the pandemic. Prominent among this will be the cohort of post-intensive care survivors who have been mechanically ventilated and will likely experience short- and medium-term consequences. The notion that patients surviving intensive care and mechanical ventilation for several weeks can be discharged home without further medical attention is a dangerous illusion. Post Intensive Care Syndrome and other severe conditions will require not only adequate screening but early rehabilitation and other interventions. Action must be taken now to prepare for this inevitable

— NICHE. NICHE Recommended Care of the Critically Ill Older Adult. 2015 (available with subscription only). The document states:

Families require special attention to prevent postintensive care syndrome-family. Teaching the caregiving role may both prepare families for caregiving duties at home and also provide them with meaningful activities that can minimize the stress of being exposed to critical illness.

Clinical Literature
We searched PubMed, EMBASE, Google Scholar, the Cochrane Library, and selected web-based resources for clinical studies relevant to this topic published between January 1, 2015, and April 23, 2020. Our search strategies included the following keywords: disability evaluation, PICS, post-intensive care syndrome, rehabilitation, therapy. Please see the Selected Resources and References section for detailed search strategies.

We included SRs that assessed interventions for diagnosing, preventing, or treating PICS and reported on diagnostic accuracy of interventions intended to detect PICS, treatment delivery, and patient-centered outcomes. To minimize double-counting patients, we reviewed the most recent or comprehensive of overlapping reports on the same outcomes or interventions. We also reviewed individual clinical studies not described in the included SRs. We reviewed full text of articles available through open access or our library subscriptions and abstracts of the remaining articles. We reviewed full text of four SRs and five clinical studies and the abstract of one clinical study described below. Table 1 summarizes the SRs’ findings. Table 2 summarizes the clinical study findings.

Of the four SRs, the largest (Geense et al. 2019) reported on several PICS interventions; however, three smaller SRs that included several of the studies also included in the Geense SR focused on specific populations or interventions in greater detail within their respective focus, so we included them despite some overlap of included studies.

We identified but excluded from review:

— 4 studies reporting on the implementation of PICS prevention or treatment interventions, but not on their effectiveness
— 2 clinical instrument validation studies

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- 2 cross-sectional studies that reported outcomes in patients stratified according to clinical evaluation instruments but did not report on the instrument’s diagnostic or prognostic accuracy(8,9)
- 2 cross-sectional studies that correlated the use of interventions with patient outcomes but did not report intervention effects(10,11)

We also excluded studies with fewer than 10 patients and conference abstracts.

Systematic Reviews

- 1 SR of 36 studies (Geense et al. 2019, n = 5,165) assessed physical rehabilitation, psychosocial interventions, dedicated follow-up services, and ICU diaries and reported on physical function and QOL in patients discharged from ICUs.(1) This was the largest SR. We also reviewed three SRs that had >15% overlap of included studies and patients. (See below.)
- 1 SR of 10 studies (Taito et al. 2019, n = 1,110) focused on physical rehabilitation in patients who received mechanical ventilation and reported on mortality.(12) We excluded two other less recent and comprehensive SRs focusing on physical rehabilitation were excluded.(13,14)
- 1 SR or 12 studies (Barreto et al. 2019, n = 2,812) focused on ICU diaries and reported on QOL and psychological morbidity.(15) This SR included more relevant studies than Geense et al.
- 1 SR of 5 studies (Schofield-Robinson et al. 2018, n = 1,707) focused on follow-up services and reported on mortality, morbidity, and QOL.(16) This SR included more relevant studies than Geense et al.

Clinical Studies

- 1 RCT (Wu et al. 2019, n = 66) compared physical therapy conducted by mobile rapid response team or by usual staff in hospitalized patients discharged from the ICU to non-critical care wards, and reported on hospitalization length and physical and mental status at 1-year follow-up.(17)
- 1 sham-controlled RCT (Patsaki et al. 2017, n = 128) reported on physical function at discharge in patients who received physical therapy and muscle neurostimulation after transfer from ICU to general wards.(18)
- 1 pre-post study (Daniels et al. 2018, n = 196) compared physical function and QOL at 6-month follow-up in patients treated at a single ICU before and after adoption of a patient and caregiver PICS education program consisting of video and written materials and in-person coaching.(19)
- 1 case series (Venni et al. 2018, n = 159) reported on QOL and PICS incidence in patients discharged from an ICU that implemented a multicomponent PICS prevention protocol consisting of sedation and ventilation reduction, early mobilization, and enhanced surveillance and response to delirium signs.(20)
- 1 case series (Stollings et al. 2018, n = 56) reported on pharmacotherapy changes in patients recently discharged from ICU and whose treatment was reviewed by a dedicated ICU recovery pharmacist.(21)
- 1 diagnostic cohort study (Milton et al. 2017, n = 82) reported on prognostic accuracy of discharge HADS and PTSS-10 scores to predict anxiety and PSTD incidence, respectively.(22)

Evidence limitations. Evidence from RCTs and controlled studies synthesized in meta-analyses is sufficient to permit limited conclusions on the utility of ICU diaries and physical rehabilitation to improve short-term QOL following ICU discharge. However, pooled confidence intervals are too wide to support conclusions on other outcomes (i.e., physical function, mortality). Furthermore, reported findings are subject to significant limitations to interpretation because studies involved different treatment protocols and patient demographics. Therefore, findings may not generalize to all intervention protocols and patient groups.

In addition, a large evidence gap remains. SRs found evidence too limited in quantity and quality to draw conclusions on other preventive and therapeutic interventions. Additional individual studies we reviewed were insufficient to draw conclusions because they had a high risk of bias from lack of randomization or controls or because results lacked additional independent validation. Only one study reported on prognostic or diagnostic interventions. Large, multicenter controlled studies and diagnostic cohort studies are needed to address the limitations and evidence gaps and define clinical pathways for optimal management of PICS.
## Table 1. Systematic Reviews

<table>
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<th>Authors’ Conclusions</th>
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<tr>
<td>Barreto et al. 2019(15)</td>
<td>“To reevaluate the current literature on the effect of ICU [intensive care unit] diaries for patients admitted in the ICU and their relatives, giving also a detailed description of the diary structure, healthcare impression on writing diaries, and patients’ feedbacks on receiving an ICU diary.”</td>
<td>Searched PubMed, OVID, EMBASE, EBSCO host, and PsydNFO in July 2019 for clinical studies comparing use of ICU diaries with no additional intervention. Included 12 studies (n = 2,812).</td>
<td>“When pooling the results, ICU diary was associated with lower risk of depression (RR 0.41, 95% CI 0.23–0.75) and better quality of life (10.3 points higher in SF-36 general health score, 95% CI 0.79–19.8), without a decrease in anxiety or post-traumatic stress disorder (PTSD). For the relatives receiving an ICU diary, there was no difference in the incidence of PTSD, anxiety, or depression.”</td>
<td>“This systematic review and meta-analysis supports the use of ICU diaries to reduce the risk of depression and preserve the quality of life of patients after ICU admission. ICU diaries do not seem to have any beneficial effect on the relatives of the patients.”</td>
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<td>Geense et al. 2019(1)</td>
<td>“To assess the effectiveness of nonpharmacologic interventions to prevent or mitigate adverse long-term outcomes among ICU survivors.”</td>
<td>Searched PubMed, CINAHL, PsydNFO, EMBASE, and Cochrane CENTRAL in July 2018 for longitudinal studies of interventions to prevent postdischarge adverse events (AEs) in ICU patients. Included 36 studies (n = 5,165). This study overlaps with 1 or more of the reviews listed above and reports on 4,066 unique patients.</td>
<td>“Interventions were subdivided into six categories: 1) exercise and physical rehabilitation programs; 2) follow-up services; 3) psychosocial programs; 4) diaries; 5) information and education; and 6) other interventions. Many outcomes favored the interventions, but significant differences were only found for... exercise programs in improving the Short Form Health Survey-36 Mental Component Score (seven studies, n = 664; mean difference, 2.62; 95% CI, 0.92–4.32).”</td>
<td>“There is thin evidence that diaries and exercise programs have a positive effective on mental outcomes. Despite outcomes favoring the intervention group, other commonly used nonpharmacologic interventions in daily ICU practice are not supported by conclusive evidence from this meta-analysis.”</td>
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<tr>
<td>Author/Year</td>
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<td>Taito et al. 2019(12)</td>
<td>“To determine whether enhanced physical rehabilitation [ICU] discharge improves activities-of-daily-living function, quality of life (QOL) and mortality among patients who received mechanical ventilation in the ICU.”</td>
<td>Searched MEDLINE, EMBASE, CENTRAL, PEDro, and WHO International Clinical Trials Registry in January 2019 for relevant randomized controlled trials (RCTs). Included 10 RCTs comparing rehabilitation with usual care alone (n = 1,110). This study overlaps with 1 or more of the reviews listed above and reports on 372 unique patients.</td>
<td>“Rehabilitation did not significantly decrease long-term mortality (RR 1.05, 95% CI 0.66 to 1.66). The analysed trials did not report activities-of-daily-living data. The certainty of the evidence for QOL and mortality was moderate.”</td>
<td>“Enhanced physical rehabilitation following ICU discharge may make little or no difference to QOL or mortality among patients who received mechanical ventilation in the ICU.”</td>
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<td>Schofield-Robinson et al. 2018(16)</td>
<td>“To assess the effectiveness of follow-up services for ICU survivors that aim to identify and address unmet health needs related to the ICU period.”</td>
<td>Searched CENTRAL, MEDLINE, EMBASE and CINAHL in November 2017 for studies that compared “an ICU follow-up service using a structured programme and co-ordinated by a healthcare professional versus no follow-up service or standard care.” Included 5 studies (n = 1,707). This study overlaps with 1 or more of the reviews listed above and reports on 171 unique patients.</td>
<td>“Follow-up services for improving long-term outcomes in ICU survivors may make little or no difference to HRQoL [health-related quality of life] at 12 months… We found moderate-certainty evidence from five studies that they probably also make little or no difference to all-cause mortality up to 12 months after ICU discharge (RR 0.96, 95% CI 0.76 to 1.22; 4 studies; 1289 participants; and in one non-randomised study 79/259 deaths in the intervention group, and 46/151 in the control group) and low-certainty evidence from four studies that they may make little or no difference to PTSD (SMD -0.05, 95% CI -0.19 to 0.10, 703 participants, 3 studies; and one non-randomised study reported less chance of PTSD when a follow-up service was used).”</td>
<td>“We found insufficient evidence, from a limited number of studies, to determine whether ICU follow-up services are effective in identifying and addressing the unmet health needs of ICU survivors.”</td>
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## Table 2. Clinical Trials

<table>
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<th>Author/Year</th>
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<th>Findings Reported by Authors</th>
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<td><strong>Randomized Controlled Trials</strong></td>
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<td>Wu et al. 2019(17)</td>
<td>Assessor-blinded, single-center study of 66 patients transferred to non-critical wards after &gt;5 days in an intensive care unit (ICU)</td>
<td>Inpatient physical rehabilitation therapy conducted as usual by acute care ward staff (n = 36) or as an early intervention by a mobile, dedicated team (n = 30)</td>
<td>“The intervention group received more physiotherapy and occupational therapy sessions per week than the usual-care group (median = 8.2 vs 4.9, p &lt; 0.001). Total length-of-stay was variable; while median values differed between the intervention and usual care groups (median 31 vs 41 days), this was not significant and the pilot study was not adequately powered (p = 0.57). No significant differences were observed in the secondary outcomes [physical function and psychological status] at hospital discharge, 6- or 12-month follow-ups.”</td>
<td>“Provision of intensive early rehabilitation to [ICU] survivors on the acute ward is feasible. A further trial is needed to draw conclusions on how this intervention affects length-of-stay and functional outcomes.”</td>
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<td>Patsaki et al. 2017(18)</td>
<td>Double-blind, single-center study of 128 patients transferred from ICU to non-critical patient wards</td>
<td>Daily physical therapy with active or sham lower-limb neurostimulation until discharge</td>
<td>“MRC [Medical Research Council], handgrip, functional status and hospital length of stay did not differ at hospital discharge between groups (p &gt; 0.05). ΔMRC% one and two weeks after ICU discharge tended to be higher in NMES [neuromuscular electrical stimulation] group, while it was significant higher in NMES group of patients with ICU-acquired weakness at two weeks (p = 0.05).”</td>
<td>“NMES and personalized physiotherapy in ICU survivors did not result in greater improvement of muscle strength and functional status at hospital discharge. However, in patients with ICU-aw [ICU-acquired weakness] NMES may be effective.”</td>
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<td>NCT01717833</td>
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# CLINICAL EVIDENCE ASSESSMENT

## Screening and Treatment for Post-intensive Care Syndrome after Discharge of Patients with COVID-19

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Intervention</th>
<th>Findings Reported by Authors</th>
<th>Authors’ Conclusions</th>
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<tr>
<td><strong>Nonrandomized Comparative Study</strong></td>
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<td>Daniels et al. 2018(19)</td>
<td>Pre-post implementation study of 193 patients discharged from a single tertiary ICU</td>
<td>Patient participation in a post-intensive care syndrome (PICS) education program consisting of videos, written materials, and in-person counseling (n = 93) or no additional intervention (n = 100)</td>
<td>“The qualitative analysis demonstrated that patients and caregivers participating in the interventions after hospitalization demonstrated increased understanding of life after critical illness and PICS. In addition, patients and caregivers participating in the support groups noted a sense of community, with decreased feelings of being left alone to cope with their ailment (PICS).”</td>
<td>“Interventions targeted to patients after hospitalization may offer subjective improvement in QOL for those at risk for PICS.”</td>
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<td>“After adjustment for patient characteristics, there was no evidence of a difference in average [SF-36] physical composite score (difference = −1.23; 95% CI = −4.60 to 2.13; P=.47) or mental composite score (difference = −0.16; 95% CI = −3.49 to 3.17; P=.92).”</td>
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<tr>
<td><strong>Case Series</strong></td>
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<td>Venni et al. 2018(20)</td>
<td>Prospective, single-center study of 159 patients treated at an ICU for &gt;3 days</td>
<td>Structured PICS prevention, including sedation and ventilation optimization, delirium monitoring and early treatment, and early mobilization</td>
<td>“Most patients positively rated their health at the 6-month follow-up and had no significant impairment in physical or mental health status. The mean normalized values of the physical and mental component of the SF-12 score were 46 ± 11 and 48 ± 14, suggesting a normal physical and mental health status in most patients. Twenty-nine patients (18.2%) showed evidence of PICS. Similar good results were found by the questionnaire of memories.”</td>
<td>“In this real-world analysis that lacks a control group, patients who used a program aimed at minimizing the risk of HRQoL deterioration and PICS reported a good perception of their state of health with a relatively low prevalence of PICS.”</td>
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## CLINICAL EVIDENCE ASSESSMENT

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<td>Stollings et al. 2018(21)</td>
<td>Prospective, single-center study of 56 patients seen at a dedicated ICU recovery center (ICU-RC) within a tertiary hospital</td>
<td>Pharmacotherapy review by ICU-RC pharmacist</td>
<td>“All 56 patients had at least 1 pharmacy intervention; 22 (39%) patients had medication(s) stopped at the clinic appointment, and 18 (32%) patients had new medication(s) started. The pharmacist identified 9 (16%) patients who had an adverse drug event (ADE); 18 (32%) patients had ADE preventive measures instituted. An influenza vaccination was administered to 13 (23%) patients despite an inpatient protocol to ensure influenza vaccination prior to discharge. A pneumococcal vaccination was administered to 2 (4%) patients.”</td>
<td>“Use of a critical care pharmacist resulted in the identification and treatment of multiple medication-related problems in an ICU-RC as well as implementation of preventive measures.”</td>
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<td>Milton et al. 2017(22)</td>
<td>Prospective study of 82 patients at single ICU</td>
<td>Hospital Anxiety and Depression Scale (HADS) and the Post-Traumatic Stress Symptoms Checklist-10 (PTSS-10) evaluation 1 week and 3 months after discharge</td>
<td>“We found correlation between early and late scores and reasonable predictive precision regarding 3-month outcomes, with an AUROC of 0.90 for PTSS-10 part B, 0.80 for the HADS anxiety subscale and 0.75 for the HADS depression subscale.”</td>
<td>“Symptoms of post-traumatic stress, anxiety and depression assessed 1 week after ICU stay correlate with 3-month psychological outcome.”</td>
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<tr>
<td><strong>Diagnostic Cohort Study</strong></td>
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### Selected Resources and Reference

**Search Summaries**

Our master’s-level medical librarians searched the following databases to identify the literature and related materials.

**ECRI Resources [searched January 1, 2015, through April 23, 2020]**

**Search Strategy:**

post* AND "intensive care" AND syndrome*

scan of Rehabilitation topic area

post* AND ("intensive care" OR ICU) and syndrome* in Hospital Inpatient topic area

**Results:** We identified three related reports.

- PSO literature request: transition of care from ICU. [Cleveland Clinic - Guidance]. 2020 Feb 5.
- Should we reconsider how often we intubate older patients? [Risk Management News]. 2018 Jun 27.
Screening and Treatment for Post-intensive Care Syndrome after Discharge of Patients with COVID-19


Search Strategy:

#1 (“postintensive care syndrome” [Supplementary Concept] OR (“post intensive care” OR “postintensive care”) AND syndrome*) OR (PICS* AND syndrome*) AND (disability evaluation OR screening OR habilitation OR rehabilitation OR therapy)


#3 screen*[tiab] OR rehabilitation[tiab] OR therapy[tiab]

#4 “Patient Discharge”[Majr] OR discharge[tiab]


#6 #1 OR (#2 AND #3 AND #4 AND #5)

Results: We identified 74 records.


Search Strategy:


#2 (“intensive care”[mh] OR “critical care”:ti,ab OR “intensive care”:ti,ab OR “critical illness”:exp/mj OR “critical illness*”:ti,ab OR “Intensive care unit”:exp/mj OR “intensive care unit*”:ti,ab OR icu*:ti,ab) AND (survivor*:ti,ab OR survivor:ti,ab)

#3 screen*:ti,ab OR rehabilitation:ti,ab OR therapy:ti,ab

#4 “hospital discharge”:exp/mj OR discharge:ti,ab

#5 (random*:ab,ti OR clinical NEXT/1 trial*) OR ‘health care quality’:exp OR (‘methodology’:exp OR search*:ab,ti OR ‘review’:ti)

#6 #1 OR (#2 AND #3 AND #4 AND #5)

Results: We identified 3 records.


Search Strategy:

#1 (“post intensive care” OR “postintensive care”) AND syndrome*

#2 (mh “Critical Care”) OR “critical care”:ti,ab OR “intensive care”:ti,ab OR [mh “Critical Illness”] OR “critical illness*”:ti,ab OR [mh “Intensive Care Units”] OR “intensive care unit*”:ti,ab OR ICU:ti,ab OR ICUS:ti,ab) AND (survivor*:ti,ab OR survival:ti,ab)

#3 screen*:ti,ab OR rehabilitation*:ti,ab OR therapy*:ti,ab

#4 [mh “Patient Discharge”] OR discharge:ti,ab

#5 #1 OR (#2 AND #3 AND #4)

Results: We did not identify any unique relevant publications.
Guidelines, Position and Consensus Statements [searched January 1, 2015, through April 23, 2020]

Search Strategy:
post* AND (*intensive care* OR icu) AND syndrome* ; intensive care ; scan of relevant society websites

Results: We identified three relevant documents.

Selected Standards and Guidelines


─ Nurses Improving Care for Healthsystem Elders (NICHE). NICHE recommended care of the critically ill older adult. 2015.


Search Strategy: “intensive care”; rehabilitation

Results: We identified two relevant documents.

─ Centers for Medicare & Medicaid Services (CMS). NCD for cardiac rehabilitation programs (20.10). [effective date 2010 Feb 22].

─ CMS. NCD for pulmonary rehabilitation services (240.8). [effective date 2007 Sep 25].

─ We also identified several local coverage policies or articles. To access, search the Local Coverage Database at: Medical Coverage Database. Note: choose Local Coverage, check All Local Coverage, select All States under Geographic area, then choose Keywords, select All Words (and), type: rehabilitation, click Title, and click Search.

Selected Web Resources. [searched April 24, 2020].


─ Mikkelsen, ME, Netzer, G, and Iwashyna, T. Post-intensive care syndrome (PICS). UpToDate. [last updated 2019 Aug 5]. Note: subscription required to access full text.

─ Post-intensive care syndrome (PICS). Cleveland Clinic. [cited 2020 Apr 24].


References Reviewed (PubMed and EMBASE search dates were January 1, 2015, through April 23, 2020)


Screening and Treatment for Post-intensive Care Syndrome after Discharge of Patients with COVID-19


Screening and Treatment for Post-intensive Care Syndrome after Discharge of Patients with COVID-19

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The information presented in this Clinical Evidence Assessment is highly perishable and reflects the state of the literature on this topic at the time at which searches were conducted and the Clinical Evidence Assessment was prepared. Clinical Evidence Assessments provide a guide to the published clinical literature and other information about a topic on which we received a client inquiry. The scope is customized to address the specific information needs of the requestor. The content reflects the information identified from searches of the available, published, peer-reviewed scientific literature, gray literature, and websites at the time the searches were conducted.

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