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SYSTEMATIC REVIEW

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Quality of life in ICU survivors and their relatives with post-intensive care syndrome: A systematic review

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Abstract

Background: Post-intensive care syndrome (PICS) is characterized by all three adverse survivorship dimensions: physical function, cognitive function and mental health status.

Aim: This review aimed to describe the quality of life (QoL) of Intensive Care Unit (ICU) survivors with PICS after discharge and of their relatives with Family Post-intensive care syndrome (PICS-F) and to report anxiety, depression and Post-Traumatic Stress Disorders (PTSD) in studies investigating PICS.

Study Design: A systematic review was carried out. We searched PubMed, Scopus, Web of Science and the Cumulative Index to Nursing and Allied Health Literature. This review was registered in the PROSPERO database (CRD42022382123).

Results: We included 19 studies of PICS and PICS-F in this systematic review. Fourteen observational studies report the effects of PICS on depression, 12 studies on anxiety and nine on post-traumatic stress disorder and 10 on QoL. Mobility, personal care, usual activities and pain/discomfort in QoL were the domains most affected by PICS. A significant association was demonstrated between a high level of ICU survivors' anxiety and high levels of ICU relatives' burden. Strain-related symptoms and sleep disorders were problems encountered by ICU relatives with PICS-F.

Conclusion: PICS and PICS-F were widespread experiences among ICU survivors and their ICU relatives, respectively. The results of this review showed the adverse effects of PICS and PICS-F on QoL.

Relevance to Clinical Practice: PICS and PICS-F strongly impact the rehabilitation process and are measured in terms of health costs, financial stress and potentially preventable readmission.

KEYWORDS

ICU, post-intensive care syndrome, relatives, survivors, systematic review

1 | BACKGROUND

Every year millions of patients who survive critical illness are faced with a new and complex set of consequences and challenges called survivorship.[1] Intensive care unit (ICU) survivors have to deal with a different version of themselves after ICU discharge, characterized by all three adverse survivorship dimensions of physical function, cognitive function and mental health status.[2]

Many ICU survivors do not return to their initial health status.[3] Indeed, as described in the literature, many risk factors are significantly associated with post-intensive care syndrome (PICS), such as older age,[4] female gender,[5] previous mental health problems[4] and specific situations developed during the ICU stay, such as high disease severity,[6] negative ICU experience,[4] and delirium and its duration,[7] which negatively impact quality of life (QoL).[2,6] Authors observed that ICU survivors face different and wide sequelae after ICU discharge,[8] which are identified as the three dimensions of the PICS. Psychological sequelae are common, such as depression, anxiety and post-traumatic stress disorder (PTSD).[9] Cognitive impairments such as difficulty with memory, concentration and attention are observed.[10] Also, physical consequences such as being exhausted, pain,[8,11] muscular weakness[12] and loss of appetite and weight[13] are described.

The three dimensions (physical, psychological and mental) characterize the core properties of PICS.[14] In 2021, Yuan et al. defined the concept of PICS as 'new or worsening co-occurrence of physical dysfunctions, psychological disorders, cognitive impairments or failed social reconstruction with these impairments persisting beyond ICU and hospital discharge'.

This definition of the syndrome thus expresses the need to identify all three dimensions in order to develop a more comprehensive and holistic insight into PICS. In contrast, in 2020 Lee et al. found in their meta-analysis that only one study[15] reported on all three attributes of PICS.[4] The reason may be because PICS has been discussed for a relatively short time.[14]

In 2015, systematic reviews and meta-analyses were published about the impact of routine follow-up consultations on the anxiety, depression, PTSD and QoL of ICU survivors after discharge.[16]

The fifth edition of the Diagnostic and statistical manual of mental disorders (DSM-5™) defines anxiety, depression and PTSD.[17] Anxiety symptoms include conditions that share characteristics of elevated levels of fear or anxiety and related behavioural disturbances. Depressive symptoms refer to disruptive mood dysregulation disorder, while PTSD is a psychiatric disorder that develops in people who have experienced a traumatic event.[17] This review considers all three PICS dimensions, but recent research by Yuan and colleagues[18] reported that many authors chose and evaluated only a single domain of PICS rather than evaluating PICS comprehensively. Furthermore, the authors showed that anxiety and depression could be detected by a single tool and later described as PICS without consideration of the cognitive and physical dimensions.[18]

However, PICS affects not only the ICU survivors' health but also their relatives' health. Family post-intensive care syndrome (PICS-F), which encompasses the psychological and cognitive repercussions that ICU survivors' relatives suffer after the ICU stay, influences QoL.[2,6] This syndrome has been defined by the Society of Critical Care Medicine (SCCM) to identify psychological distress experienced by ICU family members during the post-ICU period, including symptoms of anxiety, depression and PTSD,[19–21] in view of family-centred care as an approach 'that is respectful of and responsive to individual families' needs and values'. Furthermore, an essential aspect of caregiver research is determining the emotional burden described as reduced functional status during daily activities and depression and anxiety symptoms.[22] Together with patient-centred care, it represents the crucial components of the quality of global care, as stated in 2001 by the Institute of Medicine Committee on Quality of Health Care in America.[23] Indeed, family support in the ICU can improve survivors' outcomes by allowing families to be relatives for all intents and purposes.[24]

Renner explains the benefit of ICU diaries written by nurses or family members to record events about the period that critically ill patients usually cannot remember in a recent Guideline on multimodal rehabilitation for patients with post-intensive care syndrome.[25] In follow-up programs, critical care nurses manage the post-discharge period by detecting the sequelae of PICS on ICU survivors and PICS-F on ICU relatives.[16,26] Furthermore, the introduction of nurse-managed ICU diaries allows for reductions in the risks of anxiety, depressive symptoms and PTSD.[25]

Although several authors have focused their studies on analysing the effect of PICS on the health of ICU survivors[27–29] and their relatives,[5] no systematic review has been conducted to summarize the knowledge about the effect of PICS on both ICU survivors and their relatives. Indeed, to our knowledge, systematic reviews[4,30] on PICS have been more focused on understanding the risk factors and less on the consequences, especially the multidimensional concept of the syndrome. Furthermore, a recent systematic review was published about this topic; however, authors were more focused to investigate the characteristics of existing instruments used to measure this syndrome.[18] To our knowledge, researchers have been focused more on ICU survivors than on their relatives.[4,13] This represents a gap in the literature because knowing PICS, identified as a comprehensive three-dimension syndrome, and its effects on both the QoL of ICU survivors and their relatives will provide a different perspective to detect and implement tools and interventions aimed at these two populations.

What is known about the topic

- Post-intensive care syndrome (PICS) and post-intensive care syndrome-family (PICS-F) affect survivors and their relatives after critical illness survivorship.
- PICS is common after acute care admission in three domains: physical, mental and cognitive.
- PICS-F is characterized by psychological sequelae such as anxiety and depression.

What this paper adds

- PICS was associated with poor quality of life in ICU survivors and is explained predominantly by the mental component.
- The mental components of PICS, such as anxiety, depression and PTSD, adversely impact ICU survivors after discharge.
- Relatives who experience PICS-F report increased strain-related symptoms and sleep disorders.

1.1 | Aim and hypothesis

This review aimed to describe the impact of PICS on QoL in ICU survivors after discharge and the reporting of anxiety, depression and PTSD in studies investigating PICS. Furthermore, we investigate a relationship between PICS-F and their relatives 'QoL, regardless of whether the patient displays PICS.

We tested the following hypothesis:

PICS is associated with a negative impact on QoL in ICU survivors. Furthermore, as described in the literature, PICS evaluation was mainly investigated only in term of the mental component.[18] We therefore assume that the mental components of PICS, such as anxiety, depression and PTSD, negatively impact ICU survivors after discharge.

PICS-F was associated with a negative impact on ICU relatives 'QoL' after discharge.

2 | DESIGN AND METHODS

2.1 | Design

This systematic literature review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[31] and registered in the PROSPERO database (CRD42022382123).

2.2 | Search strategy and research questions

A comprehensive bibliographic search was conducted on PubMed (via MEDLINE), CINAHL (via EBSCO), Scopus and Web of Science (via EBSCO) in March 2022. The search strategy included combinations and synonyms of free text and MESH (medical subject headings) terms. To identify additional studies, we also examined the reference lists of retrieved articles.

We included the search terms such as (family* OR caregiver* OR 'care partner' OR carer OR survivor OR dyad OR patient OR carereceiver) AND ('intensive care unit' OR 'intensive care' OR 'critical care' OR ICU) AND ('post intensive care syndrome' OR 'post care syndrome') AND ('quality of Life' OR QoL OR HRQoL OR 'Health Related Quality of Life' OR anxiety OR depression OR stress OR burden OR 'sleep disorder' OR mutuality OR preparedness). The research question was: *How does the onset of post-intensive care syndrome and family post-intensive care syndrome influence QoL in ICU survivors and their ICU relatives?*

2.3 | Study selection

We included original studies with the following inclusion criteria: (1) adult ICU survivors (> = 18 years old); (2) each outcome evaluation within the mental component of PICS; (3) study design: cohort, case–control studies, cross-sectional studies, randomized control trials (RCTs) and longitudinal studies.

Regarding ICU relatives, we included articles according to the following criteria: (1) adult relatives or family (> = 18 years old); (4) any outcome evaluation within the dimensions of PICS-F; and (2) study design: cohort, case–control studies, cross-sectional studies, randomized control trials (RCTs) and longitudinal studies.

Exclusion criteria were (1) studies that did not report the three dimensions of PICS as an outcome variable; (2) study design: reviews; (3) studies that had not been peer reviewed (e.g., abstract, report, editorial, and conference proceedings); and (4) studies not in English.

Regarding relatives, we excluded articles according to the following criteria: (1) studies that did not assess PICS-F as an outcome variable; (2) study design: reviews; (3) studies that had not been peer reviewed (e.g., abstract, report, editorial, conference proceedings); and (4) studies not in English. We limited the search to human studies without temporary restrictions applied.

2.4 | Outcome

The primary outcome of this review was the QoL of ICU survivors. The secondary outcomes were to evaluate a mental component of PICS, such as anxiety, depression, PTSD. Regarding relatives, the primary outcome was to evaluate a Qol.

2.5 | Data extraction

The references obtained from the search string of each database were exported to Endnote v.x7, where duplicates were removed. The results were then uploaded to Rayyan, where two independent reviewers (FG and FT) conducted the initial screening of titles and abstracts. Subsequently, the remaining studies were examined in full text, and data extraction was performed. Non-conformities and disagreements regarding inclusion of the studies were resolved by consensus between the two evaluators; otherwise, the conflicts were resolved by a third reviewer (GP). Data extraction was performed in Microsoft Excel® 2016 via a tool built by the research team. The following information was extracted: authors and years, study design, time to follow-up, setting, PICS or PICS-F, sample size, outcome, main findings, age, gender, type of ICU, length of ICU stay, ICU delirium, acute respiratory failure, mechanical ventilation, number of PICS dimensions investigated, type of dimension explored and country.

2.6 | Evaluation of quality and data extraction

Two independent reviewers (FG and FT) assessed the methodological quality of a review through the full text and the risk of bias through the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Cohort Studies[32] and JBI Critical Appraisal Checklist for RCTs.[33] We used the JBI Critical Appraisal Checklist for analytical cross-sectional studies to evaluate the cross-sectional studies.[34] Quality evaluation was expressed as a percentage frequency of items (yes rating) for each checklist.

We extracted the following data from each study included in this review: (1) origin/country of origin (2) authors and years, (3) aims/purpose (4) study design, (5) time to follow-up, (6) setting, (7) PICS or PICS-F, (8) outcome, (9) tool and (10) main findings. One reviewer (FG) performed data extraction and entered it into an Excel spreadsheet for building the summary tables.

3 | RESULTS

3.1 | Search results

The literature search generated 6301 files, with three potential articles identified from the citations of the retrieved paper. Duplicate removal led to the exclusion of 2908 papers, and a further 2865 records were excluded by title and abstract screening. Eight full texts were not retrieved for screening. A total of 528 potentially relevant full-text articles were assessed for eligibility, leading to 19 papers in the review. Figure 1 shows the flow chart of the review selection process. More details of the review selection process are presented in the figure.

3.2 | Study characteristics

We included 19 studies in this systematic review: 14 studies (73.7%) about the outcome in ICU survivors with PICS, three studies (15.8%) about the effect on relatives with PICS-F and two studies (10.5%)

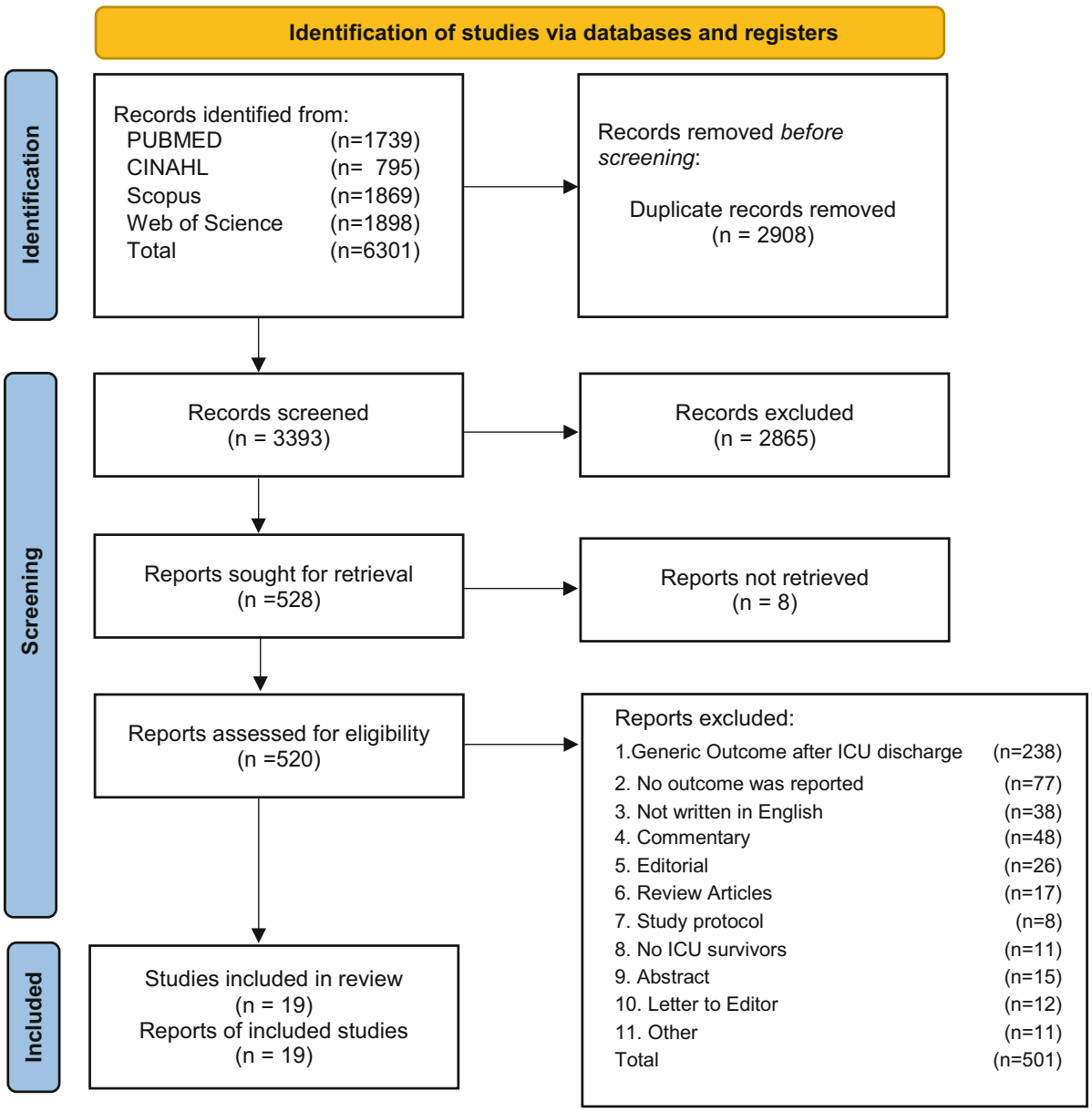

FIGURE 1 Flowchart of study selection.

about PICS and PICS-F. The characteristics of the studies are shown in Table 1. Eleven studies[35–45] reported the three dimensions of PICS, four studies[46–49] reported two, while one study[50] reported only one dimension. The most investigated dimension was mental (16 studies),[35–48,50] while cognitive[35–47] and physical[35–45,48,49] were measured in 13 studies each.

Study designs were as follows: six longitudinal studies,[35,44,46,48,51,52] two retrospective studies,[43,45] nine cohort studies,[36–41,47,49,50] one RCT,[53] and one cross-sectional study.[42] All included studies described that the two groups were similar and drawn from the same population. Also, authors applied the same valid and reliable measures for all included studies.[35–53]

We included 3106 ICU survivors and 279 relatives in this systematic review. The sample was composed predominantly of male survivors (over 60%) in 11 studies,[37–41,43–46,49,50] with an average age above 60 in nine studies.[36,38,40,43–45,48–50] Six studies reported results on survivors hospitalized in a general ICU,[46,36,47,37,41,48] four studies on a COVID ICU,[41,42,44,45] and four studies on a medical/surgical ICU.[39,40,43,49] One study each was conducted on trauma ICU survivors,[35] cardiac surgery ICU survivors,[50] and mixed ICU survivors.[38] Fifteen studies reported on ICU length of stay.[35–39,41–50] Six studies attested that ICU length of stay was around 20 days,[35,36,42,44,45,47] while six studies showed an ICU length of stay of <10 days.[38,39,43,46,48,49] Seven studies measured ICU delirium during ICU stay.[35,38,40,41,45,46,48] Four studies reported an elevated prevalence of ICU delirium (up to 70%).[35,40,45,46] Two studies showed that ICU survivors with acute respiratory failure were between 74% and 85.7%.[35,47] An increasing number of survivors (up to 89%) were mechanically ventilated in four studies.[40,44,45,48] Two COVID ICU survivor studies showed that around 30% of ICU survivors were nursed in a prone position during the ICU stay.[41,45] Three studies[51–53] showed that relatives were predominantly women aged 55, while two studies[51,52] reported that 33% were a spouse. Five studies were conducted in the United States,[36,40–42,45] three in Japan,[38,43,48] two in Australia,[37,47] and one each in Sweden,[46] Portugal,[49] Belgium,[44] the Netherlands,[39] and Scotland.[50]

3.3 | Quality of life in ICU survivors

Of the 19 included studies, 10 studies reported on QoL in ICU survivors with PICS.[36–39,41–44,47,50] Thirty-seven percent of ICU survivors were affected in more than one domain, and 73% had sequelae after one year, as Farley and Henderson reported.[47,50] The mental component of PICS negatively affected the QoL of ICU survivors.[38,39,43] A more substantial home rehabilitation setting was associated with increased QoL ($p = .008$).[36]

QoL was affected by PICS on different domains. QoL issues varied across different time points post-ICU discharge, with fluctuations in mobility – moderate impairment 8% of ICU survivors after 3 months, 18% after 12 months.[37,41,44,50] Self-care issues were reported to be 6% after 3 months, and to be increased to 15% after 12 months.[39] Pain and discomfort were reported as moderate impairment at 13% after 3 months and increased to 27% after 12 months.[37] Anxiety and depression were reported in 18% of the ICU survivors after 12 months.[36]

Morelli et al. reported no statistically significant differences in the QoL of ICU survivors from COVID-19.[42] Two studies attested to moderate and high levels of disability in ICU survivors with a PICS component,[40,41] and one reported a high prevalence of sleep disorder (75%)[44] (Table 1).

3.4 | PICS and anxiety, depression and PTSD of ICU survivors

PICS is prevalent in ICU survivors at 43% to 96%.[35,36,40,45,49] Five studies reported PICS prevalence in three domains.[35,36,38,40,46] The most prevalent domain was physical impairment.[35,36] Bottom-Tanzer et al. showed that 92.9% ($n = 65$) of ICU survivors had a physical impairment, while Dubin et al. attested to 80% ($n = 40$) of cases.[35,36] Cognitive impairment was described in four studies. Dubin et al. reported that in 72% ($n = 36$) of ICU survivors, cognitive decline occurred after discharge, while in three other studies, cognitive decline occurred in between 34% and 41.4%.[35,36,38,46] Three studies measured the prevalence of anxiety, depression and PTSD in ICU survivors ($n = 14$, 14.6%[38]; $n = 16$, 31%[36]; $n = 30$, 42.9%[35]).

Sixteen studies reported results of the mental component of PICS on anxiety in ICU survivors.[35–37,39–41,43–50] Six observational studies reported a moderate prevalence of anxiety (approximately 21%) in ICU survivors as the mental health component of PICS.[43–45,47–49] Severe anxiety appeared in 18% of the cases in the study by Dubin et al. and 41% of the cases in the study by Henderson et al.[36,50] Two longitudinal studies described increased anxiety levels three to 6 months after discharge.[35,37] Cognitive impairment in PICS was related to high levels of anxiety.[46] ICU survivors with a walking disability had a higher probability of developing anxiety symptoms (score, [min, max], 2 [1,4], 4 [1,7], p-value = .013)[43] (Table 1).

Fourteen studies assessed depressive symptoms as a component of PICS in ICU survivors.[35–37,39–41,43–50] In 2019, Kerckhofs et al. showed that mental health, such as depressive symptoms, were associated with a self-reported unacceptable outcome to the question asked by the authors in the study ('I consider my current condition an acceptable outcome of the ICU treatment.') (OR = 2.06, 99% IC, 1.18–3.61).[39] Three studies reported a high level of depression in ICU survivors with PICS at 3 and 6 months, respectively.[40,41,43] Five studies reported a moderate level of depression in ICU survivors in a range of 20% to 32%,[44,45,47–49] and one study showed that 22% of cases had severe symptoms of depression.[36] In ICU survivors, two studies showed that depressive symptoms increased one to six months after discharge (baseline, $n = 4$ [8.5]; 1 month, $n = 5$ [25] p-value = .074; 6 months, $n = 10$ [66.7]).[35,37] Brück and colleagues reported a significant correlation relationship between PICS and depression at 3, 6 and 12 months ($r = 0.510$ at 3 months, $p < .001$; $r = .590$ at 6 months, $p < .001$; $r = 0.372$ at 12 months, $p = .023$)[46] (Table 1).

We identified nine studies concerning PTSD.[35,36,39,41,44–46,48,49] PTSD prevalence was identified in six studies in 11% to 28% of ICU

TABLE 1 Summaries of studies included.

Country	Authors and years	Aim	Study design	Time to follow-up	Setting
USA	Bottom-Tanzer et al., 2021	To assess the occurrence of PICS in trauma and acute care surgery patients	Longitudinal study	T1 = 2 weeks; T2 = 12 weeks; T3 = 24 weeks.	Level I trauma center and Surgical ICUs
Sweden	Brück et al., 2019	To investigate the correlation between subjective cognitive function in ICU survivors. The second objective was to assess whether depression, anxiety and posttraumatic stress symptoms in ICU survivors correlate to cognitive impairment.	Longitudinal study	T1 = 3 months; T2 = 6 months; T3 = 12 months.	General ICU
USA	Cairns et al., 2019	To assess the feasibility and acceptability of a 3-day intervention on symptoms of PICS-F in spouses of patients undergoing mechanical ventilation in the ICU.	Randomized controlled trial	T1 = 1 day, T2 = 3 days; T3 = 30 days; T4 = 90 days	Level I Trauma Center ICU
USA	Dubin et al., 2021	To assess patients for functional impairments, elicit their functional and rehabilitation goals and ascertain whether they could achieve their stated functional goals.	Cohort study	6 months	General ICU
Australia	Farley et al., 2016	To determine the long-term outcome (12–24 months) and health-related quality of life of Australian survivors of prolonged mechanical ventilation in ICU	Cohort study	14, 25 months	General ICU
Scotland	Henderson et al., 2021	To describe the long-term outcomes such as PICS of cardiac intensive care unit patients and their primary caregivers	Cohort study	3, 12 months	Postoperative cardiac surgical ICU
Australia	Heydon et al., 2019	To identify critical illness survivors who had developed post-intensive care syndrome and to explore their use of community health care resources, the socioeconomic impact of their illness and their self-report.	Observational study	1, 3 months	General ICU
Japan	Kawakami et al., 2021	To evaluate the co-occurrence of PICS symptoms and the assessment of baseline HRQOL in Japanese patients admitted to multicenter ICUs. Additionally, we assessed the subjective significance of changes in SF-36 parameters before and after ICU admission among the patients.	Multicenter cohort study	6 months	Mixed ICUs
Netherlands	Kerckhofs et al., 2019	To investigate the effect of overall HRQoL and the components of PICS on the risk of a self-reported unacceptable outcome of ICU Treatment.	Cohort study	1 year	Mixed ICUs
USA	Marra et al., 2018	To describe the frequency of co-occurring newly acquired cognitive impairment, disability in activities of daily living and depression among survivors of a critical illness and to evaluate predictors of being Post-Intensive Care Syndrome (PICS)-free.	Cohort study	3,12 months	Medical and surgical ICUs
USA	Martillo et al., 2021	To determine the characteristics of post-intensive care syndrome in the cognitive, physical and psychiatric domains in coronavirus disease 2019 ICU survivors.	Cohort study	1 month	General and COVID-19 ICUs
USA	Morelli et al., 2022	To examine Dual Task performance in patients surviving severe and critical COVID-19 compared with patients with chronic lung disease and to determine the psychometric properties of the Timed-Up-and-Go test in patients surviving COVID-19.	Cross-sectional study	1,3 months	COVID-19 ICU
Japan	Nakamura et al., 2021	To investigate the relationship between grip strength and mental status/quality of life using outcome data from our PICS clinic.	Retrospective study	1 month	Medical and surgical ICUs
USA	Petrinec and Martin, 2017	To examine the relationship between coping strategies used by family decision-makers of critically ill patients, the severity of PICS-F symptoms and the relationship between family decision-makers PICS-F symptoms and health-related quality of life.	Longitudinal study	T1 = days 3–5; T2 = 1 months; T3 = 2 months.	Medical and surgical ICUs

TABLE 1 (Continued)

Country	Authors and years	Aim	Study design	Time to follow-up	Setting
USA	Petrinec, 2017	To examine indications of post-intensive care syndrome, coping strategies and health-related quality of life among family decision-makers during and after Patients' long-term hospitalization.	Longitudinal study	1,3 months	General ICU
Belgium	Rousseau et al., 2021	To describe the mid-term outcomes and assess the prevalence of the main PICS symptoms in critically ill COVID-19 survivors referred to face-to-face consultation in our post-ICU follow-up clinic 3 months following a prolonged ICU stay.	Longitudinal study	T1 = 1 month; T2 = 3 months; T3 = 12 months	Mixed ICU and COVID-19 ICUs
Japan	Shima et al., 2020	To describe and elucidate the epidemiology of PICS in Japan.	Longitudinal study	3, 12 months	General ICU
Portugal	Torres et al., 2017	To evaluate patient post-intensive care syndrome (PICS) and caregiver burden 3 months after discharge from the (ICU) and determine the impact of different PICS components upon caregiver burden.	Observational study	1,3 months	Medical and surgical ICUs
USA	Weidman et al., 2021	To describe a group of COVID-19 ICU survivors who attended a post-ICU recovery clinic, determine the prevalence of PICS problems and assess associations between PICS and ICU-related factors.	Retrospective cohort study	3 months	General ICU

Country	PICS or PICS-F	Sample size	Outcome	Tool	Main findings
USA	PICS	70 ICU survivors	Anxiety, depression, post-traumatic stress symptoms and return to work	Activity Measure for Post-Acute Care (AM-PAC), 6-Minute Walk Test (6MWT) and Timed Get Up and Go (TUG); Patient Health Questionnaire (PHQ-9) and PTSD Checklist (PCL-5)	1. The prevalence of PICS was $n = 67$ (95.7%). 2. Overall visits in follow-up clinic ($n = 116$), $n = 26$ (37.1%) one PICS criterion, $n = 24$ (34.3%) patients with two and $n = 17$ (24.3%) with three. 3. During all follow-ups ($n = 116$ visits), $n = 25$ (38.4%) presented with one PICS criterion, $n = 23$ (35.4%) with two PICS criteria and $n = 17$ (26.2%) with three. 4. Cognitive impairment: $n = 29$ (41.4%) ICU survivors; psychiatric symptoms: $n = 30$ (42.9%) and physical symptoms: $n = 65$ (92.9%). 5. Anxiety or depression [2 weeks, $n = 18$ (54.5); 12 weeks, $n = 11$ (37.9); 24 weeks, $n = 10$ (66.7)]. 6. Post-traumatic stress disorder symptoms score [2 weeks, $n = 9.5$ (3–23); 12 weeks, $n = 21$ (3–30); 24 weeks, $n = 20$ (9–38)]. 7. Assessment of preadmission anxiety or depression score (one criterion) was moderate [$n = 18$ (69.2)]; review of no preadmission anxiety or depression score (one criterion) was moderate [$n = 10$ (43.5)]. 8. Post-traumatic stress disorder score was high [Preadmission Post-traumatic stress symptoms, $n = 3$ (100); NO preadmission post-traumatic stress symptoms, $n = 10$ (30.3)]. 9. ICU survivors returned to work (Unable to return to work):2 weeks [41/43 (95.3)],12 weeks [23/30 (76.7)],24 weeks [11/18 (61.1)]. 10. ICU survivors returned to work (Returned to work):2 weeks [1/43 (2.3)],12 weeks [7/30 (23.3)],24 weeks [7/18 (38.9)].
Sweden	PICS	100 ICU survivors	Anxiety, depression and posttraumatic stress symptoms	Cognitive Failures Questionnaire (CFQ); Cambridge Neuropsychological Test Automated Battery (CANTAB®)- [Cognitive assessment software]; Stockings of Cambridge (SOC); Pattern recognition memory (PRM); Spatial span (SSP); Rapid visual information processing (RVP); Post-Traumatic Stress Symptoms Scale-10 (PTSS-10); Hospital Anxiety and Depression Scale (HADS)	1. Cognitive impairment (Neuropsychological Test) was [$n = 20$ (34%) at 3 months; $n = 9$ (18%) at 6 months, and $n = 7$ (16%) at 12 months]. 2. Significant association with cognitive impairment at three, six and 12 months [RVP—RVP A, $n = 57$ mean score = 0.87, SD =0.06, IC (0.85–0.88); n = 47 mean score = 0.89, SD = 0.06, IC (0.87–0.91) p-value = .01; n = 41 means = 0.90 SD = 0.06, IC (0.88–0.92) p-value <0.001; SOC—minimum moves, $n = 57$ means = 8.4 SD =1.9, IC (7.9–8.9), $n = 49$ means = 8.8 SD = 1.9 IC (8.3–9.3), p-value = .19, $n = 45$ means = 9.4 SD = 1.9 IC (8.9–10.0) p-value <.001. 3. Positive correlation between cognitive impairment and cognitive failure at 3, 6, and 12 months (r = −0,134–0,207, $p > 0,05$; r = −0,106–0,257, $p > 0,05$; r = − 0,070–0,109, $p > 0,05$). 4. Low correlation between cognitive failure and anxiety/depression total score (r = −0,348, p-value = 0,015) and posttraumatic stress disorder (r = −0,319, p-value = 0.008) at 3 months. 5. Significant correlation between cognitive failure and anxiety subscale ($r = .550$ at 3 months, $p \leq .001$; $r = .645$ at 6 months, $p < .001$; $r = .552$ at 12 months, $p < .001$). 6. Significant correlation between cognitive failure and depression subscale ($r = .510$ at 3 months, $p < .001$; $r = .590$ at 6 months, $p < .001$; $r = .372$ at 12 months, $p = .023$). 7. Significant correlation between cognitive failure and posttraumatic stress disorder symptoms e ($r = .710$ at 3 months, $p \leq .001$; $r = .710$ at 6 months, $p \leq .001$; $r = .440$ at 12 months, $p \leq .01$).

(Continues)

TABLE 1 (Continued)

Country	PICS or PICS-F	Sample size	Outcome	Tool	Main findings
USA	PICS-F	10 caregivers	Stress, anxiety, depression, post-traumatic stress symptoms	Perceived Stress Scale (PSS); Hospital Anxiety and Depression Scale (HADS); Impact of Event Scale (IES).	1. SAF-T intervention reduces the stress level in SAF-T caregivers ($z = -3.5$, $p = .01$).
USA	PICS	50 ICU survivors	Quality of Life, anxiety, depression, or post-traumatic stress symptoms	European Quality of Life 5 Dimensions; Quality of Life Goals Inventory; Hospital Anxiety and Depression Scale (HADS); Post-traumatic Stress Syndrome 10-Questions Inventory (PTSS-10); Montreal Cognitive Assessment (MoCA); Medical Research Council (MRC)	1. PICS prevalence was $n = 48$ (96%) of patients; physical impairment was $n = 40$ (80%) patients; Cognitive impairment was $n = 36$ (72%) patients, mental health $n = 16$ (32%) patients. 2. Severe anxiety $n = 9$ (18%), severe depression, $n = 11$ (22%) and post-traumatic stress disorder $n = 11$ (22.5%) 3. Pharyngeal dysfunction $n = 37$ (74%) patients, pharyngeal weakness $n = 31$ (62%); aspiration risk $n = 36$ (72%). 4. A significant association between discharge to the home or an acute rehabilitation with greater strength [physical impairment (p-value = .002); Quality of life domains of mobility ($p = .008$), self-care ($p = .04$) and pain and discomfort ($p = .02$)].
Australia	PICS	27 ICU survivors	Quality of Life, anxiety, depression	European Quality of Life 5 Dimensions; Hospital Anxiety and Depression Scale (HADS)	1. Quality of life problems was $n = 16$ (59%), in ≥1 domains $n = 10$ (37%) in ≥2 dimensions, $n = 8$ (30%) in ≥3 dimensions. Psychological symptoms, $n = 10$ (37%) patients. 2. Anxiety and Depression were borderline or abnormal scored [$n = 6$ (22%); and 4 (15%)].
Scotland	PICS PICS-F	27 ICU survivors 23 ICU caregivers	Quality of life, anxiety, depression, insomnia, pain and strain related to care (caregivers)	European Quality of Life 5 Dimensions; Hospital Anxiety and Depression Scale (HADS); Carer Strain Index (CSI); Insomnia Severity Index (ISI); Brief Pain Inventory (BPI)	A. ICU Survivors: 1. ICU survivors with one quality of life problem are 92% (baseline); after 1 year, it is 73%. 2. ICU survivors with more quality-of-life problems are 22% (baseline), and after 1 year, it is 18%. 3. Forty-one per cent of ICU survivors have severe anxiety problems, and 22% have depression. Pain appeared in 52% ($n = 14$) of cases. 4. 56% of ICU survivors had a drug-related problem. 5. Issues were related to cardiovascular drugs (70%). B. ICU Caregivers: 1. Strain related to care was 20%. 2. Eleven caregivers (48%) had anxiety symptoms, and six (26%) had symptoms of depression. 3. The caregivers' anxiety outstripped that of the patients in the baseline phase. 4. 77% of caregivers expressed problems with sleep.
Australia	PICS	39 ICU survivors	Quality of life, anxiety, depression, pain and return to work	European Quality of Life 5 Dimensions; Functional Activities Questionnaire (FAQ)	1. Mean Functional Activities Questionnaire scores increased from 1.8 (baseline) (95% confidence interval [CI]: 0–3.5) to 8.9 at 1 month after ICU discharge (95% CI: 6.5–11.4; $p = <.001$); 2. Functional function increased from 8% at baseline to 54% and 33% at 1 and 3 months after ICU discharge. 3. Quality of life: Mobility: Moderate problems: Baseline n (%) [4 (8.5)]; 1-month, n (%) [7 (35)] p-value <.001, 3 months, n (%) [6 (18.2)] p-value <.026; Personal care: Moderate problems: Baseline n (%) [3 (6.4)]; 1-month, n (%) [5 (25)] p-value <.001, 3 months, n (%) [6 (15.2)] p-value <.002; Usual activities: Severe problems: Baseline n (%) [0 (0)]; 1-month, n (%) [5 (25)] p-value <.001, 3 months, n (%) [5 (15.2)] p-value <.001; Pain/discomfort: Moderate: Baseline n (%) [6 (12.8)]; 1-month, n (%) [8 (40)] p-value <.008, 3 months, n (%) [9 (27.3)] p-value <0.417; Anxiety/depression: Moderate: 3 months, n (%) [6 (18.2)] p-value =0.048; 4. Meagre rates of return to work were observed, with 35% of respondents at 3 months. 5. ICU survivors return to work: 35% of respondents indicated they were experiencing financial difficulty because of their critical illness at 3 months.
Japan	PICS	96 ICU survivors	Quality of life and return to work	Short-Form Health Survey 36 (SF-36); Physical component scale (PCS); Mental component scale (MCS); Short-Memory Questionnaire (SMQ)	1. PICS among the ICU survivors, at least one PICS impairment was high in 84% of the patients. The prevalence of two or more PICS impairments was 56%. 2. A total of $n = 61$ (63.5%) ICU survivors were in the PICS group, and $n = 35$ (36.5%) were in the non-PICS group, with one criterion of PICS, while ≥2 measures of PICS occurred in 17 (17.8%) ICU survivors. 3. Among non-PICS ICU survivors, $n = 22$ (62.9%) were discharged home, while among PICS ICU survivors, 24 (39.3%) were discharged home from the hospital ($p = .026$). 4. Physical, mental and cognitive impairments occurred in $n = 31$, 32.3%, $n = 14$, 14.6% and $n = 36$, 37.5% of ICU survivors. 5. Quality of life: Among PICS ICU survivors, the physical component at baseline and 6 months were 37.6 [18.9–50.8] and 21.5 [11.4–34.8], respectively ($p < .001$), and the mental component at baseline and 6 months were 49.7 [42.5–55.0] and 53.4 [44.2–63.4], respectively ($p = .037$). 6. The physical and mental components occurred in 31 (32.3%) and 14 (14.6%) patients. 7. All ICU survivors without PICS returned to work, while ICU survivors $n = 15$ (75%) patients with PICS returned to work.

TABLE 1 (Continued)

Country	PICS or PICS-F	Sample size	Outcome	Tool	Main findings
Netherlands	PICS	1453 ICU survivors	Quality of life, anxiety, depression and post-traumatic stress symptoms	European Quality of Life 5 Dimensions; Barthel index; Cognitive failures questionnaire (CFQ); Hospital Anxiety and Depression Scale (HADS); Impact of Event Scale (IES).	1. A lower score overall to measure the quality-of-life score [unacceptable vs. acceptable (0.57 vs. 0.81; $p < .001$)]. 2. Quality of life [self-reported unacceptable outcome (OR = 2.09, 99% CI 1.62–2.69, p-value<.001, OR = 2.05 (1.56–2.70), p-value <.001, OR = 2.20 (1.64–2.94) p-value<.001], depression and anxiety [self-reported unacceptable outcome (OR = 2.20, 99% CI 1.60–3.02, p-value<0.001, OR = 2.04 (1.47–2.84) p-value<0.001, OR = 2.05 (1.45–2.89) p-value <.001, OR = 2.06 (1.18–3.61) p-value <0.001)] and PSTD [self-reported unacceptable outcome (OR = 1.74, 99% CI 1.26–2.40, p-value<.001, OR = 1.64 (1.17–2.30) <0.001, OR = 1.57 (1.09–2.26) p-value = .002, OR = 1.13 (0.68–1.88) p-value = .525)]. 3. Post-traumatic stress disorder [median (IQR) 21 (0–36.8) 9 (0–25) 6 (0–17) 6 (0–19). 4. Self-reported unacceptable outcomes in ICU survivors are significantly associated with the mental component of PICS (anxiety and Depression) OR of 2.06 (99% CI 1.18–3.61).
USA	PICS	406 ICU survivors	Disability and depression	Repeatable Battery for the Assessment of Neuropsychological; Status (RBANS): the Katz Activities of daily living (ADL); Beck Depression Inventory Second Edition (BDI-II); Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)	1. At 3 and 12 months, one or more PICS problems were present in n = 74, 64% and 56% (24/43), respectively. 2. PICS problems (i.e., in two or more domains) were current at 25% at 3 months and 21% at 12 months. 3. PICS problems in all three fields were present in only 6% at 3 months and 4% at 12 months. 4. More severe frailty was associated with lower odds of being PICS-free (p = .005 at 3 months and P = 0.048 at 12 months). 5. The proportion of patients with one or more PICS problems decreased by 5% at 3 and 12 months. 6. 3-month follow-up, disability n = 332 (99%), depression n = 363 (95%), n. At 12 months, disability n = 383 (99%), depression n = 313 (94%). 7. Of these, n = 97 (33%) had cognitive impairment, n = 69 (21%) had disability, and n = 97 (31%) had depression.
USA	PICS	45 ICU survivors	Quality of life, anxiety, depression, post-traumatic stress symptoms, disability and pain	European Quality of Life 5 Dimensions; Insomnia Severity Index; Patient Health Questionnaire-9 (PHQ-9); Modified Rankin Scale (mRS); Dalhousie Clinical Frailty Scale (DCFS) (25), the Quality of Life in Neurologic Disorders (Neuro-QoL); Post-traumatic Stress Syndrome Checklist (PCL-5); Montreal Cognitive Assessment (T-MoCA)	1. Ninety-one per cent of coronavirus disease 2019 ICU survivors fit the diagnostic criteria for PICS. 2. Physical Domain: n = 30 ICU survivors (66.7%) had mobility difficulties: n = 29 reported 'some problems in walking about,' and one said being 'confined to bed.' Sixteen patients (35.6%) reported problems with self-care, and 30 ICU survivors (66.6%) reported problems with usual activities. Twenty-seven ICU survivors (60%) said moderate or extreme pain or discomfort, n = 26 patients (57.7%) had some degree of disability: n = 14 (31.1%) had scores indicating 'moderate disability. 3. Psychiatric Domain: 22 ICU survivors (48.9%) presented with psychiatric impairment, with depression endorsed most commonly, followed by insomnia; n = 17 ICU survivors (37.8%) reported feeling 'moderately anxious or depressed; two patients (4.4%) reported feeling 'extremely anxious or depressed; n = 17 ICU survivors (37.8%) had scores in the range of at least mild depression (score >4), with eight (17.8%) scoring in the field of moderate to severe (score >9). Eight patients (17.8%) reported post-traumatic stress symptoms (score ≥31); 4. Cognitive Domain: Twenty-four of 30 patients (80%) scored 19 and above, suggesting no cognitive impairment, whereas six of 30 patients (20%) scored less than 19, which reflects impaired cognition. 5. N = 41 (91.1%) met the criteria for PICS. Of these, 22 (53.6%) had impairments in two domains, and two (4.9%) had impairments in all three. 6. Impaired quality of life: mobility [n, (%)] 30 (66.7); pain/discomfort [n, (%)] 27 (60.0); self-care [n, (%)] 16 (35.6); usual activities [n, (%)] 30 (66.7)
USA	PICS	92 ICU survivors	Quality of life	European Quality of Life 5 Dimensions; Timed-Up-and-Go (TUG); Short Physical Performance Battery (SPPB); 6 Min Walk Test (6MWT); Montreal Cognitive Assessment (MOCA).	1. N = 31 (86%) of critical-COVID and n = 20 (60%) severe-COVID patients demonstrated either a physical or cognitive indicative of an impairment related to PICS 1-month after hospital discharge. 2. Ability to perform motor and cognitive tasks simultaneously score n = 17.1 (7.3%) in critical COVID-19, n = 12.9 (4.8%) in severe COVID-19, n = 13.3 (3.6), p-value <.009. 3. No statistical difference in the quality of life between critical COVID-19 and severe COVID-19 (mean = 70.6 (SD = 17.7); means = 70.1 (SD = 19.1).
Japan	PICS	133 ICU survivors	Quality of life, anxiety and depression	European Quality of Life 5 Dimensions; Barthel index; Functional status score for ICU (FSS-ICU); Impact of Event Scale-Revised (IES-R); Hospital Anxiety and Depression Scale (HADS); Mini-Mental State Examination (MMSE); Short-Memory Questionnaire (SMQ)	1. In the PICS clinic: walking disability n = 80 (60.2%), muscle volume loss n = 70 (52.6%), respiratory dysfunction n = 29 (21.8%), Depression n = 17 (12.8%), Anxiety n = 20 (15%), sleep disorder n = 23 (17.3%), memory impairment n = 43 (32.3%), executive function disorders n = 27 (20.3%). 2. Physical status: Barthel index (n = 57) was 100 (IC 90, 100); the functional status (n = 57) score for the ICU was 35 (IC 35, 35), the Medical Research Council (n = 57) score was 58 (IC 54, 60), grip strength (kg) was 20.75 (IC 15.75, 28.25), grip strength ≥ age/gender was 6 (4.5%). 3. Mental status: Depression [score (min, max)] was 5 (3, 10), Anxiety score was 3 (1, 6), and Impact of Event Scale was 4 (1, 9). 4. Cognitive status: Mini-Mental State Examination [score (min, max)], (n = 40) score was 27.5 (23, 30),

(Continues)

TABLE 1 (Continued)

Country	PICS or PICS-F	Sample size	Outcome	Tool	Main findings
					Short-Memory Questionnaire score was 36 (26.5, 41). 5. At the PICS clinic, Physical status [No Walking Disability (n = 53) Vs Walking Disability (n = 80)], Barthel index [score (min, max)] was 100 (100, 100) vs 100 (80, 100), p-value = .012, functional status [score (min, max)] score was 35 (35, 35) vs 35 (34, 35), p-value = .0025, Medical Research Council score [score (min, max)] was 60 (58, 60) vs 58 (53, 60), p-value .0010, grip strength (kg) [score (min, max)] was 24.75 (18.20, 31.30) vs 20.10 (13.10, 26.35), p-value .0021. 6. At the PICS clinic, Mental status [score (min, max)]: [No Walking Disability (n = 53) Vs Walking Disability (n = 80)], depression [score (min, max)] was 4 (1, 7) vs 7 (4, 10) p-value = .013, anxiety [score (min, max)] was 2 (1, 4) vs 4 (1, 7) p-value = 0.046, Quality of life [score (min, max)] was 0.96 (0.84, 1) 0.77 (0.62, 0.89) p-value <.0001. 7. There were negative correlations with total depression/anxiety scores and quality of life scores in the PICS clinic. Correlation coefficients were r = −.25 (p = .011) and r = .47 (p < .0001) between grip strength and depression/anxiety and quality of life scores in the PICS clinic, respectively.
USA	PICS-F	48 family decision-makers	Anxiety, depression, post-traumatic stress symptoms, quality of life and return to work	Hospital Anxiety and Depression Scale (HADS); PTSD Checklist (PCL-5); Brief COPE instrument; Medical Outcomes Study 36-item Short-Form General Health Survey version 2 (SF-36v2).	1. The authors found a significant prevalence of anxiety (45.8%), depression (25%) and post-traumatic stress disorder (11.1%) symptoms among family decision-makers throughout the study. 2. Family decision-makers (n = 25) had a previous self-reported psychiatric history of anxiety, depression, or post-traumatic stress disorder and n = 32 were employed, with n = 23 (47.9%) stating that they had to decrease their work hours because of a family member's illness. 3. PICS-F symptoms [T1, T2, T3 mean (SD)]: Anxiety score was 10.04 (4.65) vs 8.42 (4.79) vs 7.80 (2.03), Significant decrease from T1, F (2,68) = 3.94, p < .05, Depression score was 6.92 (3.63) vs 6.34 (4.33) vs 6.92 (4.82), and post-traumatic stress disorder score was 10.56 (7.31) vs 16.05 (13.65) vs 18.00 (13.54), significant increase from T1, F (1.51,51.26) = 14.05, p < .05; 4. Coping strategy [T1, T2, T3 mean (SD)]: Avoidant score was 1.49 (0.34) vs 1.67 (0.52) vs 1.69 (0.50) significant increase from T1, F (2,64) = 4.91, p < .05; Emotion-focused score was 2.77 (0.41) vs 2.36 (0.53) vs 2.43 (0.48), significant decrease from T1, F (2,64) = 9.40, p < .05; Problem-focused score was 3.51 (0.42) vs 2.43 (0.63) vs 2.46 (0.85), significant decrease from T1, F (2,64) = 32.54, p < .05 5. Quality of life [T1, T2, T3 mean (SD)]: Physical component summary score was 49.48 (10.47) vs 49.06 (9.48), Mental component summary score was 45.03 (10.65) vs 41.72 (12.47), a significant decrease from T1, t (35) = 2.35, p < .05. 6. Family decision-makers were employed: n = 32; n = 23 (47.9%) declared they had to reduce working hours because of a family member's illness.
USA	PICS-F	30 family decision-makers	Anxiety, depression, post-traumatic stress symptoms and quality of life	Hospital Anxiety and Depression Scale (HADS); PTSD Checklist (PCL-5); Brief COPE instrument; Medical Outcomes Study 36-item Short-Form General Health Survey version 2 (SF-36v2).	1. PICS-F symptoms [T1 = at admission, means (SD); T2 = 1 month means (SD); T3 = 2 months means (SD)]: Anxiety score was 8.10 (3.73) vs 7.88 (2.34) vs 6.17 (3.27), Significant decrease from time of admission and 30 days later: F2,44 = 6.68, P = .003, Depression score was 6.77 (3.28) vs 7.31 (3.87) vs 7.04 (3.88), Post-traumatic stress disorder score was 10.70 (7.56) vs 13.46 (9.24) vs 13.38 (11.75); 2. Coping strategy [T1 = at admission, means (SD); T2 = 1-month means (SD); T3 = 2 months means (SD)]: Problem-focused score was 3.54 (0.45) vs 2.71 (0.81) vs 2.72 (0.78), Significant decrease from time of admission: F2,44 = 14.05, P < 0.001. 3. Quality of life [T1 = at admission, means (SD); T3 = 2 months means (SD)]: Physical component summary score was 47.08 (9.91) vs 47.83 (9.83), Mental component summary score was 48.00 (10.28) vs 46.03 (9.49), 2009 US norms for each scale component: mean, 50 (SD, 10).
Belgium	PICS	32 ICU survivors	Quality of life, sleep disorder, post-traumatic stress symptoms, anxiety and depression	Montreal Cognitive Assessment (MoCA); Hospital Anxiety and Depression scale (HADS); Pittsburgh Sleep Quality Index (PSQI); Impact of Event Scale (IES); Barthel Index of activities of daily living (ADL); European Quality of Life 5 Dimensions	1. The main observed disorders were sleep disorder score [score >5 (75%, 24/32)], cognitive impairment score [score < 26 (44%, 14/32), activities of daily living score [Barthel<100 (31%, 10/32)] and post-traumatic stress disorder score [score ≥ 33 (28%, 9/32)]. Joint disorders were observed in 13/32 (40.6%) ICU survivors. 2. The quality-of-life visual scale was rated 71 [61–80]. A quarter of patients (8/32) demonstrated persistent inflammation based on CRP blood level (9.3 [6.8–17.7] mg/L); 3. The anxiety score was 12.5%, the depression score was 25%, the post-traumatic stress disorder score was 28%, the low grip of the straight score was 31%, the sleep disorder (low quality) score was 75%, and cognitive impairment score was 83.8%.

TABLE 1 (Continued)

Country	PICS or PICS-F	Sample size	Outcome	Tool	Main findings
Japan	PICS	204 ICU survivors	Anxiety, Depression and post-traumatic stress symptoms	Barthel index (BI),13 Hospital Anxiety; Depression Scale (HADS); Impact of Event Scale-Revised (IES-R)	1. At 3 months, ADL disability, anxiety, depression and post-traumatic stress disorder symptoms were 32%, 42%, 48% and 20%, respectively. 2. At 12 months, the prevalence was 22%, 33%, 39% and 21%, respectively. Most of any symptoms were 66% at 3 months and 55% at 12 months 3. Barthel index [3-month means (SD) vs 12-month means (SD)] was 37 (32) vs 15 (22), $p < 0.001$; Anxiety [3-month means (SD) vs 12-month means (SD)] was 37 (42) vs 20 (33), Depression [3-month means (SD) vs 12-month means (SD)] score was 44 (48) vs 24 (39), post-traumatic stress disorder [3-month means (SD) vs 12-month means (SD)] score was 17 (20) vs 12 (21).
Portugal	PICS-F PICS	168 caregivers 245 ICU survivors	Anxiety, Depression and post-traumatic stress symptoms	Medical Research Council Scale for Muscle Strength; Hospital Anxiety and Depression Scale (HADS); Post-traumatic Stress Syndrome Questions Inventory (PTSS-14); Zarit index.	1. ICU survivors with PICS symptoms were n = 106 (43%), and those without PICS were n = 139 (57%); 2. ICU caregivers with no overburden were n = 84 (50%), Low overburden n = 58 (34.5%) and Moderate to high overburden was n = 26 (15.5%). 3. Three months after their ICU stay, 106 ICU survivors (43%) reported at least one component of PICS: 20% had depression, 19% had anxiety, 11% had post-traumatic stress disorder, 11% had mobility impairment and 20% had ICU-acquired weakness. 4. ICU survivors' anxiety and Depression 3 months after ICU discharge significantly influenced the presence of caregiver burden. 5. Anxiety [ICU caregivers, no overburden (Zarit ≤21), Low overburden (Zarit 22–40), Moderate to High overburden (Zarit ≥41), median (min-max)] was 7 (0–17) vs 8 (0–18) vs 12 (0–20) p-value = 0.03. 6. Depression [ICU caregivers, no overburden (Zarit ≤21), Low overburden (Zarit 22–40), Moderate to High overburden (Zarit ≥41), median (min-max)] was 6 (0–19) 5 (0–16) 9 (1–20) p-value = 0.008. 7. Post-traumatic stress disorder [ICU caregivers, no overburden (Zarit ≤21), Low overburden (Zarit 22–40), Moderate to High overburden (Zarit ≥41), median (min-max)] was 27 (14–83) 32 (14–65) 40 (14–96) p-value = 0.178.
USA	PICS	87 COVID-19 ICU survivors	Anxiety, Depression and post-traumatic stress symptoms	Hospital Anxiety and Depression Scale (HADS); Post-Traumatic Symptom Scale-10 (PTSS-10); European Quality of Life 5 Dimensions; Montreal Cognitive Assessment (MoCA)	1. The overall prevalence of PICS was 90% in ICU survivors post-COVID-19. 2. The main results describe that depression was 29%, anxiety was 21%, post-traumatic stress disorder symptoms 13% and cognitive impairment was 25%.

Abbreviations: ADL, Activities of daily living; CRP, C-reactive protein; HRQoL, Health-Related Quality of Life; ICU, Intensive care unit; IQR, Interquartile Range; OR, Odds Ratio; PICS, Post-intensive care syndrome; PICS-F, Post-intensive care syndrome-family; PTSD, Post-traumatic stress disorder; RVP, Rapid visual information processing; SAF-T, Sensation Awareness Focused Training; SD, Standard deviation; SOC, Stockings of Cambridge; USA, United States of America.

survivors.[36,39,41,44,48,49,45] Two studies showed a significant correlation between cognitive impairment and PTSD at 3 months ($r = .710$, $p < .001$), 6 months ($r = .710$, $p < .001$) and 12 months ($r = .440$, $p = .001$).[35,46]

3.5 | PICS-F in ICU relatives

We found five studies about PICS-F.[49–53] One RCT evaluated the effectiveness of a coaching intervention for PICS-F reduction,[53] and four studies described the long-term outcomes of PICS-F on relatives.[49–52] The prevalence of PICS-F was reported at 15.5% moderate to high overburden, but there was an increase above 80% for family members with a history of prior anxiety and depression.[49,52] There were significant levels of anxiety, depression and PTSD. Still, there was a significant association between increased anxiety and depression among ICU survivors and a substantial increase in overburden among relatives.[49–51] In a cohort study, 20% of relatives suffered of strain related to care; 48% reported anxiety symptoms, and 26% symptoms of depression; moreover, the majority of the sample (77%) expressed problems with sleep[50] (Table 1). Two longitudinal studies of PTSD reported symptoms prevalence.[52,53] Also, Petrinec and Martin reported that relatives reduced working hours because of the family member's illness.[53] (Table 1).

3.6 | Quality of included studies

The quality assessment of the studies reported a score between 46% and 82%. Seven studies scored 72%, three scored the highest at 82%, three scored 64% and three scored 55%. Three studies totalled 75%, 63% and 46%, respectively.

In one RCT, the items reporting the allocation to treatment group were not declared,[53] but in all studies, the groups were similar and recruited from the same population.[35–53] Furthermore, in all studies, the exposures were measured with similar methods and reliably.[35–53] In 15 studies, the identification and strategies for confounders were unclear.[36–41,43,44,47–52] In all studies included, the researcher measured the outcomes validly and reliably.[35,37–53] The reasons for incomplete follow-up are unclear in only four studies,[36,47,50,52] while nine used strategies to address the incomplete follow-up bias.[39–41,43–45,48,52,53] All studies applied appropriate statistical methods to answer the research question.[35–50,52,53] No studies were excluded based on quality evaluation or risk of bias. More details are in Table 2.

TABLE 2 Assessment of the quality of the included studies.

Study analysed with The Joanna Briggs Institute critical appraisal checklist for randomized controlled trials

Author and years	Study design	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
Cairns et al., 2019	RCT	+	U	+	U	U	U	+	+	+	+	+	+	+	(9/13)

Studies analysed with The Joanna Briggs Institute critical appraisal checklist for cohort studies

Author and years	Study design	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	
Bottom-Tanzer et al., 2021	Longitudinal study	+	+	+	N	N	U	+	+	+	U	+	(7/11)
Brück et al., 2019	Longitudinal study	+	+	+	N	N	U	+	+	N	U	+	(6/11)
Dubin et al., 2021	Cohort study	+	+	+	U	U	U	+	+	U	U	+	(6/11)
Farley et al., 2016	Cohort study	+	+	+	U	U	+	+	U	U	U	+	(6/11)
Henderson et al., 2021	Cohort study	+	+	+	U	U	+	+	+	U	U	+	(7/11)
Heydon et al., 2019	Cohort study	+	+	+	U	U	+	+	+	+	U	+	(8/11)
Kawakami et al., 2021	Cohort study	+	+	+	U	U	U	+	+	+	U	+	(7/11)
Kerckhofs et al., 2019	Cohort study	+	+	+	U	U	U	+	+	+	+	+	(8/11)
Marra et al., 2018	Cohort study	+	+	+	U	U	U	+	+	+	+	+	(8/11)
Martillo et al., 2021	Cohort study	+	+	+	U	U	U	+	+	+	+	+	(8/11)
Nakamura et al., 2021	Retrospective study	+	+	+	U	U	U	+	+	+	+	+	(8/11)
Petrinec and Martin, 2017	Longitudinal study	+	+	+	U	U	U	+	+	+	+	+	(8/11)
Petrinec, 2017	Longitudinal study	+	+	+	U	U	U	+	U	U	U	+	(5/11)
Rousseau et al., 2021	Longitudinal study	+	+	+	U	U	+	+	+	+	+	+	(9/11)
Shima et al., 2020	Longitudinal study	+	+	+	U	U	+	+	+	+	+	+	(9/11)
Torres et al., 2017	Cohort study	+	+	+	U	U	+	+	+	+	U	+	(8/11)
Weidman et al., 2021	Retrospective study	+	+	+	U	U	+	+	+	+	+	+	(9/11)

Study analysed with The Joanna Briggs Institute critical appraisal checklist for analytical cross sectional

Author and years	Study design	Q1	Q2	Q3***	Q4	Q5	Q6	Q7	Q8	
Morelli et al., 2022	Cross-sectional study	+	+	+	+	U	U	+	+	(6/8)

Note: + = yes, − = no, U = Unclear, N = Not applicable, RCT: Randomized controlled trial.

4 | DISCUSSION

This review aimed to examine the impact of PICS and PICS-F on QoL in ICU survivors and their relatives after discharge, respectively, and the reporting of anxiety, depression and PTSD in studies investigating ICU survivors with PICS. Our main findings were (1) mobility, pain, discomfort and disability as the domains of QoL most affected by PICS in ICU survivors; (2) the mental component of PICS negatively affects the QoL of ICU survivors; (3) a high prevalence of PICS and moderate prevalence of PICS-F and (4) strain-related symptoms and sleep disorders as the most affected dimensions by PICS-F in ICU family members.

Relevant differences in QoL domains such as mobility, pain, discomfort and disability were observed among the ICU survivors with PICS. In 2017, Hodgson and colleagues reported a moderate or severe disability in survivors of critical illness.[15] Similar results were obtained in our review. In the literature, it is described how long periods of immobility can negatively affect disability after ICU discharge.[15] Interestingly, the predictors of disability included a history of anxiety/depression.[15] This review focuses on the three dimensions of PICS, but the psychological sequelae are described in the literature as PICS without considering the cognitive and physical domains.[18]

In 2017, Makinen and colleagues reported a high prevalence of persistent pain in ICU survivors.[54] The same result was described in our review.

Our review shows that the mental component of PICS negatively affects the QoL of ICU survivors. As the literature describes, patients with severe mental health problems have a lower quality of life than the general population.[55,56] Patients with mental health problems find it harder to accomplish many of their daily chores, such as washing and dressing, reducing self-confidence.[56] In 2020, Berghöfer and colleagues assessed QoL in patients with severe mental illness.[56] The authors observed that patients with anxiety disorders and depressive symptoms reported lower Qol scores.[56] Similar findings were obtained in the studies included in the review.[38,39,43] Guideline on multimodal rehabilitation for patients with post-intensive care syndrome by Renner reported that psychological interventions, such as ICU diary, can counteract PICS's psychological sequelae such as anxiety, depression and post-traumatic stress.[25] ICU diaries are essential non-pharmacological interventions written by nurses, therapists, or family members to record events about the period that critically ill patients usually cannot remember.[57]

Our results showed that the PICS prevalence lies in an extensive range between 43% and 96%. The studies in our review included ICU survivors discharged from different types of ICUs with varying admissions to the ICU. A recent systematic review describes that ICU admissions, such as emergency admission and ICU type, are considered risk factors for the onset of PICS symptoms.[4]

Indeed, the ICU survivors discharged from general and medical/surgical ICUs have a PICS prevalence between 43% and 54%.[36,40,49] That percentage has a sharp increase in those ICU survivors discharged from COVID-19 ICUs (90%),[45] with a further rise in ICU survivors discharged from trauma ICUs (96%).[35] A recent systematic review with meta-analysis describes that negative ICU experience and delirium are important risk factors for the onset of PICS.[4] Our result showed an extensive range of prevalence of PICS. Furthermore, Bottom-Tanzer et al. reported a high prevalence of ICU delirium (prevalence = 81%)[35] compared with other studies, including those which measure ICU delirium. Moreover, the severity of critical illness appears to be an independent risk factor for the onset of ICU delirium.[58,59] Six out of 19 studies measured ICU delirium. Bottom-Tanzer et al. found the highest range in the survey, with a higher prevalence of PICS than in other included studies. Bottom-Tanzer et al. did not study the relationship between PICS and ICU delirium, but we hypothesize that it may have influenced onset. Therefore, future research should describe how these phenomena interact with each other and ICU survivors' outcomes.

The prevalence of PICS symptoms varies depending on the areas involved, such as cognitive, physical and mental status. ICU survivors with PICS may develop impairment in one or more domains. Bottom-Tanzer et al. reported that in trauma ICU survivors, PICS developed in 34.4% ($n = 24$) with one criterion. At the same time, it decreased among ICU survivors with two or more standards,[35] in COVID-19 survivors, this result increased by up to 90%.[41,42]

Cognitive impairment was a key component of PICS and was referred to as a more permanent condition[60,61] in ICU survivors. Several studies in our systematic review showed a correlation between cognitive impairment and anxiety, depression and PTSD.[35,38,46] Critical illness and intensive care treatment are associated with long-term cognitive impairment.[11] This decline could cause significant problems in survivors' daily life and professional settings, such as memory, visual construction, processing speed and executive functioning.[62] Furthermore, ICU patients experiencing anxiety and depression need more intensive health care than usual to accomplish activities of daily living.[63] In 2022, Smith and Rahman observed that these sensations were increased by feelings of isolation, fear and dehumanization, which would justify the relationship with the psychiatric sequelae of the PICS area after discharge.[64]

A fundamental component for reducing PICS is the introduction of family members in the care process of ICU survivors.[49] Furthermore, ICU relatives will experience various burdens attributable to PICS-F.[19] Several family members who provided care for critically ill survivors report that it was somewhat difficult to pay for basic needs such as food, housing, medical care and heating, thus creating anxiety and depression.[65,66]

Our results show that ICU relatives experienced sleep disorders with PICS-F. Previous studies described that relatives with sleep disorders had moderate to severe depression and anxiety.[26] The cause could be the patient's concern about vigilance activity during the night, which caused some anxiety.[22,67] In 2003, Mahoney defined vigilance as the continuous supervision by relatives of their patients' activities.[67] This activity consists of five phases: supervision, protective intervening, anticipating, always on duty and being there.[67] Vigilant relatives considered themselves 'on duty' even when they weren't 'doing stuff', explaining the moderate to severe depression and anxiety among relatives.[67]

The literature described how intensive treatment changes relationships within the family, with negative repercussions on the quality of sleep for relatives.[26] After intensive treatment, ICU survivors cannot be fully independent at discharge.[63] Our results describe how PICS negatively affects mobility, personal care, usual activities and pain/discomfort. Several factors can negatively impact the QoL by creating dependence in daily activities, such as older age, male sex, ICU delirium, illness severity and duration of mechanical ventilation.[68]

ICU admission is an experience that makes a difference to patients. Some ICU survivors have fragmented memories; others remembered the darkness, were unable to speak and had a severe illness and could not get out of bed.[69] Memories are foundational to our experience and can often be influenced by ICU survivors.[70] Recently, Cohen and Kahana developed a theory on how episodic memory patterns re-establish themselves from context, and memories form associations with the contexts in which they are encoded, including emotional valence and arousal.[71]

Acute care admission is a period that significantly impacts survivors and family members. Feeling useless when the death of a family member could become a real possibility is one of the feelings that relatives of ICU survivors experience.[69]

The quality assessment of the included studies was good. Only one study scored low, while most of the included studies scored over 70%, confirming good methodological quality. Recently, Wang et al. and Jeong et al. developed specific tools for detecting PICS, but we are unaware of any tools for PICS-F.[8,10]

4.1 | Limitations

This review has several limitations. Our results were based on studies not using a specific PICS or PICS-F detection tool. In 2010, the SCCM defined PICS as new impairments in ICU survivors in the physical, cognitive and mental components.[21] PICS was detected according to the SCCM model, detecting the ICU survivors' central disturbances.[21] The researcher detected each disorder with a specific scale, but the long-term outcomes of ICU survivors are numerous. Even though we used a rigorous search and screening strategy, considering that the definition of PICS encompasses extensive domains, our search strategy may not have detected all related studies. Furthermore, we purposely focused only on the mental component of PICS because we were interested in evaluating mental aspects underestimated in ICU survivors and their relatives, providing a vision of the humanization of after-discharge care. Given the clinical complexity of the survivors, not all are detectable, leading to bias.[36] In addition, the tools used were not always specific to ICU survivors. Another limitation is that we could consider observational studies only, except for one RCT. This is probably because the topic is relatively new in the literature, especially with respect to the relatives of the ICU survivors. Indeed, only five studies on PICS-F were identified in this systematic review. Therefore, few RCTs studied interventions aimed at these two populations.[53] The review exclusion criteria restricting the studies to those in English only and the lack of meta-analysis are limitations.

4.2 | Implications for practice and further research

This review has several implications. The literature describes the approaches to minimize PICS and PICS-F.[72] The PICS clinic is an environment where critical care survivors are assessed through a psychiatric assessment, including self-assessment modules to test physical, cognitive and mental symptoms.[35] PICS and PICS-F are serious and outstanding issues that strongly impact cost and are measured in terms of time for disability, health care costs, financial stress, mortality and potentially preventable readmission.[73,74] Specific tools for detecting PICS would provide a more accurate estimate of the phenomenon, helping nurses to identify the ICU survivors who need treatment. Future research is expected to focus on using standardized tools to detect PICS and PICS-F in specific environments, such as PICS clinics, as a common activity for critical care nurses. Critical care nurses are essential in developing and implementing follow-up treatments. They play leadership, staffing and developing roles in different post-ICU services.[26] As per Renner et al.,[25] the latest PICS rehabilitation guidelines state that professional support is needed during the follow-up care; in particular, the role of nurses in ICU is fundamental in writing and reading along with survivors and their relatives the ICU diaries, as part of the aftercare treatment, in order to obtain better outcomes such as deeper comprehension of the ICU stay, effective coping, improvement of social relationships. Specific tools for detecting PICS would provide a more accurate estimate of the syndrome, helping nurses to identify the ICU survivors who need treatment. Furthermore, because so little has been found on PICS-F and ICU relatives, future research is expected to focus on this population as there is a gap in literature about the identification of this phenomenon through proper tools; also, there are very few interventions towards this population as only one RCT has been found.[53] Finally, more research is needed on using standardized tools to detect PICS and PICS-F in specific environments, such as PICS clinics, as a common activity for critical care nurses.

5 | CONCLUSION

PICS and PICS-F are common multidimensional cognitive, physical and mental phenomena. The authors investigated each PICS area separately from the others, and not all areas were investigated in some studies. Future studies should focus on standardized tools that detect PICS and PICS-F in all areas. They are often associated with elevated levels of anxiety and depression. In contrast, an increased anxiety level in ICU survivors is associated with increased anxiety in family members, who experience strain-related symptoms and sleep disorders. Early recognition and timely identification of these syndromes must be guaranteed by nurses, by enforcing multidisciplinary follow-up post-ICU services, where critical care nurses can develop and implement specific interventions, in order to improve survivors' and relatives' outcomes.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in PubMed at https://pubmed.ncbi.nlm.nih.gov.

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