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Illustrating PICS

People who have been admitted to an Intensive Care Unit report a reduced quality of life for up to twelve years following critical illness compared to the general population (Flaatten and Kvåle 2001). This may not be surprising for most of the readers of this journal. First and foremost, during the first year following critical illness, patients state this lower quality of life, particularly within the physical domain (experienc-

Post-Intensive Care Syndrome

Patients and families need to know they are not alone

In this article, we aim to summarise the current management of Post Intensive Care Syndrome (PICS) and Post-Intensive Care Syndrome – Family (PICS-F), understanding the need for continuum assessment and support throughout critical disease.

ing impairments in body function, basic and instrumental activities of daily living and participation) (Ohtake et al. 2018). These referred symptoms are part of a broader set, which together make up the post-intensive care syndrome (PICS), named after two expert meetings that took place in 2010 and 2012, including the Society of Critical Care Medicine and international specialists from non-critical care organisations. PICS was then defined as “as new or worsening impairment in physical, cognitive, or mental health status arising and persisting after hospitalisation for critical illness” (Needham et al. 2012; Harvey and Davidson 2016).

PICS is described in 30-50% of patients after ICU admission; differences are due to patient population included in the studies, patient comorbidities, measurement tools, and time frames. At the time of hospital discharge, between 46% and 80% of survivors experience cognitive impairment; 3 and 12 months after discharge, 40% and 34%, respectively. At 12 months, clinically significant symptoms of anxiety, depression, and post-traumatic stress are present in 20% to 30% of survivors. Patients also refer other health problems: sleep disturbances (55%), ongoing pain (52%), airway irritation (45%), gastrointestinal rhythm disturbances (40%), dyspnoea (23%), dysphagia (19%), and nightmares about their time in ICU (14%) (Rai et al. 2019). Moreover, Marra et al. (2018) demonstrated in a multicentre cohort study that one or more post-intensive care syndrome problems were present in the majority of survivors. Still, concurr-

ing difficulties were coeval in only one out of four, being able to describe the possible existence of PICS subtypes, yet to be clearly defined.

Conversely, PICS can occur in both surviving and deceased patients' families (named PICS-Family or PICS-F). The long-term consequences on families are psychological, physical, and social. Approximately 10-75% of families suffer from anxiety; around 35% of families have depression and 8-42% symptoms accordant to post-traumatic stress disorder, which can persist for years (Schmidt and Azoulay 2012) (**Figure 1**).

Managing PICS effectively requires a clearer understanding of the associated risk factors. Lee et al. (2019) performed a systematic review of the risk factors for PICS and determined their effect size. Sixty risk factors were identified: those ICU related (uncontrolled pain or inappropriate sedation, presence and duration of delirium, immobility, steroids, prolonged mechanical ventilation, prolonged length of stay...) and those associated intrinsically to the patient (such as personal traits, own previous experiences, pre-existing anxiety, sepsis or ARDS on admission ...). Significant risk factors for PICS included older age (OR 2.19), female sex (OR 3.37 for mental health), previous mental health problems (OR 9.45), disease severity (OR 2.54), negative ICU experience (OR 2.59), and delirium (OR 2.85). On the other side, major risk factors for PICS-F are poor communication between staff, lower educational level, and having a loved one who died or was close to death.

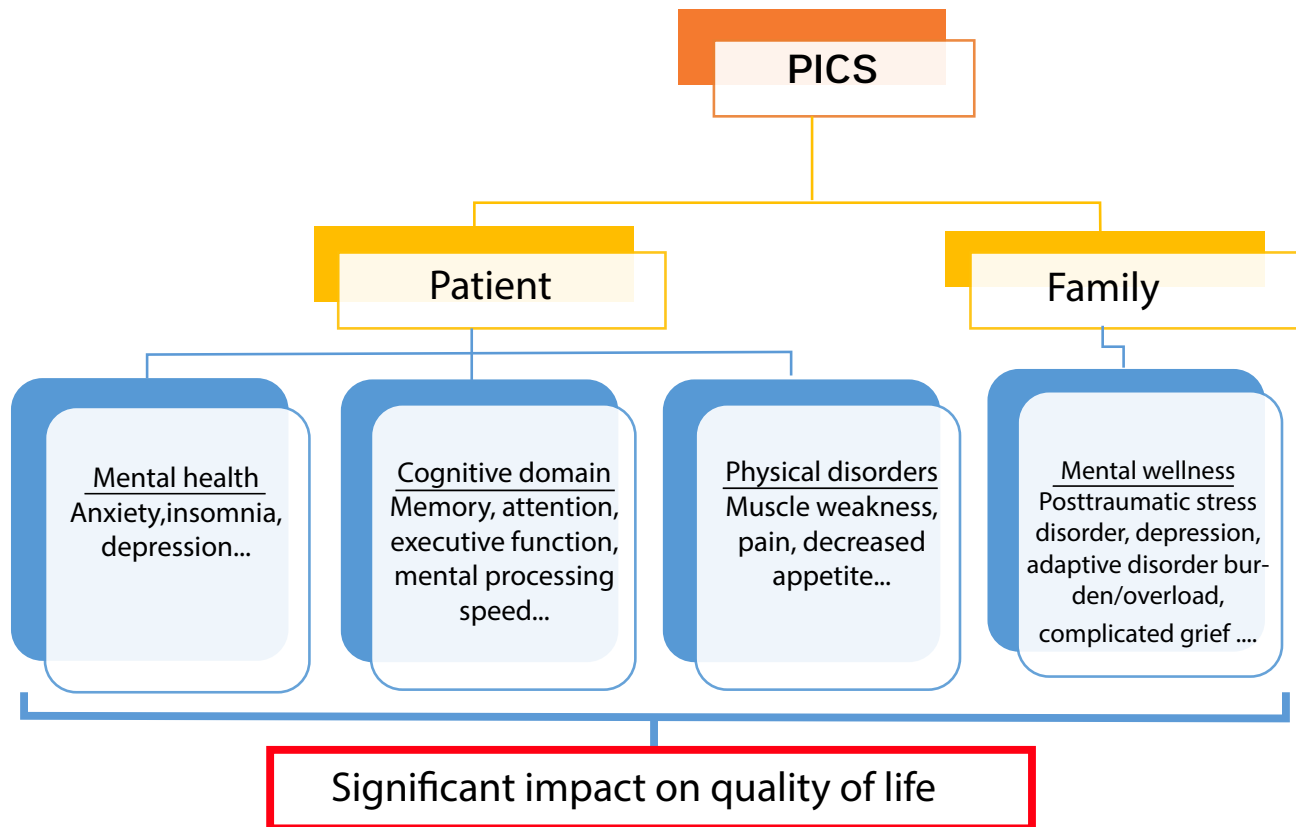


Figure 1. PICS environment

Decreasing PICS Incidence: Is it Possible?

Prevention strategies

To avoid the development of PICS, we must, as health professionals dedicated to the care of the critical patient, focus first on prevention measures:

- Following the updated Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit (ICU PAD guidelines; Devil et al. 2018), adapted into the world-wide known ABCDEF bundle (Marra et al. 2017; Lee et al. 2020) (Figure 2).
- Early mobility programmes by integrating physical therapists and occupational therapists into the ICU setting (Fuke et al. 2018).
- Early psychological interventions by integrating psychologists in the critical care team, offering both patients and

families, support, counselling, and education on stress management (Peris et al. 2011; Czerwonka et al. 2015).

- Use of ICU diaries: an illness narrative for patients written by nurses and patient's relatives, allowing patients to reconstruct the story of their critical illness, helping them understand the seriousness of the process, and filling in gaps of memory. Its maintenance has inconsistently shown (depending on the methodological differences between trials) decrease in symptoms of PTSD and could be used as a tool to provide support and care to the patient and family (Garrouste-Orgeas et al. 2019; Kredentser et al. 2018; Garrouste-Orgeas et al. 2014; Jones et al. 2010).
- Keeping favourable nutritional status and sleep quality.
- Modifying the ICU environment, using patient care space as a treatment tool (Luetz et al. 2019).

Management strategies

However, once the patient presents symptoms consistent with PICS, we must first make an early diagnosis, and then try to manage the symptoms with the tools we currently have available. One significant barrier in the assessment of PICS is the lack of a single, validated clinical tool to assess impairments in all three domains of PICS rapidly. Wang et al. (2019) managed to validate the Healthy Aging Brain Care Monitor Self Report version (HABC-M SR) psychological and functional subscales as reliable tools to measure the severity of symptoms of PICS. Besides, Jeong and Kang (2019) aimed to develop a PICS questionnaire consisting of 18 items covering all three domains, demonstrating excellent reliability (Cronbach's alpha of 0.93). Future studies in search for a quick clinical tool to rapidly assess PICS are still needed.

Regarding management of PICS, developed different strategies are:

ABCDEF bundle



Figure 2. ABCDEF bundle [Source: Marra et al. 2017]

- **Post-ICU rehabilitation programmes**, including patient-directed exercises, in-home therapist sessions and telehealth delivery of therapy, bundled with cognitive rehabilitation (Denehy and Elliott 2012; Jackson et al. 2012).

- **Post-discharge follow-up programmes** (Busico et al. 2019; Van Der Schaaf et al. 2015; Mehlhorn et al. 2014). A possible example can be seen in **Figure 3** and outlined below: *Management of acute illness within the ICU* Following ABCDEF bundle and patient's ICU discharge plan made on advance through the Continuity-of-Care Nursing team (search of patient's needs, assure a satisfactory hand-off with hospital ward team and discuss next steps with the patient and family).

Hospital recovery

- Follow-up programme by the ICU outreach team (span time and objectives agreed in advance).
- Nurse-led follow-up in the hospital ward (coordination with healthcare professionals and resource planning). Ward-discharge plan with the corresponding level of health care, guaranteeing the continuity of care.
- Optimal rehabilitation therapy: exercise, physical therapy, occupational therapy, speech-language pathology, or cognitive rehabilitation.
- Need of other subspecialties: Cardiology,

Pneumology, Psychiatry, Otolaryngology

- Support programme for families/caregivers, aimed at reducing stress and anxiety, supporting fluid communication about the patient's condition and prognosis. Priority to the patient's values and wishes in the shared decision-making process.

- Social work: assess the need for social support upon discharge (institutionalisation, Day Centre, home help...) and will inform and facilitate the necessary procedures to obtain economic and social support if needed.

Post-discharge recovery

- Targets: return the patient to baseline by promoting continuous care, sharing knowledge, professional experience, and availability of resources among professionals at all levels of care.
- Comprehensive assessment of the patient at the Primary Care Provider or PICS "clinic": screening deficits in following areas: motor and sensory functions, communication problems, swallowing problems, post-traumatic stress symptoms, symptoms of anxiety and depression, cognitive functions, psychosocial and sexual adaptation.
- Assessment to be carried out at intervals defined by each of care programme (at discharge, at one month, at three months, at six months, at 12 months...).
- The programme must also include a plan

for unforeseen health changes and what advice should be given to patients and caregivers in these cases.

Although it is widely accepted that follow-up activity at discharge is an effective intervention, research on such programmes has been disappointing. High quality randomised controlled trials with well-intentioned interventions designed and delivered by ICU teams after ICU discharge have not produced the desired results, and clinical evidence published to date is neither homogenous nor standardised (Schofield-Robinson et al. 2018; Walsh et al. 2015; Cuthbertson et al. 2009). There are several reasons why these interventions may have been ineffective. Among them: the complexity of the pathophysiology, the inability to identify and target high-risk groups, the impossibility of individualising therapy, and, in some cases, the lack of input from other expert providers such as physical therapists, neurologists, psychiatrists, geriatricians, and rehabilitation physicians. According to the data provided, it is unlikely that follow-up interventions will be useful in the future if we do not achieve greater collaboration between the different parts of the health system.

- **ICU survivor peer support groups** provide an adequate space for survivors to share experiences, feelings, empathy, advice... with others, collaborating and helping each other through problems. They allow mental reframing, effective role-modelling, information sharing, and practical advice that is not readily available to healthcare professionals. These have also proved favourable in other situations (mental health disorders, substance abuse issues, or cancer survivors) and can lead to empowerment, self-advocacy, and improved overall outcomes (Mikkelsen et al. 2016; Haines et al. 2019).

What about PICS-F?

Most critical patients cannot express their wishes, ask questions, or assert their rights. In these settings, family members (or primary caregivers) take the lead: they start making decisions, sometimes decisive ones, continually

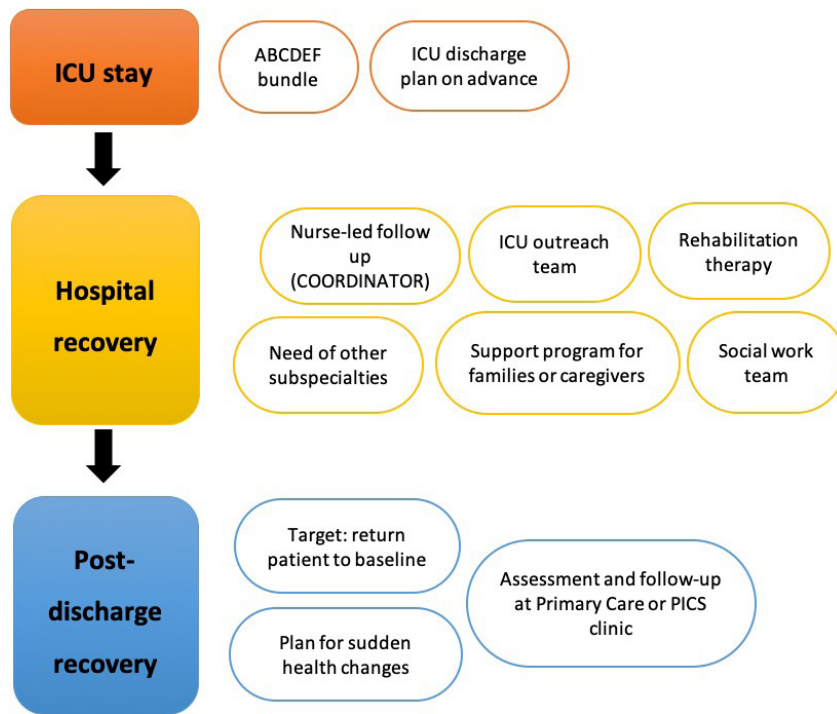


Figure 3. Post-discharge follow-up programme example

trying to think about what the patient would have wanted at any given time. It is clear that, in this situation of uncertainty and fear, there is a risk of psychological distress. Therefore, symptoms such as anxiety, depression, or acute stress disorder may appear. Withal, it is only the beginning, since once the patient is discharged, he/she requires caregiving until recovery and return to baseline. Who would not burden in this situation? (Davidson et al. 2012; Torres et al. 2017; Petrincic and Martin 2018).

Moreover, caregiver problems may start early during ICU admission. They may require the greatest support at that time, even though issues such as posttraumatic stress disorder may not appear until a few months after discharge.

Possible interventions to decrease the psychological burden and improve family members' experience could be (Schmidt and Azoulay 2012; Haines et al. 2018):

- Communication strategies: literature regarding family involvement in medical decision-making is growing, and extent data suggest that different methods of

communication and inclusion in decision-making may play a vital role in outcomes.

- Access to information (brochures, adapted explanatory documents for laypersons...).
- Family participation in care: open visiting hours, regular meetings with nurses, and ICU staff... .
- Psychological screening and support: need of psychologists during difficult times, developing coping strategies [problem-focused coping, emotion-focused coping, building resilience (Sottile et al. 2016)].
- Follow-up programmes for families: family debriefing visits, "family clinics," increasing awareness of possible long-term consequences of intensive care among ICU survivors.
- Engaging intensive care survivors and caregivers to co-design recovery programmes.
- Peer support and development of social support networks.

As previously said with PICS, PICS-F is also a complex problem, and will probably require global, proactive, and multimodal interventions.

Conclusion

PICS is a growing public health issue. We must empower healthcare professionals from a range of different disciplines who give care to ICU survivors with information, education, and resources.

In the following months, considering the COVID-19 pandemic, the teams dedicated to this issue will face the conundrum of the increase in PICS/PICS-F cases. Patients who suffered the viral infection in its most severe form will present significant deterioration.

Improving the psychological outcomes of critically-ill patients and their families is challenging, as it depends on previous mental health, social and economic background, and cultural and geographic factors. Future research requires a precise framework to risk-stratify patients and family members, a consensus regarding what are the best tools to measure outcomes, and standardised follow-up approaches. We must emphasise the prevention of cognitive, physical, and psychological sequelae. We must meet the current gap in health services. Patients and their families need to know they are not alone.

Conflict of Interest

F. Gordo has performed consultancy work and formation for Medtronic. The other authors have no competing interests. ■

Abbreviations

PICS – post-intensive care syndrome
 PICS-F – post-intensive care syndrome family
 ICU – intensive care unit
 OR – odds ratio
 PAD – Pain, Agitation and Delirium
 PTSD – posttraumatic stress disorder

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The Post-ICU Patient

Management of long-term impairments after critical illness

Survivors of critical illness and their caregivers frequently face long-term impairments of cognition, mental health, mobility and beyond, which demand for a patient-centred transition management and well-coordinated, outpatient post-ICU care.

Introduction

In recent years, the post-ICU sequelae of survivors of critical illness have become a focus of attention in research and patient care. This is the result of progress made in critical care throughout the last decades, which led to vast increases in survival rates and, therefore, growth of the cohort of post-ICU patients (Iwashyna et al. 2012; Zimmerman et al. 2013). Early investigations outlined that post-ICU patients are burdened with multifaceted consequences of critical illness summarised under the term post-intensive care syndrome (PICS). Notably, patients often perceive such functional impairments that potentially result from treatment as extremely relevant (Fried et al. 2002; Needham et al. 2012). The aim of this narrative review is to provide an overview over the established and further extended PICS domains and outpatient management of post-ICU patients.

Cognition

Studies in different patient populations and settings have established the association of critical illness and long-term cognitive impairments (**Figure 1**) (Adhikari et al. 2009; Hopkins et al. 2005; Iwashyna et al. 2010; Jackson et al. 2011; Jackson et al. 2003; Marra et al. 2018; Mitchell et al. 2018; Pandharipande et al. 2013; Wolters et al. 2013). Across studies, cognitive impairments were found in 4% to 62% of patients with follow-up periods from 2 to 156 months (Wolters et al. 2013). However, there has been no consensus on categorisation of cognitive

impairments and tools of assessment, which partially explains the variations.

Upon ICU discharge, the frequency of cognitive impairments is high, and after an initial improvement (Hopkins et al. 2005), impairments persist for years. They pertain to almost all domains of cognition, including memory, verbal fluency, attention and executive function (Wolters et al. 2013). Additionally, ICU survivors face a 60% increase in relative risk to suffer from dementia three years after discharge (Guerra et al. 2015). Presence and duration of delirium is a risk factor for long-term cognitive impairment (Girard et al. 2010; Goldberg et al. 2020), but the underlying pathophysiology is widely unknown. Few studies have considered pre-ICU cognitive functions. Two population-based, prospective cohort studies found a decline in cognitive functions in ICU survivors when compared to their pre-ICU status (Ehlenbach et al. 2010; Iwashyna et al. 2010), and in a cross-sectional study, 37% of ICU patients showed pre-existing cognitive impairments (Pisani et al. 2003).

Considering the connection between delirium and cognitive impairment (Goldberg et al. 2020), preventing delirium seems rational. Regular screening for delirium (Luetz et al. 2014), implementation of bundles such as the ABCDEF bundle (Barnes-Daly et al. 2017; Marra et al. 2017), the preference for non-benzodiazepine sedatives if sedation is necessary (Pandharipande et al. 2007; Pandharipande et al. 2010), and modifications of the patient environment can

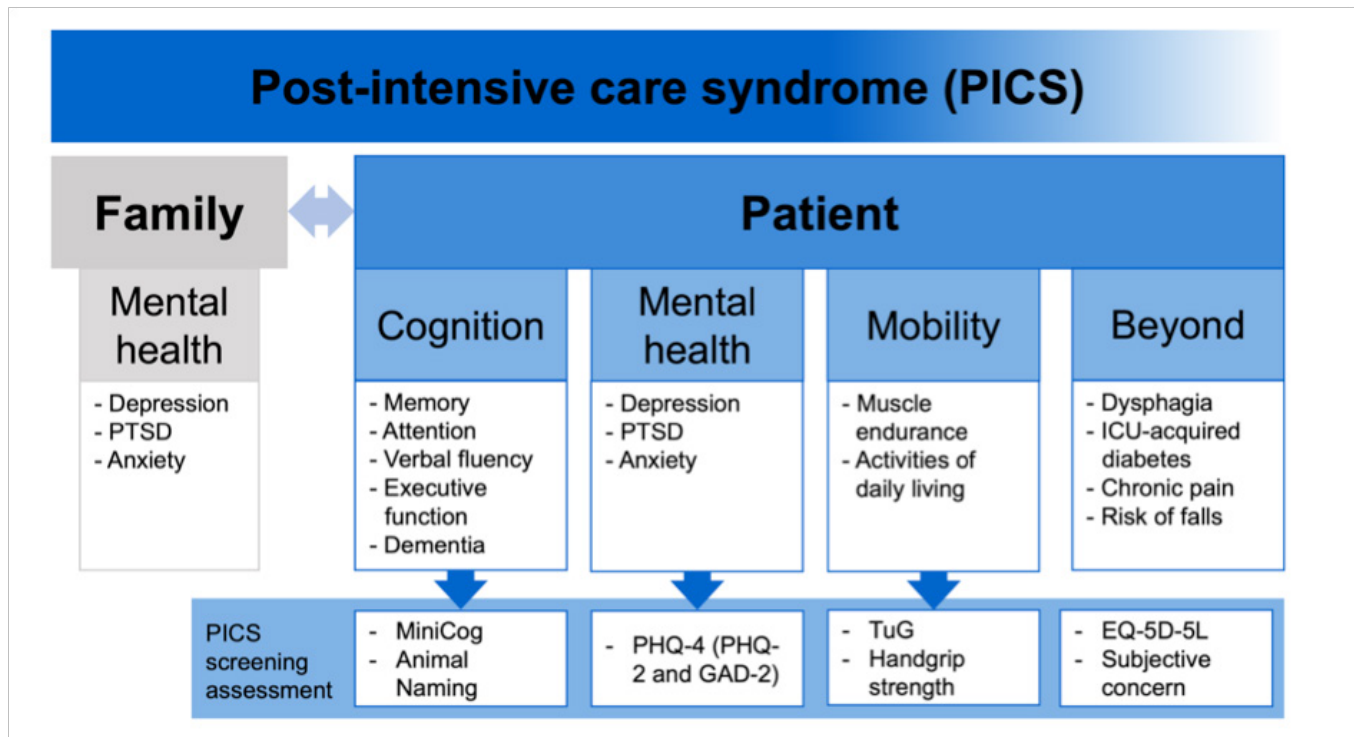


Figure 1. Domains of long-term impairments in post-ICU patients and caregivers [modified and extended from Needham et al. (2012)] and instruments used for ambulatory PICS screening after ICU treatment as proposed by Spies et al. (2020). EQ-5D-5L and items for the patients' subjective concern about functional impairments are used to assess health-related quality of life.

Abbreviations: PICS=Post-intensive care syndrome; PTSD=Post-traumatic stress disorder; ICU=Intensive care unit; PHQ=Patient health questionnaire; GAD=Generalised anxiety disorder scale; TuG=Timed up-and-go; EQ-5D-5L= European quality of life 5 dimensions 5 level.

reduce delirium (Litton et al. 2016; Luetz et al. 2019). Unlike a no-sedation strategy (Olsen et al. 2020; Strøm et al. 2010), no or light sedation has been shown to prevent delirium (Hager et al. 2013; Pandharipande et al. 2007). This is also the subject of current guidelines (Barr et al. 2013; Taskforce DAS et al. 2015).

As a brief screening for cognitive impairments, Spies et al. (2020) proposed to use the MiniCog (Borson et al. 2003) and Animal Naming test (Sager et al. 2006). If the patient is above threshold, the Trail Making test (Reitan 1958) and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph 2012) provide in-depth assessment. Data on treatment of already manifest cognitive impairment is limited. Two pilot studies showed promising results of cognitive rehabilitation (Jackson et al. 2012; Wilson et al. 2018), while another

study using a combined cognitive-physical rehabilitation did not detect an effect on executive functions (Brummel et al. 2012). In the future, larger trials need to investigate the potential of cognitive rehabilitation and have to consider pre-existing cognitive impairments. Studies also need to investigate if delirium prevention improves cognitive outcomes – an association still to be established.

Mental Health

Mental health impairments after critical illness pertain to depression, anxiety, and post-traumatic stress disorder (PTSD) (Marra et al. 2018). Symptoms of depression are present in about 30% of post-ICU patients, persisting even five years after discharge (Bienvenu et al. 2018; Davydow et al. 2009; Rabiee et al. 2016), but studies did not consistently use the same assessment tools, definitions

and time frames (Rabiee et al. 2016). With regards to anxiety, 32% to 40% of patients show symptoms within the first year after discharge (Nikayin et al. 2016). Just like depression, anxiety symptoms remain relatively stable (Bienvenu et al. 2018; Hopkins et al. 2005). For PTSD, prevalence varied from 4% to 62% across studies, with a pooled prevalence of 17% to 44% in the year after ICU discharge (Parker et al. 2015). After eight years, PTSD prevalence was still 24% (Kapfhammer et al. 2004). Notably, a large number of patients show overlapping symptoms (Huang et al. 2016; Marra et al. 2018). For instance, Wolters et al. (2016) found that 63% percent with any mental health symptoms showed symptoms of anxiety, depression and PTSD. Analogous to cognitive impairments, very few studies assessed pre-existing psychiatric symptoms, but results indicate

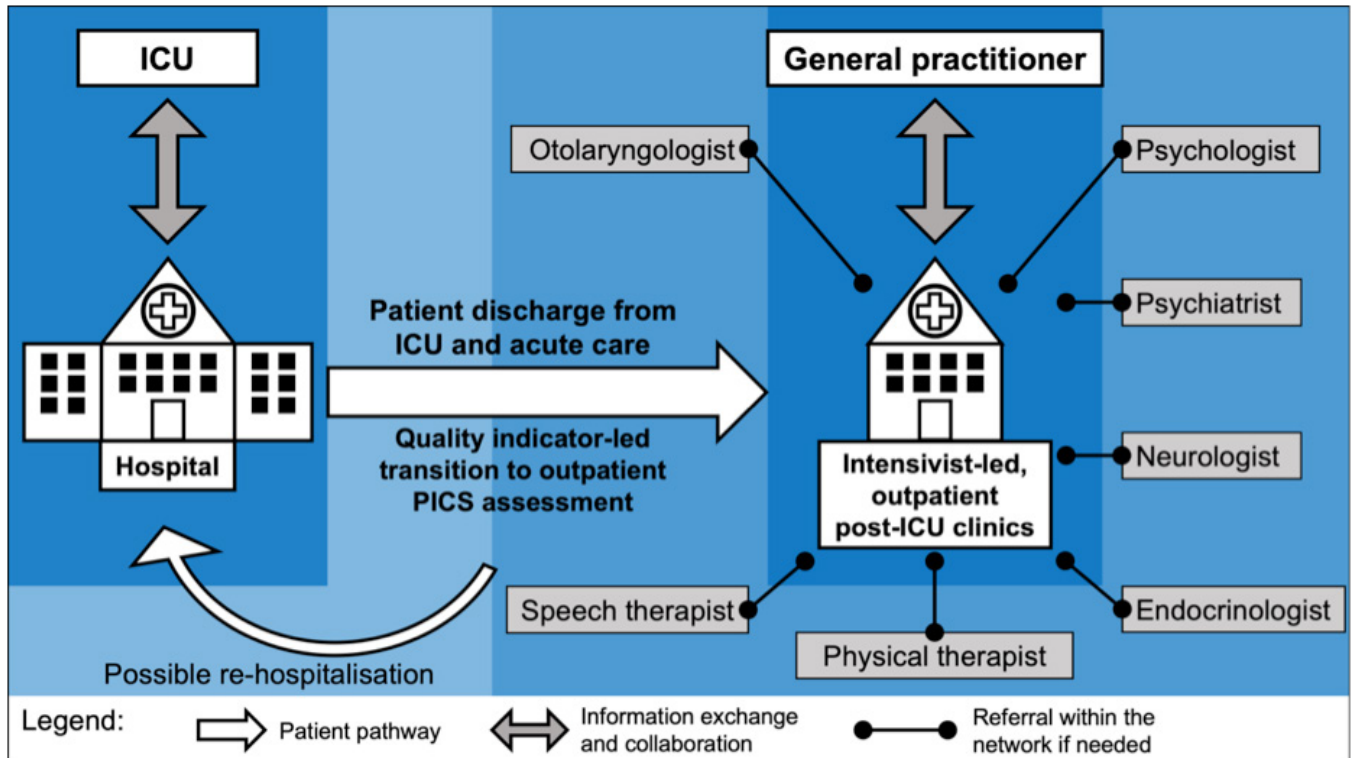


Figure 2. Management of the post-ICU patient. After a quality indicator-led discharge and transition to ambulatory care, patients are regularly assessed for PICS-related symptoms in post-ICU clinics, which work in close collaboration with the general practitioner and rely on a network of specialists for referrals. Abbreviations: PICS=Post-intensive care syndrome; ICU=Intensive care unit.

that prevalence is high (Davydow et al. 2009; Rabiee et al. 2016). For instance, 6.2% of mechanically ventilated ICU patients had a psychiatric diagnosis and about 50% received a prescription for psychoactive medication in the five years preceding their ICU stay, significantly more than in the general population. ICU treatment increased the risk for a psychiatric diagnosis and psychoactive medication prescription, with hypnotics and antidepressants being most commonly prescribed (Wunsch et al. 2014).

Risk factors associated with mental health impairments are nightmares and extreme fear in the ICU (Parker et al. 2015; Rattray et al. 2005; Samuelson et al. 2007), lack of recollection of ICU experience (Rattray et al. 2005), and delusional memories from the ICU (Jones et al. 2001; Nikayin et al. 2016). Further, pre-ICU psychiatric morbidity (Wade et al. 2012; Weinert and Meller 2006),

stress during ICU treatment (Wade et al. 2012), and psychiatric symptoms at hospital discharge were associated with post-ICU depression, anxiety and PTSD (Davydow et al. 2009; Nikayin et al. 2016; Rabiee et al. 2016; Rattray et al. 2005). Interestingly, neither age, severity of illness, or sex were identified as risk factors. Likewise, delirium, was not associated with PTSD or depression in the ICU context (Girard et al. 2007; Jackson et al. 2014; Wolters et al. 2016), even though post-operative delirium was found to be a risk factor for PTSD (Drews et al. 2015). It has been shown that mental health problems significantly diminished health-related quality of life (Davydow et al. 2009; Parker et al. 2015).

As a screening tool for mental health impairments, the Patient Health Questionnaire-4 was proposed, followed by the more detailed Patient Health Questionnaire-8 for depression, Generalised

Anxiety Disorder Scale-7 for anxiety (Kroenke et al. 2010), and Impact of Event Scale-revised for PTSD (Spies et al. 2020; Weiss 2007). For treatment, ICU diaries reduced PTSD symptoms in one large randomised controlled trial and one prospective, non-randomised study (Garrouste-Orgeas et al. 2012; Jones et al. 2010), and anxiety and depression symptoms in another small randomised controlled trial (Knowles and Tarrier 2009), whereas a recent, large randomised controlled trial published in JAMA did not detect an effect of ICU diaries on PTSD, anxiety or depression (Garrouste-Orgeas et al. 2019). Provision of a self-help manual reduced PTSD symptoms but not depression or anxiety symptoms (Jones et al. 2003), and the benefit of post-ICU follow-ups remains inconclusive (Cuthbertson et al. 2009; Schandl et al. 2012). Interestingly, physical rehabilitation has been shown to