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COVID 19 – KCE CONTRIBUTIONS

POST INTENSIVE CARE SYNDROME IN THE AFTERMATH OF COVID-19

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This document is a rapid review of scientific literature retrieved from several publicly funded COVID-19 resource collections. The literature included in these repositories is not always peer-reviewed or externally validated. KCE synthesised the evidence in short time frames to respond to urgent questions and could therefore not follow its regular methodological procedures. This work is used to inform guidance of other governmental agencies (like Sciensano, CSS/HGR, AFMPS/FAGG and SPF/FOD).

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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ABC	Activities Balance and Confidence
ADL	Activities of Daily Living
AT	Anaerobic Threshold
BDI	Beck Depression Inventory
BMI	Body Mass Index
CAMS-R	Cognitive and Affective Mindfulness Scale – Revised
CAPS	Clinician Administered PTSD Scale
CES-d	Center for Epidemiological Studies Depression Scale
CIM	Critical Illness Myopathy
CIP	Critical Illness Polyneuropathy
CFQ	Cognitive Failure Questionnaire
CPC	Cerebral Performance Category Scale
DASS	Depression Anxiety Stress Scales
DEMMI	De Morton Mobility Index
DEX	Dysexecutive Questionnaire
EQ-5D	EuroQoL 5D
FIM	Functional Independence Measure
GAD-7	General Anxiety Disorder 7-item scale
GOS	Glasgow Outcome Scale
GP	General Practitioner
GRPS	Graded Chronic Pain Scale
HABC-M SR	Healthy Aging Brain Care Monitor Self Report version
HADS	Hospital Anxiety and Depression Scale
HRQoL	Health-related quality of life
HTQ-IV	Harvard Trauma Questionnaire Part IV
IADL	Instrumental Activities of Daily Living
ICU-AW	ICU acquired weakness
ICU	Intensive care unit
ICUM	ICU Memory Tool
IES-R	Impact of Event Scale-Revised
ISWT	Incremental Shuttle Walk Test
Kg	kilogram
LOS	Length of Stay
MDI	Major Depression Inventory
Min	Minutes
MMSE	Mini Mental State Examination
MRC	Medical research Council
MRS	Modified Rankin Scale
MUST	Malnutrition Universal Screening Tool
NSS	Neuropathic Symptom Score
OMI	Outcome Measurement Instruments
PDS	PTSD Diagnostic Scale
PHQ-9/10	Patient Health Questionnaire depression scale 9/10 items

PROMIS	Patient-Reported Outcomes Measurement Information System
PTSD	Posttraumatic Stress Disorder
PTSS	Posttraumatic Stress Disorder Symptoms
PTSS-14	Posttraumatic Stress Disorder Symptoms- 14 items
QOL	Quality of Life
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RIS	Regensburg Insomnia Scale
6MWT	Six-Minute Walk Test
SCL	Symptom Checklist
SMD	Standardized mean difference
Sec	Seconds
SF-36	36-Item Short Form Survey
SF-36 PF	36-Item Short Form Survey - Physical functioning domain score
SF-36 PCS	36-Item Short Form Survey - Physical component summary score
SF-36 MCS	36-Item Short Form Survey - Mental component summary score
SPPB	Short Physical Performance Battery
STAI	State-Trait Anxiety Inventory
TICS-M	Modified Telephone Interview for Cognitive Status
TSQ	Trauma Screening Questionnaire
TST	Timed-Stands Test
TOWER	Tower Test
TUG	Timed Up and Go test
VAS	Visual Analogue Scale
XSMFA-B	Extra Short Musculoskeletal Function Assessment - disability
XSMFA-F	Extra Short Musculoskeletal Function Assessment - physical function

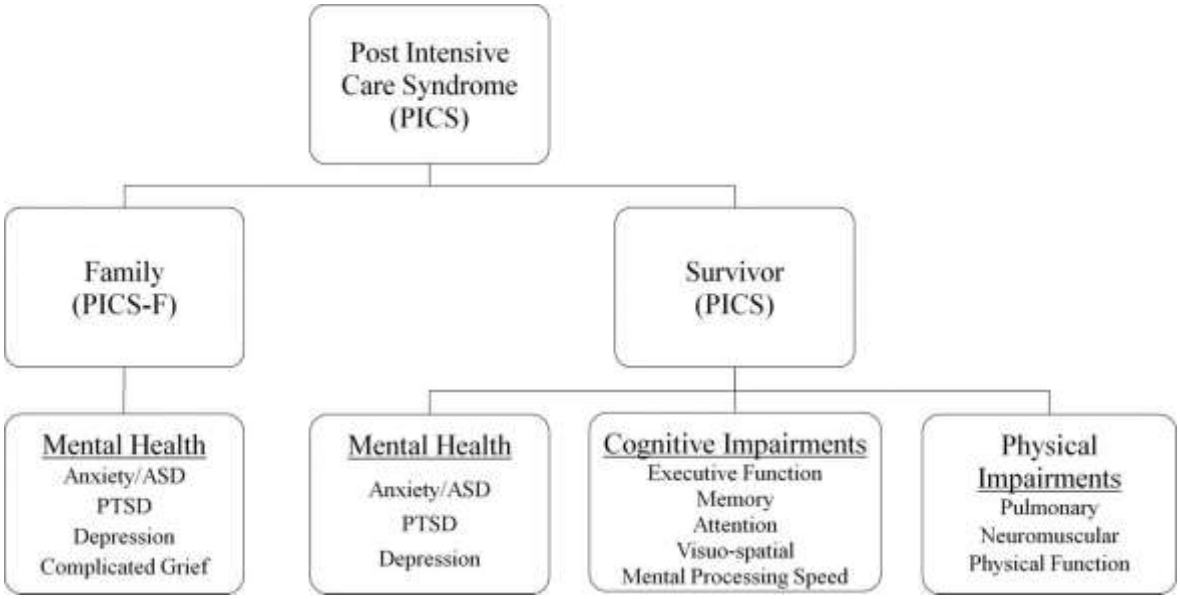
INTRODUCTION

Post-intensive care syndrome

Improvement in the management of critically ill patients over the last decades has led to an increased survival. Nevertheless, patients may develop physical, mental, and cognitive sequelae after discharge from the intensive care unit (ICU). The "Post-Intensive Care Syndrome" (PICS) concept has been established in 2012 at a stakeholder conference and is defined as *impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization*.[1] One of these disorders may occur in more than half of patients three months after a severe critical illness treated in the ICU.[2] It may lead to impairments in daily life, inability to return to work and decreased quality of life.[1]

The most frequent physical impairment is ICU-acquired weakness (ICU-AW), which may occur rapidly after ICU admission and may persist during years. Other long-term physical complications include impairments in pulmonary function, walking ability and activities of daily living. Mental health problems involve frequently anxiety, depression and post-traumatic stress disorders (PTSD). Cognitive disorders include impairments in memory, attention and concentration, verbal fluency and executive functions. Some symptoms and signs of PICS are observed at ICU discharge (such as muscular weakness) while others, such as PTSD, may appear only a few months after ICU discharge.[1] Family member of ICU survivors may also be affected by mental health impairments, and these symptoms are related to "PICS-F" (F for family). Figure 1 presents a conceptual diagram for PICS and PICS-F. Further details on symptoms, physiopathology, frequency and evolution of the PICS-related outcomes are described in Chapter 1.

Figure 1 – Post-intensive care syndrome (PICS) conceptual diagram (Needham et al)[1]



ASD: acute stress disorder; PTSD: post-traumatic stress disorder.

PICS-related disorders are favored by a variety of factors. Some factors are related to a long exposure to the ICU setting and to a number of ICU interventions, such as deep sedation, lack of contacts with family, prolonged immobility etc. However, pre-existing factors, such as socio-demographic characteristics, functionality, quality of life, or the presence of co-morbidities also play a role. The risk factors for developing PICS that are identified in the scientific literature are described in Chapter 2.

PICS and COVID-19

The current COVID-19 epidemic is likely to be followed by an "epidemic" of PICS among COVID-19 patients who survived a long ICU stay. There are no data nor evidence on PICS post-COVID so far (as of September 2020) but other authors warn that COVID-19 patients have been exposed to a high number of risk factors for PICS during their ICU treatment:[3-10]

- During the first wave of COVID-19 in Belgium, 12% of hospitalized COVID-19 patients were admitted in ICU, many had acute respiratory failure, more than half required mechanical ventilation, deep and long duration of sedation was common, neuromuscular blocking agents (NMBA) were frequently used, the length of stay in ICU was long (25% stayed ≥17 days),[11] and overloaded ICU staff may have limited time to devote to the early mobilization efforts that are recommended in ICU patients.
- The COVID-19 patients who are at higher risk of ICU admission are also those at higher risk to develop PICS, i.e. older persons with underlying diseases such as diabetes, hypertension, increased frailty and other chronic disorders.[10, 11]
- Due to deep sedation and a long ICU stay, a very high proportion of them have prolonged ICU delirium which is the major risk factor for cognitive impairment at long-term.[4] The reduction of human interactions prevents cognitive stimulation, reorientation of and reassurance to patients, which may exacerbate delirium and increase the risk for long-term cognitive impairment.
- Due to isolation and confinement, COVID-19 patients had no or very limited visits from family or friends, hindering emotional and social support.[6-8] This social isolation also prevails when COVID-19 patients are discharged from the hospital to return home or are referred to a rehabilitation center. This isolation has been associated with increased symptoms of depression and anxiety, as well as fear and hostility towards medical providers.[4] The fear of infecting loved ones, survivor's guilt, and social stigma also add to the mental stress.
- Restriction of visits or no visits at all to the ICU due to the risk of transmission and lack of personal protective equipment during the first COVID wave, may increase the risk of PICS-F. In the beginning of the COVID-19 epidemic, Family members were not able to see or speak to their loved one during ICU stay, sometimes even before their death.[7]
- Family members of COVID-19 patients admitted in the ICU were also left in the uncertainty about the survival chances of their loved ones for weeks. This was aggravated by the media news on the severity of the disease with scaring images and high fatality ratio.

Other authors plea that we should get prepared for "aftershocks of the pandemic" of for a "crisis after a crisis".[3, 9] This shows a need to raise awareness of PICS for patients treated in the ICU and their families, as well as for all members of the health care team.[4, 10] Patients surviving ICU will require adequate screening as well as early rehabilitation and other interventions.[4, 9, 10]

PICS and general practitioners

The ideal management of PICS patients requires a multidisciplinary and patient-centered approach that may involve post-ICU physiotherapy and rehabilitation care, mental health and cognitive interventions, social support etc.[1] A number of Belgian hospitals have developed specific consultations for PICS patient (post-ICU clinics) prior to the COVID-19 pandemic,[12] and some have set up specific rehabilitation services for COVID-19 patients during the COVID-19 crisis (see Chapter 5). The effectiveness and availability of potential interventions in Belgium are however unclear.

There is very limited information about PICS in Belgium (as in most other countries).[a] There are also no specific Belgian clinical pathways or guidelines for the care of ICU survivors after hospital discharge to manage their long-term consequences.[12] Patients discharged from hospitals or rehabilitation units after an ICU stay will often contact their GPs, as these are responsible for coordinating the patient care. Although there are usually followed-up by their organ specialist or surgeon, they may also rely on their GP for the detection of remaining health problems and potential

[a] Except for some documents from ICU services such as Erasme https://www.erasme.ulb.ac.be/sites/default/files/files/documents/2018/depliant_post_usi_vf_bd.pdf, CHU Liège https://www.rmlg.ulg.ac.be/show.php, or health website https://www.gezondheid.be/index.cfm?fuseaction=art&art_id=30624

referrals. Studies in other countries report that ICU survivors may be reluctant to consult their GPs or, if they do, would not easily report psychological symptoms – in particular intrusive memories from ICU.[5, 13, 14] As GPs care for their patients over many years, they are however very well placed to identify psychological distress in those patients or in their families.[5, 9, 13, 15, 16]

Nevertheless, GPs are often not aware of the risk of PICS, and lack information on how to detect and guide patients with PICS and their family. This lack of awareness and information about PICS among GPs has been reported by PICS experts but has not been studied in Belgium. It has also been reported in other countries (see Chapter 7).[5, 13] It is therefore important that primary care providers are informed about the long-term health consequences after the ICU stay. In this report, we aim to inform GPs about the PICS syndrome, as well as how to detect and manage the PICS-related problems to help patient referral.

Study objective and research questions

This study, targeted at GPs, addresses the detection and management of PICS-related outcomes among adult ICU survivors and their families (PICS-F) after hospital discharge. In the perspective of a rapid report to meet post-COVID-19 needs, we aim to provide practical information that could help the GPs in their daily practice. The objectives are to increase GP knowledge and awareness about PICS and PICS-F symptoms, frequency and evolution, help them in detecting PICS-related outcomes in ICU survivors by the use of a rapid and easy screening tool, provide them an overview of the existing post-ICU interventions and their effectiveness, describe the services, resources and other support that are currently available in Belgium to care for them, provide illustration of the experience and point of view of PICS patients and discuss the role of GPs for PICS patients.

The research questions of this study are:

1. What are the clinical tools to use among ICU survivors that could be applied in Belgian GP practices to screen them for PICS-related disorders?
2. What is the effectiveness of post-ICU interventions to improve PICS-related outcomes?
3. What are the experience and preferences of PICS patients in terms of support and care?
4. What are the current services, organizational and financial resources for the management of PICS cases or similar patients in Belgium?

This study addresses the PICS problem in adults only for feasibility reasons in the short time frame. We also focused on ICU-AW among the physical complications, as this is considered as the most important long lasting physical consequence of PICS and the most documented.[1] We do not cover the detection and management of other physical problems such as pain, respiratory impairments and fatigue, which are common health problems encountered by GPs in the daily practice. This report does not include mortality as an outcome.

This report provides information and a proposal for practical screening tools, but does not proposes recommendations.

The *prevention* of PICS (and PICS-F) related outcomes, through improved management of patients at ICU level, is addressed in another KCE study that started in 2019.

General methodology

Due to the short time frame available to prepare a response to the expected high number of post-COVID PICS, we aimed at a rapid report based on pragmatic literature reviews and consultations of key informants on PICS. Evidence was mostly extracted from recent systematic reviews, except for the section on the effectiveness of interventions, which extracted data from primary studies. No expert meeting was organized but more than 30 Belgian experts and a team of German researchers on PICS have been consulted, and the draft of this report or specific chapters have been reviewed by 7 different experts in specific fields.

The detailed methodology for the literature search and other aspects are summarized in each chapter and detailed in Appendix.

Content of the report

The report contains the following chapters:

- Chapter 1 describes the symptomatology, physiopathology, frequency and evolution of PICS and PICS-F related disorders.
- Chapter 2 lists the risk factors for developing PICS / PICF in ICU survivors and describe a few sets of predictors that can be used to identify patients at higher risk of PICS
- Chapter 3 describes tools to detect PICS-related outcomes and proposed a screening instrument to be used at GP level
- Chapter 4 describes the post-ICU interventions and their effectiveness according to the literature
- Chapter 5 provides an overview of the services, resources and support that are available in Belgium for PICS-related outcomes
- Chapter 6 report stories of PICS patient experiences and perspectives, from Belgium and similar settings
- Chapter 7 summarizes what is discussed in the literature on the potential role of GP for PICS detection and coordination
- Chapter 8 provides a summary of the proposed strategies and a conclusion

Appendices contain further details on methodologies, evidence tables and additional useful information.

1 CHAPTER 1: WHAT IS THE POST-INTENSIVE CARE SYNDROME?

Key points

- **The most frequent physical complication is the ICU- acquired weakness observed in around 40% of patients at ICU discharge. It the results of damages to both muscular and peripheral nerve systems and is characterized by a decrease of muscle mass. Recovery mostly occurs within 12–24 months, but disease persists for years in a proportion of patients.**
- **The mental health problems include mostly anxiety (35% at 1 year), depression (29% at 1 year) and post-traumatic stress disorder (PTSD, 20% at 1 year), which often co-exist and do generally not improve over time. PTSD can be unrecognized because affected patients tend to avoid contact with health care and not look for assistance**
- **Cognitive impairment (in 20-40% at 1 year) include loss of verbal fluency, capacity of concentration and memory, and may aggravate existing cognitive disorders. They may improve in the first year after discharge but not in the following years.**
- **A high proportion of ICU survivors (40%) did not return to work at 1 year after ICU discharge, and social consequences make these patients more vulnerable.**
- **PICS-related disorders are more frequent in some patients, in particular those with pre-existing health problems, with severe disease and with traumatizing ICU experience.**
- **Around 20-50% of family members of ICU survivors are also affected by mental health problems, including PTSD, which corresponds to the syndrome PICS-F (F for family).**

As noted in the Introduction, this report focuses on the following impairments of the Post-Intensive Care Syndrome (PICS): ICU-acquired weakness (ICU-AW) as physical complication, anxiety, depression and post-traumatic stress disorders (PTSD) as mental health impairments, cognitive impairments and mental health consequences on family members of ICU survivors (PICS-F). This Chapter intends to describe briefly the symptomatology, pathophysiology, frequency and evolution of these PICS-related disorders, based on the literature.

Regarding the epidemiology, there is no register nor database on PICS patients in Belgium, except for four Belgian studies including epidemiological data on a group of ICU survivors (physical and quality of life outcomes, see below). [17-20] As the high number of studies from other countries present different prevalence of PICS-related outcomes in ICU survivors, we have focused our rapid literature search on systematic reviews published in the last 10 years, see search terms in Appendix 1. A total of 15 systematic reviews have been identified by using our search strategies or through the snowball approach, and are described in Appendix 2. The frequencies presented below are influenced by the tools used to diagnose health problems and by the inclusion criteria for patients. Detailed information is included in Table 1 describing the results from the systematic reviews.

The frequency of any PICS-related disorders in ICU survivors is rarely described. In one large US study (the BRAIN-ICU study) including 531 patients with respiratory failure or shock treated in medical or surgical ICUs, 64% and 56% of patients had at least one PICS-related disorder at 3 months and 12 months, respectively.[2] Only one PICS-related problem was present in 39% and 35% of patients at 3 months and 12 months, respectively. Two problems were observed in 19% and 16% of patients at the same time points, and <10% had three problems.

1.1 ICU-Acquired Weakness

ICU-AW represents the most common physical impairment of PICS, and manifests by a symmetrical weakness of the limbs and a decrease in the muscle mass and may occur rapidly after ICU admission.[1, 21-23] Unrelated to the primary critical illness, it is characterized by a structural and functional impairment of muscles and nerves.[24-26] Notably, the diaphragm and other respiratory muscles can also be involved.[21, 27, 28] ICU-AW generates long-lasting consequences persisting in the aftermath of an ICU hospitalization resulting in difficulties with the activities of daily living.

ICU-AW is observed in around 40% of patients at ICU discharge (see **Error! Reference source not found.**). Two meta-analyses, including 14 studies and 33 studies estimated a prevalence of 39%

and 40% of ICU-AW after ICU discharge, respectively (Table 1).[29, 30] Three Belgian studies were included and estimated prevalence ranging 38-45% using electroneuromyography or MRC in studies involving 400-600 patients.[17-19] Recovery of ICU-AW mostly occurred within 12–24 months, but symptoms persisted in a percentage of patients.[31-34] Persisting ICU-AW correlated with activity limitation and reduced physical function up to two years and up to 5 years after ICU discharge in a Belgian study.[33] In other studies, significant neuromuscular weakness was associated with altered QoL,[34, 35] and long-term mortality.[21, 36]

ICU-AW can be the consequence of peripheral neural disturbances (Critical Illness Polyneuropathy -CIP) and/or primary muscle failure (Critical Illness Myopathy- CIM). Both entities can occur alone or in combination. CIP refers to a sensory-motor axonal polyneuropathy causing distal axonal degeneration of motor and sensory fibers. It can give rise to muscle denervation and atrophy. CIM refers to an acute primary myopathy not related to denervation and is characterized by the loss of thick myosin filaments, muscle fiber atrophy, and cell necrosis.[21, 24, 37] Studies also suggest that a myogenic origin of ICU-AW (CIM) had a better prognosis as compared with a neuro-myogenic origin (CIP) that left 50–75% of the patients with persisting muscle weakness.[31]

The pathophysiology of ICU-AW remains uncertain and there is little evidence of which factor or factors are causal. Current evidence supports a multifactorial origin with several interactions between risk factors (see also Chapter 2). Most of them are related to the critical illness and its severity. Others depend on the pre-existing comorbidities or specific ICU treatments.[21, 24, 38] The most important risk factors are related to the primary disease (including sepsis) and the subsequent multiple organ failure.[21, 24] Accordingly, ICU-AW can been considered as a downstream effect of the inflammatory processes following the primary insult as inflammation brings an imbalance between protein degradation and synthesis. There is growing evidence that an increased protein breakdown combined with a reduced protein synthesis leads to a decrease of muscular mass typically reported in CIM.[26, 39, 40] Particularly, CIP could be related to inflammatory-induced microvascular disturbances and the detrimental effect of hyperglycemia on mitochondrial functioning.[21] In that way, nerve biopsies have shown an axonal degeneration associated with marked fiber loss.[41]

In addition, many ICU interventions have been recognized as potential risk factors for ICU-AW such as immobilization, use of neuromuscular blocking agents (NMBA), deep sedation, aminoglycoside, corticosteroid and hyperglycemia.[21] However, there are conflicting data on the exact involvement of some of them (see Chapter 2)[36, 42, 43] There is compelling evidence that bed rest in combination with critical illness has deleterious consequences on muscle trophicity. Particularly, the duration of immobilization in the ICU is recognized as risk factor for muscle wasting.[44] This is explained by the loss of mechanical loading, called muscle silencing, which reduce the protein synthesis and promotes catabolism.[45-47] Muscle mass and function undergo a decrease throughout the first days at the ICU that may remain at long-term.[40, 44] This persistent muscle wasting is presumably related to a prolonged failure of intrinsic recovering mechanisms.[48] Furthermore, muscle structural alterations through fibrosis and fat deposition or a lower excitability has been reported.[49] In some cases, impaired contractility can durably persist independently of muscle mass recovery.[48]

1.2 Mental health problems

1.2.1 Anxiety and depression

Post-ICU psychological disorders include also mental health impairments.[50-52] Mental health impairments in PICS include post-ICU psychological disorders such as anxiety, depression and PTSD.

The prevalence of anxiety in ICU survivors was estimated at 32%, 40% and 35% at 2-3, 6 and 12-14 months post-ICU (HADS-A score >8) in a meta-analysis of 22 studies (Table 1).[53] The prevalence of depression was estimated at 29%, 34% and 29% at 2-3, 6 and 12-14 months post-ICU (HADS-D score >8) in a meta-analysis of 22 studies.[54] For both disorders, there was no significant change in prevalence over time, suggesting no improvement after discharge (up to 1 year for depression).[53, 54]

1.2.2 PTSD

Classically recognized as a neuropsychiatric response to a traumatic life threatening event, PTSD has also been identified as a long-term consequence in ICU-survivors.[55-58] It manifests as a network of interconnected symptoms such as intrusive flashbacks, avoidance of reminders of the traumatic event, hyperarousal, recurrent nightmares and alteration of reactivity.[59] Particularly, in ICU-survivors,

re-experiencing and avoidance are the most prevalent symptoms.[60] While re-experiencing symptoms are generally easily identifiable, avoidant patients may deny presenting a problem and may consequently not look for assistance. It ineluctably ensues that mental difficulties worsen. The consequences on health can be substantial. Since each simple medical care can remind the patient of the traumatic event, such avoidant behavior is generally associated with poorer concern about medical condition. The consecutive lack of appropriate medical care may lead to new hospital admissions.[60]

Of note, patients may also experience Posttraumatic Stress Symptoms (PTSS) that is characterized by an array of symptoms following a traumatic event and shares many similarities with those of PTSD. Despite similarities, both disorders differ in terms of duration and intensity.[60-63] PTSS is a common acute and adaptive stress response after exposure to an upsetting situation. Those symptoms occur within the first month following ICU discharge).[60] PTSS symptoms may resolve over time, while the persistence of more severe symptoms for several months that interfere with the daily life is characteristic of PTSD.[50-52]

The prevalence of PTSD symptoms among ICU survivors was estimated at 20% at any time point by a meta-analysis of 48 studies.[64] The proportions tended to slightly increase over time post discharge: 16%, 17%, 19% and 20% at 3, 6, 12, and > 12 months, respectively, which is in line with the pathophysiology of PTSD. Another meta-analysis of 6 studies estimated it at 25% and 17% at 1-6 and 7-12 months post-ICU.[65]

Among the mental health problems arising after an ICU stay, memories of unpleasant or stressful events are frequently described by patients. Generally, patients are misperceiving the ICU-environment because of sedation, delirium, lack of sleep, unknown environment, lights, noises, and the intrusiveness of techniques. Memories can refer to events experienced in ICU such as suctioning through the endotracheal tube or sometimes to unreal events corresponding to hallucinations. In this way, patients report delusional and fearful memories. The reported prevalence of such traumatic memories range from 25 to 48%.[66] Lack of memory is reported too.[67] There is an increasing concern about the impact of ICU memories on long-term mental health. Many studies have evaluated patient memories after ICU discharge. Some studies have identified the memories of stressful events as a risk factor for mental health impairments, see Chapter 2.[68, 69]

Besides, there is growing evidence that dissociative disorders take part in the onset of PICS [70, 71] These refer to a disconnection and a lack of continuity between memories and thoughts. They develop as a reaction to a traumatic event, such as an ICU hospitalization, and can disrupt the mental functioning.[72] Many types of dissociative events are described. Patients with depersonalization or dissociation identity problems can feel disconnected from themselves. Dissociative amnesia can also manifest and is characterized by the inability to remember information about oneself. It has been evidenced that dissociative symptoms occurring during the peri- and post-ICU period are involved in the onset of PTSD and could be a risk factor for developing long-term mental health disorders.[73, 74] The pathophysiology of those phenomena are multifactorial and alterations of neurotransmitters pathways, brain inflammation and metabolic disturbances have been reported. [75, 76]

A high proportion of PICS cases presented concurrently two or three of mental health problems.[2, 77] In a large US study among ICU survivors, most PTSD cases (94%, 139/148) showed also depression and anxiety at the 6-month follow-up.[77]

1.3 Cognitive impairment

Long-term cognitive impairments are observed in ICU survivors, and the most common impaired fields are attention, concentration, visual and working memory, verbal fluency and executive function.[59, 78] Furthermore, patients undergoing neurocognitive disorders have a poorer quality of life with intellectual, social, professional and daily-living difficulties.[79, 80]

A review estimated the prevalence of persistent cognitive impairment at 20-40% of ICU survivors based on the most solid prospective studies.[81] Two recent systematic reviews found prevalence ranging 4-78% across studies at any time point (Table 1).[80, 82] A trend toward improvement of cognitive function was observed in the 1st year in the studies in which patients were tested at multiple time points, but not in the following years, even at 5 years post-ICU discharge.[80, 82] Overall, 17-63% patients were still impaired on their last follow-up according in one review (3 months to 2 years after discharge).[82] Studies also highlight the difficulty to discriminate between new cognitive impairment and the exacerbation of preexisting cognitive decline due to the lack of data on cognitive function at

baseline. In one US study, prevalence was at 6.1% at baseline and 16.7% after discharge.[83] In another study, a 2.2 increased risk for incident dementia was observed in patients after a critical illness hospitalization compared to non-hospitalized patients (hazard ratio 2.2, 95%CI 0.9 to 5.7).[84] Authors suggest that a critical illness may cause an abrupt loss of cognitive function rather than steepening the slope of decline. Survivors of critical illness with cognitive impairment have worse quality of life compared with survivors without cognitive decline.[81]

The pathophysiology of long-term neurological disorders and its link with delirium (see below) are imperfectly understood. Since assessments in the critically ill are difficult, unravelling its pathophysiology is mainly based on animal models. Several hypotheses coexist. First, an imbalance in the neurotransmitters regulation has been proposed.[85] Second, pro-inflammatory cytokines released in response to the systemic critical illness could conceivably affect the brain function. The blood-brain barrier and cerebral microcirculation could afterwards be disrupted through cellular damages.[26, 85, 86] Structural alterations of the blood brain barrier have been observed in patients with delirium and long-term cognitive dysfunction.[85] Concurrently, anatomical changes using magnetic resonance imaging have also been observed. Patients with long-term cognitive disorders had brain atrophy particularly in the regions involved in cognition processes.[87] The duration of delirium has been associated with a worse level of cognitive problems and larger brain atrophy. White matter can also be impaired up to 12 months after ICU discharge.[88]

Delirium

Delirium is recognized as the most prevalent brain dysfunction occurring during an ICU stay, and plays a key-role in the long term cognitive disorders of PICS (Chapter 2). Patients who develop delirium during their ICU stay are at a higher risk for long-term impaired cognitive function.[81, 89-91] Delirium is characterized by an acute confusional state.[56, 87, 92] Clinical hallmarks are impairments of attention, awareness and cognition. It is highly prevalent and can affect up to 70% of ICU patients.[56] Several subtypes of delirium have been identified according to the level of activeness: hyperactive, hypoactive and mixed. Hyperactive delirium is characterized by agitation, aggressiveness, hallucinations that often make patient's safety and delivery of care difficult. Hypoactive delirium is more difficult to identify and is commonly characterized by apathy, confusion, poor responsiveness and impaired attention.[93] Hypoactive and mixed delirium are the most common with prevalence of 43.5 % and 53.1%, respectively.[56, 94] This distinction may be important as recent studies suggested that only hypoactive delirium is associated with cognitive impairment.[95]

The causes of delirium are multifactorial and encompass predisposing factors and other directly related to the underlying disease and ICU therapy. Elderly patients are more likely to develop delirium. Previous comorbid conditions, severity of illness and medications are recognized as substantial risk factors.[94] Delirium is associated with increased ICU and hospital length of stay, prolonged mechanical ventilation and mortality. Its duration correlates with increased mortality. [96]

1.4 Consequences on family members

The consequences of the critical illness can extend beyond the patient and also significantly impact the mental health of relatives, then called Post Intensive Care Syndrome-Family (PICS-F). As such, a high proportion of informal care givers such as family members can undergo psychological impairments including overwhelming anxiety, depression and even a genuine PTSD.[97, 98] PICS-F symptoms may appear from the beginning of the patient's ICU admission and can last for long.[99, 100] PICS-F is frequently undiagnosed and unmanaged.[101] Some subgroups are more likely to develop PICS-F. These subgroups include younger people, people with prior psychological problems or females, as described in Chapter 2.[99]

Among caregivers of ICU patients, a meta-analysis of 28 studies estimated the prevalence of anxiety between 15% and 24%, depression between 5% and 36% and PTSD between 35% and 57% at 6 months after ICU discharge. [100] Another review of 14 studies found a prevalence of depression ranging 34-43% at 2 months, 23-29% at 1 year and 32% at 2 years following ICU.[99] The majority of caregivers were middle age females who were spouse or partner of the ICU patient.

Studies also highlighted a restriction in activity and lifestyle in caregivers. But PICS-F can also induce socioeconomic problems combined with increasing healthcare costs.[102] Frequently reported consequences are loss or change of employment, financial burden, low health-related quality of life and increased use of antidepressant, anxiolytic, hypnotic and psychotropic medication.

1.5 Quality of life and return to work

A Belgian review of 53 studies showed that critically ill patients ≥ had a lower quality of life (QoL) 12 months after ICU discharge than an age- and gender-matched population.[103] Quality of life tended to improve slowly over the years, especially the physical components, but the mental and emotional conditions stagnated or declined even further. In the elderly, QoL decreased as well, especially in the physical domains, but elderly patients generally adapted well to these limitations and perceived their QoL as good.[103]

Delayed or no return to work is common after critical illness, in particular among those experiencing PICS, and carry substantial financial and social consequences for patients, their families, and society. The jobless rates among ICU survivors employed before critical illness, was 64%, 40%, and 32% at 1-3, 12, and 42-60 months, respectively, after hospital discharge, according to a meta-analysis of 38 studies.[104] The median time to return to work ranged from 10 to 29 weeks. Those who did return to work often experienced subsequent job loss (20-36%), changes in occupation (17-66%), worsening employment status (5-84%) such as decreased work hours. Risk factors for delayed return to work include mental health impairment following hospital discharge.[104]

Table 1 – Description of systematic reviews on prevalence of PICS-related disorders

Author, years	Outcome and timing of measurement	Criteria (and tool)	Pooled prevalence	Range across studies
Physical disorders				
Yang 2018[29]	ICU-AW at 2 weeks post-ICU	MRC (7 studies) and electrophysiology (7 studies)	Median 39%	24-69%
Appleton 2015[30]	ICU-AW at different time points	Clinical diagnosis (15), electrophysiology (20), histology (1)	Pooled 40% Median 47%	9-86%
Mental health problems				
Nikayin 2016[53]	Anxiety at different timing (2-14 months)	HADS-A >8 or >11 (severe)	32%, 40% and 35% at 2-3, 6 and 12-14 months post-ICU	5-73%
Rabiee 2016[54]	Depression, at different time points	Many instruments, HADS-D in 58%	29-30% at different time points HADS-D >8: 29%, 34% and 29% at 2-3, 6 and 12-14 months	4-64%
Righy 2019	PTSD, at different time points	Many, as defined by studies	Any time: 19.8% 16% to 20% at 3 to >12 months	4-44%
Parker 2015[65]	PTSD at ≥1 month	Many. IES or IES-R (23/40 studies), PTSS-10 (6/40)	IES >35 at 1-6 months: 25% At 7-12 months: 17% pooled	4-62%
Wade 2013[70]	PTSD at 1-12 months after discharge	Many, as defined by studies	At 1 year: median 18% in high quality studies	9-75%
Cognitive disorders				
Kohler 2019[82]	Cognitive impairment, at different time points	Not reported	NA	Range 17-78% across studies. 17-63% still impaired on last follow-up
Wolters 2013[80]	Cognitive, at 2 months to 13 years post-ICU	Many, 14/19 used neuropsychological tests	NA	4-62%
Other consequences				
Oeyen 2010[103]	Quality of life ≥1 year after ICU discharge	Many	NA (not relevant)	NA
Kamdar 2020[104]	Jobless rate at different time points	Return to work	64%, 40%, and 32% at 1-3, 12, and 42-60 months	NA
Mental health problems in family members (PICS-F)				
Haines 2015[99]	Depression, PTSD, HRQoL, at different time points	Many	NA	Depression: 34%-43% at 2 months and 23-29% at 1 year. No data on PTSD.
Van Beusekom	Anxiety, depression, PTSD, HRQoL and other consequences, at different timing	Many, mostly HADS, CES-D and IES.	NA	At 6 months: Anxiety: 15-24% Depression: 5-36% PTSD: 35-57%

HADS: Hospital Anxiety and Depression Scale, HADS-A for anxiety, HADS-D for depression; HRQoL: health related quality of life; ICU-AW: ICU-acquired weakness; IES: impact of event scale. MRC: Medical research council test; PTSD: post-traumatic stress disorder. Lee et al performed meta-analyses but they are not reported as studies differ in terms of design and outcome and on statistical level as shown by heterogeneity indicators such as tau square and I^2.

2 CHAPTER 2: RISK FACTORS AND PREDICTORS OF PICS-RELATED DISORDERS

Key Points

- **The risk factors for PICS differ per outcome:**
  - **Older age and severity of critical illness, including length of stay, were risk factors for physical impairment (ICU-AW) but not for mental health and cognitive outcomes.**
  - **Pre-existing mental health problems were risk factors for depression and PTSD.**
  - **Distress at ICU, memories of ICU negative experience (including no recall) as well as mental health symptoms at ICU discharge were consistent risk factors for the three mental health outcomes (anxiety, depression, PTSD).**
  - **Delirium in ICU was the principal risk factor for cognitive impairment.**
- **A few studies identified sets of predictors that could help GPs to identify ICU survivors at risk of PICS-related disorders after their discharge:**
  - **We found no prediction system aimed at the GP level that would allow a preliminary screening of ICU survivors based on known on risk factors**
  - **Seven studies proposed different sets of predictors to be used at ICU discharge or one week after ICU discharge, and most of them have a fair or good accuracy to predict PICS-related outcomes. However, many of these factors have been collected in a research context and are unlikely to be known by the GP.**
  - **An important part of these predictors are pre-ICU factors, related to age, comorbidities, pre-existing mental health status and social situation (social support, family and work).**
  - **Most predictor sets are unlikely to present an advantage at GP level compared to the use of simple and rapid screening tools, as proposed in the chapter 3 Tools. One exception is a simple online tool with 5 questions assessing the risk for mental health problems among ICU survivors, which could be useful at GP level.**
- **These studies provide important information that the GPs could share with the patient and the family, in particular:**
  - **The condition of the patient prior to his ICU admission is a major factor that will influence the risk for PICS and for long-term outcomes. This covers in particular age, comorbidities, pre-existing mental health problems and social support.**
- **Given the role of family and social support, it is important that the GPs knows the social environment of the patient.**

The purpose of this section is to help general practitioners (GPs) to identify which patient returning home after a long ICU stay would be more likely to develop a PICS-related disorder, based on the information that is available to the GP. We describe here the risk factors for PICS-related disorders identified in systematic reviews. In a second part, we assess which risk factors can be used as predictor for PICS-related disorders at the GP level. The Chapter 3 is providing information on a few rapid tools that could be used by the GP to screen ICU survivors for such disorder.

Three categories of risk factors are considered in the literature:

- Pre-ICU risk factors, which are related to the pre-ICU patient's health, functional and social status, which are usually known by the GP and included in the patient medical file.

- ICU risk factors, which are related to the critical illness and treatment, such as length of ICU stay, duration of mechanical ventilation, duration and type of sedation, ICU delirium, mobilization etc. Some of these factors can be documented in an ICU report sent to the GP, but some specific ones (e.g. biochemical markers, imaging, specific scores) are not automatically provided in the ICU report. Many of these factors are not known by the GP and their impact is also difficult to comprehend for a physician not working in an ICU.
- Post-ICU risk factors, which can be known by the GP because they can be assessed by the GP in a visit or are described in medical reports delivered by e.g. general wards or rehabilitation units or post-ICU clinics.

2.1 Risk factors for PICS-related disorders

The many studies that have investigated risk factors for PICS-related disorders in ICU survivors show sometimes conflictual findings. Therefore in this rapid report, we have focused our rapid literature search on systematic reviews published in the last 10 years (see search terms and criteria in Appendix 1) and completed by a snowball approach and a selection of recent narrative reviews. Overall, 10 systematic reviews on risk factors and meeting the criteria were identified in the last 10 years and their characteristics are described in Appendix 2. Many of these reviews excluded primary studies focused on specific patient groups such as patients with acute respiratory distress syndrome (ARDS) or chronic critical illness. When results of primary studies were stratified over time, we excluded periods ending earlier than 2010.[70]

Table 2 – Summary of risk factors identified in selected systematic reviews, per disorder

Outcome	Pre ICU	During ICU (ICU illness and treatment)	Post ICU
Physical health			
ICU-AW[29, 31, 105]	Likely: older age	Likely: Illness severity	None identified
Mental health			
Anxiety[53, 105]	Unlikely: age and gender	Likely: Psychiatric symptoms at ICU admission Negative ICU experience, including fear and nightmares Unlikely: illness severity, LoS, diagnosis	Likely: Memories of ICU delusional experiences Anxiety at discharge Post-ICU depression and PTSD symptoms
Depression[54, 107]	Likely: Low socioeconomic status History of pre-ICU depression or psychological morbidity[54, 108] Unlikely: age and gender	Likely: ICU distress Unlikely: illness severity, LoS, benzodiazepines, sedation Unclear for delirium	Likely: Delusional/ traumatic memories or lack of factual memories of ICU experience Psychiatric problems at discharge
PTSD[65, 70, 105]	Likely: Pre-ICU psychopathology Unclear: age and gender	Likely: ICU distress or negative ICU experience (stress, fear, agitation) Unlikely: illness severity, LoS Unclear: sedation, benzodiazepines, ventilation	Likely: Early post-ICU memories (delusional/intrusive) of frightening ICU experience or amnesia of ICU experience Post-ICU psychopathology
Cognitive impairment			
Cognitive[82, 105, 109]	No clear association with older age	Likely: Delirium (presence and duration) Unlikely: LoS, mechanical ventilation, sedation and analgesia	None described
PICS-F			

Mental health in family (PICS-F): depression[99]	Likely: Female caregiver High health risk behavior (inadequate rest and exercise, skipping meals)	None	Likely: Patient functional dependency and institutionalization

ICU-AW: ICU-acquired weakness; LoS: length of stay; PTSD: post-traumatic stress disorders.

Table 2 summarizes the risk factors that were identified in the primary studies included in each systematic review. We categorized as *likely* risk factors for PICS-related disorders that were significant in >50% of primary studies or in meta-analyses pooling studies, as *unlikely* those that were significant in none or in <20% of primary studies. We labeled as *unclear* those factors that were significant in between 20% and 50% of studies. The results of each review are summarized in Table 3, including the number of primary studies that reported significant associations. The results of meta-analyses were not reported when they pooled studies that are largely heterogeneous in terms of outcome measurement and study design, such as those of Lee et al.[105] In those situations, only the results from the primary studies were taken into account.

2.1.1 Pre-ICU risk factors

Older patients had a higher risk to develop ICU-AW.[105] Patient gender and age were not likely risk factors for mental health problems.[53, 54, 105, 106] However, patients with mental health problems before ICU admission were more at risk for developing depression and post-traumatic stress (PTSD) after the ICU stay.[54, 65]

Among caregivers of PICS patients, female gender and high health risk behavior (e.g. inadequate rest and skipping meals) presented a higher risk for developing depression.[99]

2.1.2 Factors during ICU stay

Distress at ICU (or negative ICU experiences), such as fears, nightmares and agitation during ICU, were very consistent risk factors for mental health.[53, 54, 65, 105, 106]

Delirium during ICU was the most consistent risk factor for cognitive impairment, identified in all systematic reviews. Duration of delirium was associated with worse cognitive performances at 3 and 12 months.[110] Fluctuations of glucose levels, hypoglycemia and hyperglycemia during ICU were found as risk factors for cognitive outcomes in the two studies that assessed them.[110]

Severity of critical illness, including length of stay, were risk factors for ICU-AW but not for mental health and cognitive outcomes.[53, 54, 65, 105, 106, 110]

The use of NMBA and aminoglycosides were significant risk factors for ICU-AW.[29] Surprisingly, sedation (and the use of benzodiazepines) was no clear risk factors for mental and cognitive impairment in systematic reviews, although a few primary studies have shown a significant association.[54, 65, 106, 110]

2.1.3 Post-ICU factors

For the mental health problems assessed at 1-12 months after hospital discharge, two consistent risk factors were identified in all systematic reviews: memories of ICU negative experiences and mental health problems present at ICU discharge.[53, 54, 65] Memories of frightening ICU experiences that are delusional, traumatic or intrusive, including memories of hallucinations and nightmares, or the lack of factual memories of ICU experience (or poor recall), are all consistent risk factors for anxiety, depression and PTSD.[53, 54, 65, 105, 106] Anxiety, depression and post-traumatic stress symptoms identified after ICU discharge, were generally risk factor for mental disorders at 2-12 months after hospital discharge.[53, 54, 65, 105, 106] For physical health and cognitive impairment, no post-ICU factor has been identified.

The risk for depression in relatives of ICU survivors was higher in those caring for institutionalized patients or patients with functional dependency after discharge.[99]

Table 3 – Description of findings of systematic reviews on risk factors, per dimension

Author, years	Outcome and time	Patients	Significant risk factors (number of studies with association / total studies assessing this factor)
Physical disorders			
Yang 2018[29]	ICU-AW at 2 weeks post-ICU	Adults	In meta-analyses: ICU use of NMBA and aminosides (OR>2)
Lee 2020[105]*	Impaired physical ability, any time	Adults	Older age (3/4), illness severity (5/5). Unclear: female (0/4 but found in meta-analysis)
Mental health problems			
Lee 2020[105]*	Mental health problems, no timing	Adults	Anxiety: negative ICU experience (3/3). PTSD: negative ICU experience (5/5), previous psychological morbidity (4/5) NOT: age, sex, disease severity (LoS), MV
Nikayin 2016[53]	Anxiety at different timing (2-14 months) using HADS-A	Adult, studies with >50% ICU patients	Psychiatric symptoms during admission (3/3 studies), ICU fear and nightmares (3/3), memories of in-ICU delusional experiences (3/3). Anxiety at discharge (3/3). Post-ICU PTSD symptoms and depression (5/5). NOT age (0/5), gender (0/4), severity of illness, diagnosis, and LoS (0/4)
Rabiee 2016[54]	Depression at 1-12 months after hospital discharge	Adults, not specialized ICU	Low socioeconomic status (3/3 studies), employment (2/2), psychological morbidity pre-ICU (4/5), ICU distress (4/4), psychiatric problems post-ICU (5/5), delusional memories of ICU experience (2/2), lack of factual memories (3/5) NOT age (2/11), sex (0/8), illness severity and LoS (0/6), benzodiazepines (0/3), sedation (0/4). Unclear for delirium (1/3).
Parker 2015[65]	PTSD at ≥1 month post-ICU	Adults, not specialized ICU	Pre-ICU psychopathology (5/9, others studies were smaller), early post-ICU memories of frightening ICU experience (10/12), post-ICU psychopathology (4/4) NOT illness severity (1/12), LoS (2/14), sedation (0/4), delirium (0/2) Unclear for ICU benzodiazepine use (2/4), age (7/16), sex (5/18), MV (5/8)
Wade 2013[70]	PTSD at 1-12 months after discharge	Adults, survivor of general ICU, >24h LoS	In 2008-12 studies: Post-ICU delusional/ intrusive memories and/or amnesia of ICU experience (12/14 studies), ICU distress (9/10), MV (3/4) Negative ICU experience, such as fear and agitation (5/5) NOT sex (1/6), illness severity (1/6), LoS (0/6) Unclear for age (2/6), sedation (2/4) and delirium (1/2), psychiatric history (1/2)
Cognitive disorders			
Kohler 2019[82]	Cognitive impairment	Adults, non-surgical patients	No quantitative data on risk factors
Sakusic 2018[110]	Cognitive deficits (modifiable factors only)	Adults, 2 months post discharge, not specific patients	Delirium and duration of delirium (5/8 studies) Glucose levels (2/2) NOT sedation and/or analgesia (0/4), LoS (1/7), MV (2/14)
Lee 2020[105]*	Cognitive impairment, any time	Adults	Delirium (2/3 studies) Not age (1/5)
Mental health problems in family members (PICS-F)			
Haines 2015[99]	Psychosocial in family / informal caregivers and QoL. Different timing	Informal caregivers of ICU patients >48h	For depression: female, high health risk behavior, patient functional dependency and institutionalization For lifestyle disruption: patient male gender, functional dependency, education and tracheostomy

*ICU-AW: ICU-acquired weakness; LoS: length of stay; MV: mechanical ventilation; PTSD: post-traumatic stress disorders. *: Risk factors identified in majority of individual studies (not in meta-analyses), as Lee et al performed meta-analyses of very heterogeneous studies, on clinical aspects as they differ in terms of study*

design and outcome (tool and timing post-ICU) and on statistical ground as shown by heterogeneity indicators such as tau square and I².

2.1.4 Discussion

A consistent finding in all reviews is that older age as well as severity of the critical illness (including length of stay) were risk factors for physical outcomes but not for mental health and cognitive outcomes. Distress at ICU, memories of ICU negative experience (including no recall) as well as mental health symptoms at ICU discharge were consistent risk factors for anxiety, depression and PTSD. Pre-existing mental health problems were risk factors for depression and PTSD. Delirium in ICU was the principal and consistent risk factor for cognitive impairment.

The lack of or the unclear association between sedation and PICS-related disorders problems in systematic reviews was not expected. Indeed, sedation and the use of specific drugs such as midazolam has been significantly associated with PICS-related disorders problems, such as PTSD, in a number of primary studies.[106] There are however more studies that showed no association with sedation.[54, 65, 70, 110] We also excluded older studies (e.g. 1997-2007 studies in Wade et al).[70] The role of mechanical ventilation and its duration was also not clear across the body of literature, with conflicting results e.g. for PTSD and cognitive impairment.[65, 70, 110]

A limitation of this review of reviews is that diagnostic tools for PICS-related disorders varied widely across primary studies, and that sample sizes of many studies were too limited to detect a significant association. The quality of included studies was not assessed in this rapid study and may have influenced the results. A limitation in the assessment of delirium as a risk factor in mental and cognitive health problems may be that hypoactive and hyperactive delirium were not discriminated in all studies.[111]

2.2 Predictors for PICS-related disorders

In this section, we assessed whether combinations of risk factors can be used to predict the occurrence of PICS, as this could help GPs to suspect PICS-related disorders based on known factors. In other terms, we searched for studies that did not only measure the strength of association between the risk factors and the outcome, but also calculated the proportion of PICS cases (and non-cases) that could be predicted by using a set of these factors by multivariate analysis. Only a few studies have estimated the predictive value of risk factors. The literature search (Appendix 1) has identified 4 studies and manual search has retrieved 3 additional studies describing predictors of PICS-related disorders and their predictive values.[108, 111-116] Studies predicting mortality or based on a subset of patients were not included.

Five studies from the same Swedish team (two with Danish and Dutch contribution) investigated the predictive value of screening ICU survivors at ICU discharge or at 1 week after discharge (in ICU clinics).[108, 111, 113-115] Together with the 2 other predictive studies,[112, 116] they are described in Table 17 and presented below by group of outcome being predicted. We did not find studies assessing the predictive value of criteria applied at a GP consultation. The predictors are summarized in Table 4 and the studies are described below and in Table 17.

2.2.1 Predictors for physical outcomes

A multinational study conducted in 2016 in Sweden, Denmark and the Netherlands including 404 patients assessed the predictive value of 16 risk factors for new-onset physical disability assessed 3 months after ICU discharge by a ≥10 points reduction of the Barthel index compared the pre-ICU status (see Chapter 3).[114] Only one predictor was identified, the physical status at ICU discharge assessed with the by the first 5 items of Chelsea critical care physical assessment tool (CPAx), and was a relatively poor predictor (area under the ROC curve or AUC 0.68). The sensitivity of CPAx ≤18 at ICU discharge was 73% and specificity was 60%. In that study, the negative predictive value (NPV) for a low-risk group (CPAx >18) was 88% and positive predictive value (PPV) for a high-risk group (CPAx score ≤18) was 32%. A length of ICU stay ≥72 hours was a poor predictor. This CPAx predictor is proposed as a tool to rule out patients unlikely to need physical interventions in the post-ICU period.

A Swedish study conducted in 2011 involved 148 ICU survivors who were assessed for new-onset physical disability 2 months after ICU discharge, defined as a reduction in activities of daily living (ADL staircase questionnaire) compared to two weeks before hospitalization, or being in sick leave for physical reasons while working prior to ICU admission.[115] The final model contained a set of 4

predictors which showed a good accuracy (AUC 0.80): low educational level, inability to sit without support in ICU, fractures in ICU and ICU length of stay >2 days. Low educational level (elementary school of lower) was the strongest predictor, and previous studies have suggested that patients with low education employ more avoidant way of coping (see Chapter 5). The criteria ICU length of stay >2 days alone has a lower accuracy (0.70). Furthermore, it is known that LoS depends on many other factors related to the context.

Table 4 – Summary of combinations of risk factors predicting PICS-related disorders at 2-12 months after ICU discharge

Outcome and time post-ICU discharge	Sets of predictors	Predictive value*
New physical disability (Barthel Index) at 3 months[114]	Physical status at ICU discharge, defined according to Chelsea critical care physical assessment tool (CPAx), first 5 items	0.68
New physical disability at 2 months defined as reduction in ADL staircase questionnaire or sick leave[115]	Four factors at ICU discharge: Low educational level Inability to sit without support in ICU Fractures in ICU and ICU length of stay >2 days	0.82
Mental disorders: depression, anxiety and PTSD at 3 months[108]	Four factors at ICU discharge: Middle age (peak at 49-64 years) Lack of social support after hospital discharge Symptoms of depression (based on PHQ-2) Traumatic memories (PTSS-14)	0.76
Mental disorders: PTSD, anxiety and depression at 3 months[113]	Mental disorders at 1 week post-ICU: PTSD (PTSS-10 >34) Anxiety (HADS-A >7) Depression (HADS-D >7)	PTSD: 0.90 Anxiety: 0.80 Depression: 0.75
Mental disorders: PTSD, anxiety and depression at 2 months[111]	Six factors at ICU discharge: Major pre-existing diseases (Charlson score >3) Having children <18 years Previous psychological problems ICU agitation Being unemployed at ICU admission Appearing depressed at ICU	0.77
Quality of life at 1 year[116]	Twelve factors at ICU admission: QoL at baseline, age, activity of daily living, imaging, APACHE II-score (P=0.001), ≥80 years, mechanical ventilation, hematological patient, SOFA-score, tracheotomy, surgical admission and comorbidity (Charlson - CCI)	0.39
Disability moderate or severe (WHODAS II score 25–95%) at 6 months[112]	Four factors, timing not specified: History of anxiety/depression Being separated or divorced Duration of mechanical ventilation Not being discharged to home from the acute hospital	0.71

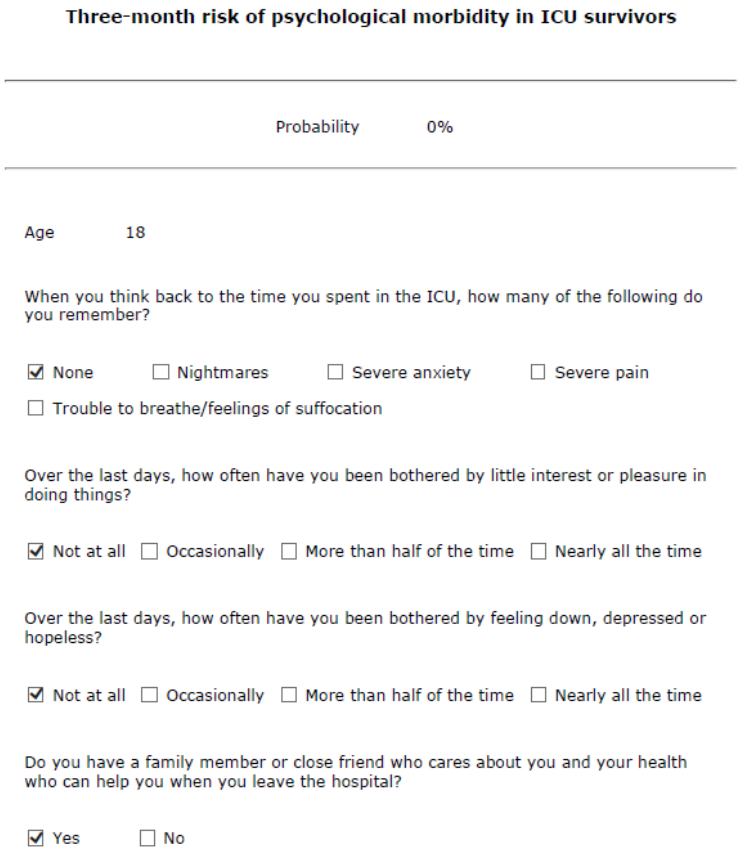
*CCI: Charlson comorbidity index; HADS: Hospital Anxiety and Depression Scale, HADS-A for anxiety, HADS-D for depression; QoL: quality of life; PTSD: post-traumatic stress disorder. *: Values for sensitivity, specificity, negative and positive predictive values are provided in Table 17.*

2.2.2 Predictors for psychological outcomes

The same multinational study conducted in 2016 assessed the predictive value of 18 risk factors identified by a literature search for psychological morbidity (depression, anxiety and PTSD) at 3 months.[108] Among 404 survivors who stayed ≥12 hours in ICU, the final model with four predictors achieved a fair accuracy (AUC 0.76) and included age, lack of social support after hospital discharge, symptoms of depression (based on PHQ-2) and traumatic memories (PTSS-14) at ICU discharge. Regarding age, the risk for psychological morbidity increased in the middle age, with a peak risk at

49-64 years. The NPV and PPV would be 37% and 58% at a pre-test predicted risk of 30-60%, which is close to the prevalence described in ICU survivors (30-50%, see Chapter 1). Based on these four predictors, authors have developed a simple and practical on-line tool to be used at post-ICU discharge for assessment of the 3-month risk for psychological problems and the need for further support (http://www.imm.ki.se/biostatistics/calculators/psychmorb/). This simple and rapid tool includes only four questions and could potentially be used at GP level (Figure 2). It has been internally validated by the authors but still requires external validation.

Figure 2 – ICU discharge instrument proposed by Milton et al (online)[108]



An earlier study among adult survivors who stayed ≥24 hours in ICU in Sweden (2012-13) found that symptoms of post-traumatic stress (PTSS-10 part B >34), anxiety (HADS-A >7) and depression (HADS-D >7) assessed at 1 week post-ICU in post-ICU clinics, were predictors for PTSD, anxiety and depression (using the same case definition) at 3 months after ICU stay.[113] The AUC was 0.90 for PTSD, 0.80 for anxiety and 0.75 for depression. When using lower thresholds for outcome at 1 week (PTSS-10 >29, HADS-A >5 and HADS-D>4, the high NPV (>90%, Table 17) in this population suggests that the absence of these criteria at an early screening can help rule out patients that can be categorized at low risk for psychological symptoms at 3 months. The PPV at that lower threshold was low (range 37-50%), likely due to the low pre-test probability of 13-21% in this patient group with an average length of ICU stay of 3 days.

A similar study was conducted in 2011 in Sweden.[111] Prevalence of psychological morbidity in the 150 patients was 31%. A model of 6 predictors, assessed at ICU or at ICU discharge, achieved a fair accuracy (AUC 0.77) to predict psychological morbidity at 2 months. These 6 predictors are major pre-existing diseases (Charlson score >3), having children <18 years, previous psychological problems, ICU agitation, being unemployed at ICU admission, and appearing depressed at ICU. Traumatic memories were not included as a risk factor.

2.2.3 Predictors for cognitive impairment

No studies of predictors for cognitive impairment have been found. Delirium in the ICU has been consistently found to be a predictor of subsequent cognitive impairment in a majority of studies (see

2.1), but the predictive values have not been quantified.[82, 110] A 2013 study stated that studies had so far been unable to identify patients at higher risk of cognitive impairment after critical illness using brief cognitive screening tools.[117]

2.2.4 Predictors for global outcomes

Quality of life

A model to predict quality of life at 1 year post-ICU discharge (using EuroQol-5D) has been developed by a Belgian study involving 1831 ICU patients.[116] The 16 variables included in the model were all available on the first day of ICU admission (see Table 17). A model including 12 factors (QoL at baseline, age, activity of daily living, imaging, APACHE II-score (P=0.001), ≥80 years, mechanical ventilation, hematological patient, SOFA-score, tracheotomy, comorbidity (Charlson - CCI) and surgical admission) could explain 40% of the variability in the quality of life (R^2 0.39) at 1 year after ICU discharge.

Disability

Predictors for disability or global function at 6 months post-ICU (using WHO Disability Assessment Schedule or WHODAS II) were evaluated in an Australian study involving 262 patients who had been ventilated >24h in ICU.[112] The best model included four predictors: history of anxiety/depression, being separated or divorced, duration of mechanical ventilation and not being discharged to home from the acute hospital. It achieved a fair accuracy (AUC 0.71) to predict moderate to severe disability (WHODAS score 25–95%). No further values are provided. Factors that were not associated with disability included age, illness severity, comorbidities and cognitive impairment.

2.2.5 Discussion

Despite a growing awareness of physical, mental health and cognitive impairments following critical illness, there is still no effective system to prospectively identify patients at risk.[118] We also found no study that assessed predictors at GP level. However, seven studies proposed sets of predictors to be used at ICU discharge.

For physical outcomes, a set of 4 predictors (low educational level, inability to sit without support in ICU, fractures in ICU and ICU length of stay >2 days) showed a good accuracy (AUC 0.80) to predict new-onset physical disability at 2 months post-ICU. However, its use would require knowledge about the ICU stay (ability to sit and fractures) that might not be systematically available at GP level. However, it would not add value to the use of a simple and rapid tool for physical screening of ICU survivors proposed in Chapter 3.

For mental health PICS-related outcomes, the set of 6 predictors assessed in an EU multinational study and presented a fair accuracy to predict mental health problems at 3 months, and the existence of an online tool makes it very attractive. Although meant to be used at ICU discharge, it consists in six simple questions that could be asked by the GP, and possibly by phone (Figure 2). It should be noted that it includes two questions of the PHQ-2 tool for depression, which are the same questions as those of the Whooley test proposed in the Chapter 3 and recommended as a screening tool for GPs by the two scientific societies of general medicine.

For cognitive outcomes, no predictive study was identified, but two simple and rapid tools proposed in the Chapter 3 would allow an easy screening at GP level and is.

We found no predictive study for relatives of PCS survivors (PICS-F).

3 CHAPTER 3: DETECTION OF PICS-RELATED DISORDERS IN PRIMARY CARE SETTING

Key-points

- **A set of measurement instruments has been proposed for the detection of PICS-related disorders, and would take <10 minutes to complete:**
  - **Physical function: Timed Up-and Go test and handgrip strength**
  - **Mental health: Whooley questions and GAD-2**
  - **Cognition: Mini-Cog and animal naming**
- **Based on the findings of this rapid screening of the patient, the GP can decide if referral is needed for a more comprehensive assessment or for the appropriate management.**

3.1 Introduction

Main health domains affected by post-intensive care syndrome (PICS) are physical function, mental health and cognition (see Chapter 1).[119] Since these ICU survivors are not or less frequently followed-up by specialised (rehabilitation) or ICU care, the general practitioner is often one of the key care professionals to recognize these impairments. Since there is heterogeneity and lack of consensus about the appropriate and feasible detection tools for PICS, the following research question served as guidance through the analysis of the literature: “What are the clinical tools to identify patients suffering from PICS-related disorders, which ones could be applied in Belgian general practitioner (GP) practices, and what is the validity of these selected tools?”.

This chapter focuses on the (rapid) detection of PICS in primary care settings and in particular by the GP. This detection, which follows a screening approach, should ideally consist of a set of detection tools, which are easily used in GP practice or at patient’s home. This set is not meant for definite clinical diagnosis, but rather to suspect potential underlying impairments and indicate the need for further assessment and management.

We also focus on the specific PICS-related domains as explained in the introduction, i.e. ICU-acquired weakness (ICU-AW) for physical health, anxiety, depression and post-traumatic stress disorder (PTSD) for mental health impairment (in ICU survivors and in families – PICS-F) and cognitive impairments. We did not include broader outcomes such as quality of life (QOL) and participation (activities of daily living (ADL) activities), which could be covered by more extensive assessment after referral, if needed.

The more comprehensive assessments, for example more elaborated test batteries to obtain a definite diagnose or to measure the amount of impairment, are thus considered as out-of-scope for this chapter. These are mainly performed by specialists in secondary care.

Research question: What are the clinical tools to identify patients suffering from PICS-related disorders, what is the validity of these selected tools and which ones could be applied in Belgian GP practices?

3.2 Methods

3.2.1 Literature search strategy

Due to the urgent need for an answer due to the COVID epidemic, the methodological approach of an exploratory review was chosen. This consists of a search for systematic reviews and primary studies in one database (PubMed) with following key terms ‘critical illness’, ‘post-intensive care syndrome’ and ‘patient outcome assessment’ (full search strategy can be found in appendix 1) for the period of 2010 up to 2020. A variety of hand searches via google searches and via reference lists was applied to identify additional sources of information. No critical appraisal of the included studies was performed.

3.2.2 Search results

The search for primary studies revealed 2568 hits of which 89 references were selected based on title and abstract. Within this list of 89 references, only 11 studies could be identified as validation studies, looking at the psychometric characteristics of the clinical tools. The remaining studies were more epidemiological studies in which a tool was used to compare a sample of ICU survivors versus other type of patients, or to describe the evolution over time in a selection of outcomes, measured with the clinical tool. In a first approach to retrieve all potential clinical tools, all clinical tools, mentioned in all 89 references, were listed and grouped per health domain.

Our search strategy could not identify any suitable systematic review. Hand searches via google searches and via references lists revealed some recent (mostly consensus-based) overviews, which were mostly in specific health domains of PICS (e.g. specific overview of clinical tools for depression in ICU survivors). The following references were found: outcome measures in acute respiratory failure survivors (Needham, 2017[120]); outcome measures in ICU survivors (Turnbull, 2016[121]; Robinson, 2017[122]); outcome measures for depression (Rabiee, 2016[54]); outcomes measures for anxiety (Nikayin, 2016[53]); outcome measures for physical health (Major, 2016[123]); outcome measures for PTSD (Parker, 2015[65]).

Additionally, a recent paper was identified in which a German team of ICU experts determined a set of outcome measurements in outpatient care settings (Spies et al, 2020)[119]. The reviews and the paper of Spies et al (2020) were considered as important sources of information to describe the currently existing clinical tools to detect PICS (see below).

3.2.3 Selection criteria for screening tools at GP level

In order to make a selection within the variety of existing tools, a set of predefined selection criteria were set up by the KCE team, mainly based on clinical experience and suitability in clinical practice, to identify the most suitable tools for use in clinical practice by the GP:

- Rapid screening: the tool should only have a short administration time (a few minutes per tool)
- Easy use in clinical practice: the tool should be easy to use, without preceding training of the assessor. No additional material is requested to perform the test, so the GP could easily screen for one or more domains related to PICS, in his clinical practice or even at the patient's home. Also cut-off scores should be available, so that the GP could easily interpret the results and decide if further follow-up (such as more comprehensive assessment or management) is needed.
- Recommended in Belgium (in guidelines or by professional associations) or commonly used in Belgian clinical practice
- Validated tools: ideally the tool should be validated to detect PICS in ICU survivors. This validation is determined by the diagnostic accuracy of a tool, and more in particular the sensitivity and specificity of a tool. In a screening approach, we aim at a high sensitivity (i.e. tool detecting the relevant clinical problem if present, very few false negative results) and the preference was thus given to the tool with the highest sensitivity in the comparison of the different tools assessing the same health domain.
- Open access: this criterion points out the need for open access to the existing tools, free of charge. A restricted access (e.g. due to fees) will be a major barrier in the use in clinical practice.
- Available in national languages: the aim of this report is to provide help to the GP on how to screen for PICS. This selection criterion has been added in line with this aim, i.e. validated tools with a (validated) version in Dutch and/or French will be preferred over others.

A similar selection process was done by a German group of experts to select screening instruments for outpatient care setting in Germany[119] and they used a very similar list of selection criteria:

- time for completion of the set not exceeding 20-30 min in total;
- potentially administrable by a variety of clinical practitioners;
- validated measurement properties in clinical patient populations including adults of all age groups, application in and psychometric data from ICU survivorship research were considered beneficial but not necessary;

- free-of-charge, non-commercial application;
- existence of a validated German version.

3.3 Detection of PICS in primary care setting

Based on our literature search, including search for validation studies, systematic reviews, expert consensus-based papers, and hand searches, a long list of detection tools was set up regardless of the setting in which it was used. Only validation studies were included for further analysis, while all other studies on ICU survivors were examined to determine which clinical tools were used to assess the outcomes of their patient populations. Only for a minority of the cited detection tools, validation studies were found in our search (restricted to the last 10 years). The main restriction of our methodological approach is the lack of a systematic search in different databases. This limitation is mainly solved by a variety of hand searches and consultation of Belgian and international clinical experts.

For mental health (anxiety and depression) 7 detection tools were found, of which only for 2 tools (HADS and PHQ-2) validation studies were found. For the majority of the 7 detection tools found for PTSD, also validation studies were retrieved. Only for half of the 8 detection tools for cognition, some validation studies could be found. Many detection tools were found for physical function, however only 1 validation study was found comparing the Medical Research Council (MRC) criteria to handgrip dynamometry. Per health domain, an overview of all retrieved detection tools and the validation data are presented in Appendix 3.

3.3.1 Selection of detection tools for GP level

A selection was made based on its potential applicability in GP's clinical practice, as defined by the selection criteria (see section 3.2.3) for a rapid screening tool for one (or more) of the domains of PICS. The methodological process behind the selection of the tools can be found in Appendix 3.

Shortly, we started from the set of tools proposed by the Spies et al study, as they thoroughly applied 3 of our 6 criteria (referring to rapidity, open access and validated tools).[119] In addition, they tested these tools among a number of practitioners and patients, in three different rounds, to assess the feasibility, burden, time of completion and acceptability of each of them. We assessed each of the tools selected by Spies for the Belgian context, in particular for the criteria of availability in national languages, open access in Belgium, and its current use in clinical GP practice (e.g. in a guideline). When the decision for specific tools was unclear, we communicated with the German team for clarification and additional information.

As stated above, we do not include the broader dimensions of QOL or ADL. A GP who regularly sees the patient, including in her/his environment, may have a good overview of these dimensions without having to use specific tests. Formal QOL instruments are more useful for research purpose and do not help the GP to decide when and where to refer the patient. The choice to leave out the QoL measurements was confirmed by Belgian experts, mainly due to the fact that more complex and longer questionnaires are less easy to use in a average GP consultation of 15 minutes. However, these dimensions may be assessed by a more comprehensive assessment, at the level of a rehabilitation unit or a post-ICU follow-up.

An overview of the final proposed set of tools is presented in Figure 3 and Table 5 per PICS domain.

Figure 3 – Overview of detection tools per health domain

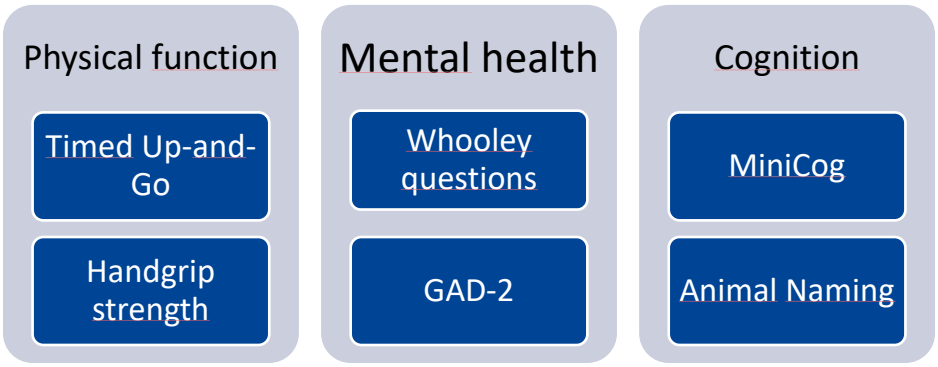


Table 5 – Overview of the selected detection tools per PICS domain

	Timed Up-and Go test (TUG)	Handgrip strength	Whooley Questions	GAD-2	Mini-Cog	Animal Naming*
Aim	Physical function	Physical function	Depression	Anxiety	Cognition	Cognition
Type of tool	The person needs to rise from chair, walk 3 metres, turn around, walk back and sit down.	Maximum squeeze in hand-held dynamometer	2 questions on anhedonia and depressed mood	2 questions on symptoms of genera-lized anxiety disorder	a 3-item recall test and a clock drawing test	naming as many animals as possible in 60s
Administration time	<10s->30s	2min	1min	1 min	3min	1min
Use in Belgian clinical practice	Clinical guidelines on diagnosis of Parkinson[124] + Clinical guideline on fall prevention in elderly at home[125]	Several guidelines mention the assessment of muscle strength, but not specific handgrip strength	Clinical guideline on diagnosis of depression in adults[126] + Clinical guideline on screening and detection of perinatal mental impairments[127]	Clinical guideline on the screening and detection of perinatal mental impairments[127]	Clinical guideline on the diagnosis of dementia in GP practice[128] + cited on the website of the SPF/FOD	Not cited in guideline for GP, but mentioned in test batteries for cognitive function[b]
Validation studies in ICU survivors	Not retrieved in search 2010-2020	Braganca, 2019[129]	Downey, 2016[130]	Not retrieved in search 2010-2020	Ketterer, 2016[131]	Not retrieved in search 2010-2020
Open access**	yes	yes	yes	yes	yes	yes

**: Or any other test known by the GP to assess the verbal fluency; **: Dutch and French versions can be retrieved in the standalone document.*

3.3.2 Physical function

Testing for impairments in the physical health domain could relate to specific physical functions or to more general activities, such as activities of daily living. In the scope of this research, the choice was made to screen for physical impairments by performing simple mobility and strength tests. More comprehensive assessment of the physical function of the patient should be performed by the appropriate care service, e.g. rehabilitation service in hospital, ambulatory physical therapist, occupational therapist, etc. (see Chapter 6 for Belgian care services).

Spies et al proposes the **Timed Up-and-Go test (TUG)** (see Table 6 and Box 1) as the preferential instrument to test mobility in ICU survivors. This test was also considered by (international) expert consensus (including a Belgian expert in physical therapy) as an important instrument to test physical functioning in critical illness survivors[123]. Some Belgian clinical guidelines for primary care also mentioned the TUG as one of the evaluation instruments in Parkinson patients[124], and in fall prevention in elderly at home[125]. Although no recent validation studies about this test could be found in our exploratory literature search, a review on the outcome measurements in ICU survivors found that the TUG is the second most frequently used physical test, next to the 6 minute walk test (which is more useful for research purposes)[121]. Another reason to select this test, is the context independency of the test. This means that the score on the test will not depend on the context in which the test is performed, for example for the 6min walk test more space is needed and the walking abilities could be affected by the underground or the restricted space. The time required to perform

[b] https://www.arteveldehogeschool.be/kronkels/wp-content/uploads/2017/06/140403_Bijlage-7-Vlaamse-ACE-R_Handleiding.pdf; https://vvkp.be/teleneuropsychologie#Geheugen

the TUG test gives an objective measurement of the mobility of the person, and even more specifically on the risk of fall. Several cut-off scores were found, depending on the gender and the age of the person. The consulted Belgian experts reported that most GPs may not use a timer to score the test but will rather informally observe the way the patient is getting up from the chair, and walks to the examination table. Although this pragmatic consideration is important to consider, we would like to highlight that this clinical observation without the use of clear cut-off scores will not help to inform the GP when to refer the patient for a more comprehensive assessment.

Box 1 – Timed-Up-and-Go Test: English version

TIMED UP-AND-GO TEST (TUG)

- Material
  - A 44 to 47 cm high chair placed against a wall to stabilize it.
  - A line drawn on the ground at a distance of 3 meters from the chair in a place without obstacles.
  - A timer
- Instruction
  - Start the timer as soon as the start signal is given and stop it as soon as the patient is seated with his/her back against the chair back
  - Intruction for the patient 'When I say 'Go', you have to get up, walk at a comfortable speed until the ground mark. You will then have to turn around and come back to sit on the chair with your back resting on the chair back. 3-2-1 Go'
- Scoring[132] : A test is positive when :
  - Age ≤60y: >9 sec
  - Age 61-79y: >14s
  - Age ≥80y: >19 sec

  Higher scores indicate higher impairment

The TUG test was developed by Podsiadlo, D. et Richardson, S. (1991). The Timed "Up & Go": A test of basic functional mobility for frail elderly persons. Journal of the American Geriatric Society, 39 (2), 142-148. It is free to use.

Table 6 – Characteristics of the TUG

Instrument	Timed Up-and-Go Test (TUG)
Aim	Detection of physical function in the domain of mobility
Type of tool	Performance test: person is sitting on a chair with armrests, with the back on the backrest. The person stands up, walks 3m in a straight line, turns around, walks back to the chair again, and sits down with the back at the backrest
Scoring system	The time to complete in seconds
Administration time	<10-≥30sec
Use in Belgian practice	Clinical guideline on Parkinson[124] Clinical guideline on fall prevention in elderly at home[125]
Validation studies	Original validation study[133] No validation studies were retrieved in the search 2010-2020.

To assess the muscle function (and more in particular the muscle strength), Spies et al[119] selected the **handgrip strength** for the screening of muscle strength. We found a statement of a group of US clinical experts[123] who also agreed on the importance of using **handgrip strength** and handheld dynamometry (see Table 7 and **Error! Not a valid bookmark self-reference.**). One validation study was found on handgrip strength to assess ICU-AW in ICU survivors,[129] and the authors stated that handgrip dynamometry is easier and quicker to perform when compared to MRC examination and the use of the diagnostic tool may save time and increase ICU-AW recognition. One question is however whether the Belgian GPs have hand-held dynamometer at their disposal at practice level

or for home visits. According to the consulted Belgian experts, handheld dynamometry is not yet fully implemented in clinical practice. In case of suspicion of ICU acquired muscle weakness and if the GP is not able to perform muscle strength testing, the patient should be referred for a more comprehensive assessment in for example a rehabilitation service, or an ambulatory physical therapist practice.

Box 2 – Handgrip Strength Test: English version

HANDGRIP STRENGTH TEST

- Material
  - Hand-held dynamometer
- Instruction
  - The patient should be standing with the arm outstretched or sitting with the arm at a 90 ° angle (please refer to the instructions for your device)
- Scoring
  - The norm values of the test vary according the age and the gender of the patient (please refer to the instructions for your device).
  - The test is positive when:
    - ♂ : Age ≤60 : <25kg ; 61-79y :<23kg ; ≥80 :<19kg
    - ♀ : Age ≤60 : <15kg ; 61-79y :<14kg ; ≥80 :<13kg

  Lower scores indicate higher impairment.

Table 7 – Characteristics of Handgrip Strength Test

Instrument	Handgrip Strength Test
Aim	Detection of physical function in the domain of muscle strength
Type of tool	Performance test: person is sitting on a chair, the arm of the dominant hand at right angles. Person holds hand dynamometer in a vertical position and squeezes it with maximum strength without changing position of arm and hand; three trials; can also be performed while lying in bed
Scoring system	The muscle strength, measured in kg
Administration time	1min
Use in Belgian practice	Several guidelines mention the assessment of muscle strength, but not specific handgrip strength
Validation studies	Original validation study[134], and Braganca, 2019[129]

3.3.3 Mental health domain

3.3.3.1 Depression

To screen for depression, Spies et al (2020)[119] selected the PHQ-2, which has been validated in relatives of ICU survivors.[130] The Belgian guidelines[126, 127] recommend rather the use of the Whooley questions for the detection of depression in adults, which are similar to the PHQ-2 questions but use a different time frame and scoring system. These questions are also available in national languages in the GP guidelines[126]. Therefore, we propose the Whooley questions as rapid screening tool to detect **depression** in ICU survivors (see Box 3).

Box 3 – Whooley Questions: English version

Whooley Questions	Yes	No
1. During the past month, have you often been bothered by feeling down, depressed or hopeless?	0	1
2. During the past month, have you often been bothered by little interest or pleasure in doing thing?	0	1
Scoring: "Yes" to one (or both) questions = positive test (and requires further evaluation); "No" to both questions= negative test (not depressed)		

Copyrights © K. Kroenke, 2007, all rights reserved. This test is free to use for clinical practice. For research information, contact Dr. Kroenke at kkroenke@regenstrief.org . Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med. 2007;146:317-25

Table 8 – Characteristics of the Whooley Questions

Instrument	Whooley questions
Aim	Detection of depression
Type of tool	questionnaire, consisting of 2 questions (first 2 items of the PHQ-9 on anhedonia and depressed mood)
Scoring system	Yes/no answers
Administration time	1 min
Use in Belgian practice	Clinical guideline on depression in adults[126] Clinical guideline on the screening and detection of perinatal mental impairments[127]
Validation studies	Original validation study,[135] Downey, 2016[130]

More information about the administration of the test can be found in Table 8. According to the Belgian experts, GPs do not often use structured questionnaires to assess mental health impairments. But we suggest that this very short screening questionnaire (2 questions) may be effective to help the GP to decide if further referral is needed for a more comprehensive assessment of a potential depression.

3.3.3.2 Anxiety

For the detection of **anxiety**, Spies et al selected the second part of the PHQ-4, which is also called the Generalized Anxiety Disorder 2-item (GAD-2, see Box 1Box 4).[119] This tool is also recommended in the Belgian guideline on the screening and detection of perinatal mental impairments, and is also available in the two national languages. The structure of the questionnaire is very similar to the Whooley questions/PHQ-2 with two questions screening for a generalized anxiety disorder. The Belgian experts confirmed that the GAD-2 is not yet well known in clinical practice, however its similarity to the well-known Whooley Questions, will facilitate its use for the screening for anxiety. More information about the administration of the test can be found in Table 9.

Box 4 – GAD-2: English version

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on the edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
Scoring: A total score of ≥3 is considered positive for screening of anxiety				

Copyrights © K. Kroenke, 2007, all rights reserved. This test is free to use for clinical practice. For research information, contact Dr. Kroenke at kkroenke@regenstrief.org . Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med. 2007;146:317-25

Table 9 – Characteristics of GAD-2

Instrument	GAD-2
Aim	Detection of anxiety
Type of tool	Questionnaire, consisting of 2 questions (2 items of the GAD-7)
Scoring system	4 point Likert scale (0=not at all; 1=several days; 2= more than half of the days; 3= nearly every day); score between 0 and 6
Administration time	1 min
Use in Belgian practice	Clinical guideline on the screening and detection of perinatal mental impairments[127]
Validation studies	Original validation study[136] No validation studies in ICU survivors were retrieved in search for 2010-2020.

3.3.3.3 PTSD

Spies et al[119] did not propose a specific screening test for PTSD. The first reason was to avoid additional burden on the GP, as existing tools such as the Impact of Event Scale (IES), PTSS-10, PTSD Checklist (PCL), Clinician Administered PTSD Scale (CAPS) and the Symptom Checklist-90-R (SCL-90-R) (see Appendix 3) take more than a few minutes to complete, and the IES was discarded in their feasibility study due to the difficulty to understand by both the patient and the health care professional. The second reason is that the PHQ-4 was considered as sufficiently sensitive to detect PTSD according to the literature. Indeed, the systematic review of Kroenke et al, 2010[137] showed that the GAD-2 has a good sensitivity and specificity to detect PTSD. A prevalence study found that the majority of the patients who scored positive on the GAD-7 (i.e. having one or more of the anxiety disorders), were diagnosed with a PTSD.[136] Also each anxiety disorder (including PTSD) had moderate levels of depressive symptom burden, indicating a relationship with non-anxiety psychiatric disorders. Another study confirmed that the majority of ICU survivors who suffered from PTSD (94%), had symptoms of anxiety or depression or both.[77] Based on these findings, we presumed that patients with a PTSD will probably score positively on the depression and/or the anxiety scale.

However, as PTSD itself is not easy to detect, interested GP could use a brief instrument to directly detect PTSD. In Spies et al[119], a more comprehensive assessment is proposed in patients reporting new or worsened health problems and showing relevant impairment in at least one the screening tests and includes the further detection of PTSD with IES-R. Our literature search indicates that the IES-6 is a very brief tool (3-5 minutes), has been validated in ICU survivors,[138] and has been advised for that purpose by other authors (see Appendix 3).[6]

3.3.3.4 PICS-F

Spies et al did not include the screening for mental health impairments among family members of ICU survivors (PICS-F), to avoid additional burden on the GP, and opted to include family members in a more comprehensive assessment (personal communication H Kampe). The analysis of the literature could not give a full answer on which tools should be applied for that purpose. Since all clinical tools for the detection of mental impairments were originally developed for other patient populations, but also showed validity for the use in ICU survivors, it was assumed that these tools could also be useful in the detection of mental impairments in the family members of ICU survivors. This was confirmed by a study, found in our exploratory search, that showed that the 2-item version of the PHQ (depression) was the most reflective model of depression severity (compared to the 9- and 8-item versions). German experts suggested to use the same screening tools in family members as in the ICU survivors, (i.e. Whooley Questions for depression and GAD-2 for anxiety, personal communication H Kampe).

3.3.4 Cognitive disorders

To screen for cognitive disorders, Spies et al (2020) selected the Mini-Cog, as well as the animal naming to assess the verbal fluency. In our exploratory literature search a variety of instruments were

reported in the primary studies in ICU survivors, however only for three instruments some validation studies could be found in ICU survivors (Mini-Cog, MMSE and CFQ) (see Appendix 3).

The **Mini-Cog** test (see Table 10 and Box 5) is already commonly used in Belgian practice. A recent Belgian guideline on the diagnosis of dementia in the GP practice (2020)[128] recommends, based on the better psychometric performance, the use of the Mini-Cog (or two other tests)[c] as a cognitive test instead of the more common used mini mental state examination (MMSE). In addition, the Dutch and French versions are available via the website of the Belgian Federal Ministry of Public Health (https://www.health.belgium.be/nl/mini-cog). According to the Belgian experts, the MMSE is more known in clinical practice. However, the Mini-Cog was preferred for a short screening tool for PICS-related cognitive impairment, due to its easy use and its shorter administration time, and its recommended use in Belgium for similar purposes, compared to the longer questionnaire of the MMSE. However, both tools are useful and validated to assess the cognitive status of the patient.

Box 5 – Mini-Cog: English version

Step 1: Three word registration

Look directly at person and say, "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember. The words are [select a list of words from the versions below]. Please say them for me now."

Version 1: Banana Sunrise Chair

Version 2: Leader Season Table

Version 3: Village Kitchen Baby

Version 4: River Nation Finger

Version 5: Captain Garden Picture

Version 6: Daughter Heaven Mountain

Scoring: No scoring in this step. If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing).

Step 2: Clock Drawing

Say "Next, I want you to draw a clock for me. First, put in all of the numbers where they go." When that is completed, say: "Now, set the hands to 10 past 11." Repeat instructions as needed as this is not a memory test.

Scoring: Normal clock = 2 points. A normal clock has all numbers placed in the correct sequence and approximately correct position (e.g., 12, 3, 6 and 9 are in anchor positions) with no missing or duplicate numbers. Hands are pointing to the 11 and 2 (11:10). Hand length is not scored. Inability or refusal to draw a clock (abnormal) = 0 points.

Step 3: Three Word Recall

Ask the person to recall the three words you stated in Step 1. Say: "What were the three words I asked you to remember?"

Scoring: 1 point for each word spontaneously recalled without cueing

Total score: word recall score (0-3 points) + clock draw score (0 or 2 points)

<3 points has been considered as a positive screen and may indicate a need for further evaluation of cognitive status

Permission to use in clinical practice given by https://mini-cog.com/permission/

Table 10 – Characteristics of the Mini-Cog

Instrument	Mini-Cog
Aim	Detection of cognitive impairments in the subdomains of memory, visuospatial and visuoconstructional skills
Type of tool	Performance test consisting of a 3-item recall test (the patient should listen to and remember 3 unrelated words and then to repeat the

[c] Together with GPCOG (General Practitioner Assessment of Cognition), MIS (Memory Impairment Screen)

	words) and a clock drawing test (the patient is instructed to draw the face of a clock and to draw the hands of the clock to read a specific time). After the CFT the patient is asked to repeat the 3 previously presented words.
Scoring system	Total score (0-5 points): word recall score + clock draw score
Administration time	The patient can take as much time as necessary to complete
Use in Belgian practice	Clinical guideline on the diagnosis of dementia in the GP practice (2020)[128]
Validation studies	Original validation study[139] Ketterer, 2016[131]

Spies et al (2020)[119] added the **Animal Naming** test (i.e. naming as many animals as possible in 60s, with a cut-off score of 14) to assess the verbal fluency of the ICU survivor. This test (see Box 6 and Table 11) could however not be retrieved in the Belgian guidelines for primary care. However, the review of Wolters et al (2013)[80] stated that verbal fluency as one of the most frequently impaired cognitive functions, and we thus propose the use of animal naming – or any equivalent test - in the screening tool for GPs. The Belgian experts confirmed that verbal fluency testing is not common in GP's clinical practice, however the short test could easily be performed during the consultation.

Box 6 – Animal Naming: English version

Animal Naming
Ask to your patient to name as many animals as possible in 60s **Score**: <14 animals, indicative for impairment in verbal fluency

Table 11 – Characteristics of Animal Naming

Instrument	Animal Naming
Aim	Detection of cognitive impairments in the subdomains of verbal fluency
Type of tool	Performance test consisting of naming as many animals as possible in 60s
Scoring system	1 point per named animal
Administration time	1min
Cut-off points	Positive score: < 14 named animals
Use in Belgian practice	Not cited in Belgian guidelines for primary care, however mentioned in test batteries for cognitive functions
Validation studies	Original validation study[140] No studies were found in ICU survivors, except for the feasibility paper of Spies et al (2020)[119]

3.4 Applicability in Belgian clinical practice

This chapter aims to suggest a set of detection tools which could help the GP to recognize signs and symptoms of PICS-related disorders, and which could serve as a decision-aid if referral for other care services is needed for more comprehensive assessment or management. The current offer and organisation of care services in Belgium is described in Chapter 5.

Within the limitations of the pre-defined selection criteria, a preference was given to a set of tools, easy to use in clinical practice, with a short administration time, validated in ICU survivors and that are preferably already implemented in Belgian practice (including the access to a French and Dutch version of each tool). The preference for already implemented clinical tools implied also that no training was considered as necessary before this set of screening tools could be used in GP practice. This additional time (for training) was considered as a major barrier given the increasing number of COVID-19 patients at risk for PICS. Another barrier could be the additional time needed by the GP to administer the different tests. Therefore a preference was given to instruments with less than 5

min of administration time for each. Also the set of tools aimed not to require additional material; the sole exception of this selection criterion was the use of a handgrip dynamometer for the measurement of handgrip strength. However, it was considered that the purchase of this dynamometer is of very reasonable price, and could also serve for other types of patients, e.g. elder persons.

The Belgian experts agreed with the need for a short and easy to use screening tool for the detection of PICS-related disorders. For the fluency of the consultation, the GPs would prefer to have access to the screening tool via the medical file of the patient instead of searching for the tool on a separate website. Reporting the scores in the medical file will also facilitate further follow-up of the patient. Another more important information for the medical file are the consequences and the clinical interpretation of the tests, Another option, mentioned by the Belgian experts, to encourage the use of the screening tool, is to have the patient fill in the questionnaires at home. This is, however, only partly possible, because the tests for physical and mental domains, are performance tests, rather than questionnaires.

During the development of this set of detection tools, comparable research projects were searched for in literature. The set of outcome measures in ICU survivors, developed by the German team of clinical experts (Spies et al, 2010) was the only published research project found. Other papers focused more on outcome measures for research purposes, which is different from the aim of this chapter to determine a set of detection tools for clinical practice.[120, 141]

One of the limitations of this set of detection tools is the collection of single tests, with no overall score on all PICS domains (physical function, mental health, cognition). In a recent paper of Wang et al (2019)[142], the authors aimed to validate a comprehensive tool (the Healthy Aging Brain Care Monitor Self Report version (HABC-M SR) for ICU survivors, however the 27-item self-administered tool demonstrated low correlation with the cognitive performance measures, suggesting that the cognitive subscale may have limited validity. In this chapter it was decided not to take into account this comprehensive tool, due to its restricted validity for all subdomains and the lack of similar studies using the HABC-M SR in clinical practice. The methodological process of selection of the detection tools and other detection tools found in literature can be retrieved in Appendix 3.

4 CHAPTER 4: EFFECTIVENESS OF INTERVENTIONS: REVIEW OF EVIDENCE

4.1 Introduction

As shown in chapter 1, PICS and PICS-F are common in patients who experienced a stay in ICU and can last for months or even years.[1]

This chapter presents the evidence on the effectiveness of interventions aiming to improve the PICS-related outcomes, assessed at 3 months after ICU discharge or later.

4.2 Method

4.2.1 Literature search

Electronic searches

We searched PubMed from 2010 to May 2020. Languages were restricted to English, French, Dutch and Spanish. Editorial, Letter and Case Reports were excluded from the electronic search.

Detailed search strategies are provided in Appendix 1.

Searching other resources

All reference lists of all retrieved and relevant publications identified by the electronic search were hand searched. Belgian experts in the field were contacted for additional relevant publications.

4.2.2 Selection criteria

Types of studies

We included all systematic reviews, RCT, quasi-randomized studies, and observational studies (prospective cohort and before and after design) that evaluated the effectiveness of interventions

Types of participants

We included all adult patients who were discharged from an ICU and their family members whatever the underlying conditions. The studies focused on a specific groups of patients such as cancer, stroke and traumatic brain injuries are excluded. Studies were included irrespective of patient critical illness severity and country.

Types of interventions

All interventions after ICU discharge targeting ICU survivors and their families after the ICU stay were considered, including those that started at the ICU or hospital ward.

Types of outcome measures

Outcomes are focused on patients recovering from an ICU stay and their family members. They have to be measured by validated tools at 3 months post-ICU discharge or later. The primary outcomes are ICU acquired weakness (ICU-AW), post-traumatic stress disorder (PTSD), anxiety, depression, cognitive function and health-related quality of life (HRQoL). The secondary outcomes are ability to return to work and patient's care satisfaction.

4.2.3 Data collection and analysis

Selection of studies

From the initial electronic search, we excluded duplicate records. Two review authors (NB and GH) assessed titles and abstracts of retrieved studies for relevance. After this first selection, full versions of all potentially eligible studies were retrieved. One author (NB) checked the full papers for eligibility. In case of doubt, two authors (GB, AD) checked the proper application of inclusion and exclusion criteria. Discrepancies were discussed by mutual discussion.

Assessment of the evidence quality

Due to the rapid process of this study, the systematic reviews were used as sources of quality appraisal for the RCT that are included, when the Cochrane Collaboration's Risk of Bias Tool for RCT was used. [143]

Additional RCT were appraised by NB. The overall risk of bias is determined by the least favourable assessment across the domains of bias.[143]

The quality of observational studies was assessed by Barreto et al[144] using ROBIN-1.

Data synthesis and summary of findings

We have conducted a structured narrative summary of the reviewed studies based on a preformatted template. No meta-analysis were performed because of the heterogeneity in study populations, study design, interventions, timing of outcome assessment and tools used to assess outcomes.

In this chapter, the term 'significant' means 'statistically significant' and the term 'clinically important difference' is used when the treatment effect reached the Minimal clinically important differences (MCID). The MCID is 'the smallest difference in score in the domain of interest which *patients* perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's *management'*.[145] The terms 'PTSS' and 'PTSD' are used according the definitions reported in the Chapter 1. In the result reporting, we used the outcome term used by the authors of the primary study.

Box 7 – MCID used in this report for tools assessing health related quality of life, physical and mental health

Scale	MCID	Legend
Physical Health		*6MWT: Six-Minute Walk Test, ISWT: Incremental Shuttle Walk Test, TUG: Timed Up and Go test, HADS-D: Hospital Anxiety and Depression Scale-Depression, HADS-A: Hospital Anxiety and Depression Scale – Anxiety, GAD-7: General Anxiety Disorder 7-item scale, PTSD: Posttraumatic Stress Disorder, IES-R: Impact of Event Scale-Revised, PTSS-14: Posttraumatic Stress Disorder Symptoms-14 items, SF-36 PF: 36-Item Short Form Survey - Physical functioning score, SF-36 PCS: 36-Item Short Form Survey - Physical component score, SF-36 MCS: 36-Item Short Form Survey - Mental component score*
6MWT[146]	35 m	
ISWT[147]	47.5 to 78 m	
TUG[146]	9.5 sec	
Mental health		
• Depression		
HADS-D[148]	2.5 points	
• Anxiety		
HADS-A[148]	2.5 points	
GAD-7[149]	4 points	
• PTSD		
IES-R[148]	0.2 points	
PTSS-14.[150]	4 points	
• Cognition		
Montreal Cognitive Assessment[151]	2 points	
HRQoL		
SF-36 PF[152]	3 points	
SF-36 PCS[153]	5 points	
SF-36 MCS[153]	5 points	

4.3 Results

4.3.1 Search results

Our literature search identified 24 systematic reviews. Three additional reviews were found by hand searching the reference list of relevant publications.[154-156] Among those, 7 were excluded because they did not meet our inclusion criteria[99, 157-163] and one was a summary of a Cochrane review.[164]

All these reviews were used as sources of primary studies and are not extensively described. Only meta-analyses are discussed in section 4.4. The retrieved reviews cover several interventions such as exercise and physical rehabilitation [54, 65, 154, 165-169], follow-up services[54, 65, 156, 165, 166, 170, 171], diaries[54, 144, 165, 166, 172-175], peer support group[176] and psychosocial programme.[165] A last review dealt with PICS-F.[177] Details regarding each intervention are provided in the section results.

4.3.2 Description of included studies

The retrieved interventions were exercises and physical rehabilitation programs, follow-up consultations, mental health interventions, cognitive interventions, and peer support groups (see

Table 12). We found only one study dedicated to relatives of deceased ICU patients[178] and 7 studies assessing the effect of interventions for ICU survivors on relatives' outcomes.[150, 179-184] The table below gives a rapid overview of the included studies. More details can be found in evidence tables in the appendix. Overall, large variations were observed across studies in the interventions (content and duration) and in the outcome assessment (timing and method).

The overall quality of the retrieved evidence is very low or unclear, mainly because of methodological issues including very low sample size. Details on the quality assessment of included studies is reported in appendix

4.3.3 Exercises and physical rehabilitation

Physical rehabilitation was studied in 11 publications[146, 152, 185-193]. Among those, 6 papers reported physical rehabilitation combined with follow-up consultations[188, 192], with education session[187, 193], with nutritional supplement[191] or with a combined cognitive and functional intervention.[190] Except one non-randomized control trial[185], all papers were monocentric [146, 186, 187, 190, 193] or multicentric[152, 188, 189, 191, 192] RCTs occurred mainly in UK[152, 186-188, 191-193] but also in Australia[146, 189] and USA.[190] Except for one trial[190], the duration of studies ranged from 2 to 4 years. All publications reported a low sample size leading to underpowered size to demonstrate statistical significant intervention effectiveness. The number of recruited patients ranged from 20 to 286 adult patients defined as > or ≥ 18y except in 2 studies including only patients ≥ 45y[191] or patients from 18 to 65y.[185] Some authors restricted the inclusion of patients based on the reason of admission or underlying condition, the ICU length of stay,[146, 186, 189, 191, 192] the duration of mechanical ventilation[146, 152, 185, 187, 189, 192, 193] or the distance between patient's residence and hospital.[146, 186, 189] The reported interventions started at the earliest at ICU admission up to 12–16 weeks post-hospital discharge at the latest. They included self-directed exercises,[188, 192] supervised exercises[146, 187, 189] or both.[152, 185, 186, 190, 191, 193]

Table 12 – Overview of included studies – Exercises and physical rehabilitation

Study ID	Design	Patients	Country	Start of intervention	Intervention	Control	Max. follow-up	Tools for outcome assessment
Exercises and physical rehabilitation alone								
Batterham 2014[185]	Non randomized controlled trial	59 patients 18-65y Ventilation ≥ 3 days Trauma or sepsis	UK	8-16 weeks after discharge	Supervised and self-directed exercise sessions during 8 weeks	Usual follow-up care by physicians but no formal rehabilitation programme	26 weeks	AT, SF-36, EQ-5D, Peak VO_2, HADS
Battle 2009[186]	RCT	60 patients ≥18y Burns or cardiac conditions	UK	12 weeks post-hospital discharge	Supervised exercise programme during 6 weeks	No intervention	12 months	6MWT, HADS, BERG Balance Score, GRIP
Denehy 2013[146]	RCT	150 adult patients ICU LOS ≥5 days	Australia	At ICU, at ward and after hospital discharge	Cardiovascular, progressive resistance strength training and functional exercise until 8 weeks post-hospital discharge	No outpatient exercise classes	12 months	6MWT, TUG, SF-36, AQoL utility
Elliott 2011[189]	RCT	195 patients ≥ 18 years ICU LOS ≥48 h Ventilation ≥24h	Australia	1 week post-discharge	Supervised and self-directed exercise sessions during 8 weeks	Usual community-based care after hospital discharge and the three study assessment visits	26 weeks	SF-36, 6MWT
McDowell 2017[152]	RCT	60 patients ≥18y ventilation >96h	UK	48.9 days post discharge on average (SD)	Standard care + 2 supervised and 1 unsupervised exercise sessions per week during 6 weeks to 11 weeks if not complete adherence + weekly call to monitor treatment	Standard care	6 months	SF-36 PF, VAS for functional limitations, ISWT, Chronic disease self-efficacy scale
Physical rehabilitation combined with other interventions								
Physical rehabilitation combined with follow-up consultations								
Cuthberts on 2009[188]	RCT	286 patients >18y Level 3 ICU unit	UK	3 months after discharge	Self-directed physical rehabilitation programme during 3 months + 2 follow-up consultations (at 3 and 9 months post discharge) with a nurse to discuss ICU experiences	No ICU follow-up	12 months	SF-36, Davidson trauma score, HADS, return to work

					and assess progress, psychological morbidity and requirement for referral			
Jones 2003[192]	RCT	126 patients ICU ≥48h Ventilated patients	UK	8 weeks after discharge to home	Routine ICU Follow-Up (i.e. 3 telephone calls + ICU follow-up clinic visit at 8 weeks and 6 months) + rehabilitation manual (educational material on psychological, psychosocial, and physical problems and a self-directed exercise programme) + 3 weekly monitoring telephone calls during 6 weeks	Routine ICU Follow-Up (i.e. 3 telephone calls + ICU follow-up clinic visit at 8 weeks and 6 months)	6 months	SF-36 physical function score, HADS, Norbeck Social Support Questionnaire, IES
Physical rehabilitation combined with educational sessions								
Connolly 2015[187]	RCT	20 patients ≥ 18y ICU-AW diagnosis Ventilation ≥48h	UK	2 weeks post-hospital discharge	16 supervised exercise sessions + education sessions covering breathlessness management, benefits of exercise, and nutrition during 3 months	Weekly telephone call to monitor general progress of recovery without specific advice on exercise rehabilitation	3 months	ISWT, 6MWT, SF-36, HADS
McWilliams 2016[193]	RCT	73 patients > 18y Ventilation ≥5 days	UK	6 weeks post discharge	supervised and self-directed exercise sessions and education sessions during 7 weeks including education on exercise, relaxation techniques, managing breathlessness, smoking cessation, anxiety management and a group discussion forum	No intervention	14-16 weeks	Peak VO_2, AT, SF-36
Physical rehabilitation combined with nutrition								
Jones 2015[191]	RCT	93 patients ≥ 45 years	UK	at ICU discharge	Supervised physiotherapy	Placebo nutritional	3 months	6MWT, HADS

		Pre ICU + ICU LOS ≥ 5 days			sessions + unsupervised exercise program (PEPSE) + nutritional supplement	supplement or placebo nutritional supplement + PEPSE or nutritional supplement		
Physical rehabilitation combined with cognitive intervention								
Jackson 2012[190]	RCT	20 patients >18y medical or surgical intensive care	UK	At post-hospital discharge	Cognitive, physical, functional rehabilitation during 12 weeks at patient's home	Physical and occupational therapy, and nursing care, to in-patient, out-patient, or home-health settings	3 months	TOWER, DEX, MMSE, TUG, ABC, Katz

4.3.3.1 Exercises and physical rehabilitation alone

We found 5 primary studies analysing the effect of exercises and physical rehabilitation without any additional intervention.[146, 152, 185, 186, 189] Among these latter, two proposed supervised exercises[146, 189] with the other mixed supervised and unsupervised exercises at home.[152, 185, 186] Two studies[152, 186] proposed a 6-week programme and the other studies proposed an 8-week programme.[146, 185, 189] The programmes started during the ICU stay [146] or early after the hospital discharge (≤ 1 week)[189] or later at 12 weeks after hospital discharge[186] and the programme of 1 study started at 8 to 16 weeks.[185] Three trials included less than 100 patients[152, 185, 186] while 150 patients were included in the fourth study[146] and 195 patients in the last one.[189]

Reported outcomes are related to physical health, mental health and health related quality of life.

Physical health

Six-Minute Walk Test (6MWT) is used to evaluate cardiopulmonary and musculoskeletal performance during exercise. The minimum clinically important difference (MCID) for 6MWT has been defined as 35 m walked.[146] This test was performed in 3 RCTs.[146, 186, 189] At different time points ranging from 3 to 12 months, no significant difference was observed between control and intervention groups. However, one study found a clinically important advantage in the distance walked in 6 minutes in patients receiving a combination of supervised and unsupervised exercises in comparison with those receiving no exercise but this difference was not statistically significant (*Mean difference after 12 months (95%CI), p-value (negative values are in favour of intervention group): -49.94 meters (-223.7–123.63), p=0.373)*.[186] In another study[146], patients benefiting from a supervised exercise programme showed a significant larger and clinically important progression than those who did not benefit from it *(mean difference in progression at 3 months 63.67m (14.17 to 113.18), p < 0.05, mean difference in progression at 12 months 72.55 (9.29 to 135.81) p < 0.05)*.

Ambulation ability is assessed in 1 study[146] by the Timed Up and Go (TUG) test. The TUG Test consists in stand up from a chair, walk 10 feet, return to the chair, and sit down. The score refers to time in seconds and higher scores reflect worse performance.[190] A clinically important difference was defined as a MCID of 9.5 seconds.[146] The study[146] found no statistically significant nor clinically important differences between the control and intervention groups after 3 and 12 months (*the difference in mean change in TUG test score from first assessment during recruitment to 3 months between intervention group and control group (95% IC) was −8.31 sec (−24.90 to 8.28) and from first assessment to 12 months was −9.57 sec (−27.42 to 8.28)*. Subgroup analyses were performed according to the duration of ventilation, medical condition or surgical condition.[146] These analyses did not show any change TUG outcomes (results not shown).[146]

The incremental shuttle walk test (ISWT) was used in a publication to assess the exercise capacity.[152] During the test, the patient is required to walk around two cones at faster rhythm each minute. A higher distance indicates a better exercise capacity. The MCID ranges from 47.5m (slightly better improvement) to 78 m (better improvement).[147] The study assessed the exercise capacity at 6 months and found no significant and clinical important difference between intervention and control groups. However, this trial showed an increase in ISWT score across time in both control and intervention groups but this increase was not significant different between groups *(data reported in graph)*.[152]

Balance is studied in 1 publication using BERG Balance Test.[186] Higher scores reflect a better balance. This study found a significant difference between intervention and control group at 12 months but not at 6 months *(mean difference in score between groups at 6 months (95%CI): 2.2 (not reported because not plausible), p=0.442 – 12 months: 7.0 (not reported because not plausible), p=0.040)*.[186] This results must be interpreted with caution because of not plausible 95%CI reporting.

Grip strength of left and right hand, assessed by Jamar Dynamometer, was not improved by exercise programme in one publication (details results are reported in the evidence table in appendix).[186]

Self-efficacy to exercise was assessed in 1 study[152] by the 10-point chronic disease self-efficacy scale. The authors reported no statistically significant improvement by personalised exercise programme in comparison with standard care *(results presented in graph, raw data not shown)*.[152]

The self-reported readiness to exercise was assessed in 1 study[152] by a questionnaire that classify patients as participating in no physical activity (stage pre-contemplation and stage contemplation) and participating in occasional or regular physical activity (stage preparation, action, and maintenance). From baseline to 6 months, self-reported readiness to exercise was increased in a significant larger extent in the intervention group compared with the control group *(results reported in graph, p=0.012)*.[152]

Mental health

Depression and anxiety are assessed in 2 trials [185, 186] using the Hospital Anxiety and Depression scale (HADS) and, more specially the specific sub-scales for depression (HADS-D scale) and anxiety (HADS-A scale). Higher scores reflects more severe symptomatology. Both studies found no statistically significant difference nor clinically important difference between intervention and control groups in depression at 6 months and 12 months. For anxiety, both studies also found no statistically significant difference in HADS-A score at 6 months but one study[186] found a statistically significant and clinically important difference at 12 months in favour of the intervention group *(mean difference (95%CI): -4.1 (1.23–5.24), p=0.006)*. The MCID in HADS sub-scale is 2.5 points.[148]

Health related quality of life

Health related quality of life (HRQoL) was assessed in 4 publications[146, 152, 185, 189] using functional limitations profile and the SF-36 subscales. While functional limitations profile assessed the physical and the psychosocial dimensions in an overall score ranging from 0 to 100 (a lower score indicated a better self-reported HRQoL), the SF-36 subscales assessed the physical function dimension (SF-36 PF) and global dimensions such as the physical component summary score (SF-36 PCS) and the mental component summary score (SF-36 MCS). In the SF-36 subscales, a higher score represents better self-reported HRQoL.

Functional limitations profile was not significantly improved by personalised exercise programme in one study (results presented in graph, raw data not shown).[152]

Physical function assessed by SF-36 PF was not significantly different in patients receiving exercises in comparison with those receiving no exercise at 6 months. [152,185, 189] A study[146] found a significant advantage at 3 months post-hospital discharge in favour of patients receiving personalised exercise programme in addition to the standard care but this advantage did not remain significant after 12 months post-discharge (*difference in mean change from first assessment at recruitment in SF-36 PF score between Intervention group and Control group (95% IC) at 3 months 6.8 (1.2 to 12.5) and at 12 months 3.5 (−3.5 to 10.5))*.[146] However, the MCID[152] was reached at 3 months in two studies[146, 152] and at 12 months in one study.[146]

Physical component summary score (SF-36 PCS) was assessed in 2 papers[146, 189] and no significant difference after 3 months[146], 26 weeks[189] or 12 months[146] was found between patients receiving exercises than those who did not *(difference in mean change of SF-36 PCS between Intervention group and Control group (95% IC) from recruitment to 3 months: 5.6 (0.09 to 11.1) and from recruitment to 12 months: 3.1 (-3.2 to 9.5)[146] / difference in SF-36 PCS between groups at 26 weeks (95% CI): 0.3 (-3.2, 3.7) points[189]).* The MCID[153] was reached at 3 months in one publication.[146]

Mental component summary score (SF-36 MCS) was assessed in 3 publications[146, 185, 189] and no significant difference after 3 months[146], 26 weeks[185, 189] or 12 months[146] was found between patients receiving exercises compared to those who did not *(difference in mean change of SF-36 MCS between Intervention group and Control group (95% IC) from recruitment to 3 months: 2.4 (-3.6 to 8.5) and from recruitment to 12 months: 4.9 (-2.7 to 12.5)[146] / difference in SF-36 MCS between*

groups at 26 weeks (95% CI): 1.5 (-3.1 to 6.2) points[189] and 4.4 (-2.4 to 11.2) points[185]). None of the studies reached the MCID.[153]

The finding was confirmed by using EQ5D scale in one publication[185] and by Assessment of Quality of Life Measure utility (AQoL utility) in another one[146] *(EQ-5D index score[185] mean difference between control group and intervention group (95%CI) at week 26: - 0.043 (-0.174 to 0.088), EQ-5D VAS[185] mean difference (95%CI) at week 26: -4.1 (-14.9 to 6.7) / AQoL utility[146]: difference in mean change between Intervention group and Control group (95% IC) from recruitment to 3 months : 0.12 (-0.03 to 0.26) and from recruitment to 12 months: 0.14 (-0.03 to 0.31))*

4.3.3.2 Physical rehabilitation combined with other interventions

Physical rehabilitation and follow-up consultations

We found two studies[188, 192] (old studies and with low sample size) that associated self-directed physical rehabilitation programme at home and consultations at an ICU follow-up clinic at 3[188], 6[192] or 9[188] months. A review letter on the patient's progress was sent to each patient's GP in one trial (n=286).[188] The rehabilitation programme included unsupervised exercises but a textbook with reported advice on psychological, psychosocial and physical problems was provided in one study (n=126).[192] The use of this rehabilitation manual was reinforced by 3 weekly telephone calls. The duration of intervention varied between studies from 6 weeks[192] to 3 months post-hospital discharged.[188]

- Mental health

Anxiety and depression were assessed by HADS-A and HADS-D in both studies.[188, 192] No significant and no clinically important differences between HADS-A and HADS-D scores was found between patients with a rehabilitation program in comparison to those without at 6 and 12 months *(mean difference (95% CI), p-value in HADS – A at 6 months: −0.9 (−2.0 to 0.1), p=0.09 and at 12 months −0.8 (−1.9 to 0.4), p=0.18 / mean difference (95% CI), p-value in HADS – D at 6 months: −0.0 (−1.0 to 1.0), p=0.99 and at 12 months −0.1 (−1.2 to 1.0), p=0.86).[188]* In addition, the proportion of anxious or depressed patients (defined with a HADS-A or HADS-D≥ 11) was similar in intervention and control groups at 6 months post-discharge *(proportion of patients with HADS-A score ≥ 11 at 6 months: Intervention group 32.7% vs. Control group 34%, ns / proportion of patients with HADS-D score ≥ 11 at 6 months: Intervention group 10% vs. Control group 12%, ns)*.[192] Stratified analysis based on the use of antidepressant did not show any difference in proportion of patients with depression or anxiety between intervention and control groups.[192]

Remark: the effect of delusional memory recall on HADS-A was studied in one publication.[192] A significant higher HADS-A score was found at 6 months post-discharge in patients with delusional memories than in those without (p=0.044). Since this study, the authors decided to add the screening of delusional memories in the rehabilitation programme. No analysis by study groups (intervention vs control) was provided by the authors.[192]

PTSD was assessed by Davidson trauma score in one study[188] and posttraumatic stress disorder-related symptoms were evaluated by the IES scores in another one.[192] No significant difference in incidence of PTSS was found whatever the assessment tool used *(proportion of patients with* IES score ≥ 19 *at 6 months post-discharge.[192] Intervention group 31/ 58 vs. Control groups 21/44, p=0.57 / Davidson trauma score mean difference (95% CI), p-value for incidence[188] at 6 months: −3.6 (−7.6 to 0.4), p=0.07 and at 12 months: −3.7 (−7.4 to 0.0), p=0.05 / Davidson trauma score mean difference (95% CI), p-value for severity[188] at 6 months: −3.1 (−6.7 to 0.6), p=0.10 and at 12 months: −1.6 (−5.0 to 1.9), p=0.37).*

Remark: the effect of delusional memory recall on PTSD was also studied.[192] At 6 months post-discharge, patients with delusional memories had a significantly higher IES scores (p=0.008) and a significant higher incidence of PTSD (defined as IES>19, p=0.028) than patients without delusional memories. Therefore, the authors decided to add the PTSD screening in the rehabilitation programme since this study. No analysis by study groups (intervention vs control) was provided by the authors.[192]

- Heath related quality of life

HRQoL was assessed in both studies by SF-36.[188, 192] No significant and clinically important differences were found in SF-36 MCS and SF-36 PCS at 6 and 12 months post-discharge.[188] *(mean difference (95% CI), p-value in SF-36 MCS at 6 months −0.6 (−3.9 to 2.8), p=0.74 and at 12 months*

0.4 (−3.0 to 3.7), p=0.83 / in SF-36 MPS at 6 months −0.8 (−3.6 to2.0), p=0.59 and at 12 months 1.1 (−1.9 to 4.2), p=0.46). However in one study,[192] patients receiving the intervention showed closer to normal SF-36 physical function scores at 6 months than control patients (data not shown)

HRQoL was also assessed by EQ5-D in one study.[188] No significant difference was found between control and intervention groups (*mean difference (95% CI), p-value in ED-5D at 6 months 0.0 (−0.1 to 0.1), p=0.83 and at 12 months −0.0 (−0.1 to 0.1), p=0.57).*[188]

- Return to work

The probability to return to work at 6 or 12 months post-ICU was not increased when patients attended nurse led ICU follow-up clinics and used 3-month self-directed physical rehabilitation programme.[188] *The OR (95% CI) was at 6 months 1.16 (0.43 to 3.12) and at 12 months 1.06 (0.35 to 3.21).* However, the assessment time points were relatively short to assess the return to work.

- Social support

After 6 months follow-up, one trial showed no difference in the level of social support measured by the Norbeck Social Support Questionnaire between the patients attended consultations at post-ICU follow-up clinic and supported by a 6-week rehabilitation programme and the patients who did not *(data not shown).*[192]

Physical rehabilitation and education sessions

We retrieved two studies that combined physical rehabilitation and education session.[187, 193] The first study, including 20 patients, proposed 16 supervised sessions at outpatient physiotherapy gymnasium including exercises and education related to breathlessness management, benefits of exercise, and nutrition. This intervention started within the 2 weeks after hospital discharge for 3 months.[187] The second study started later (6 weeks post-discharge) but lasted less (7 weeks).[193] This trial focused on 73 patients invasively ventilated for ≥5 days and proposed a multimodal intervention mixing exercise and education sessions supervised by a physiotherapy team. The exercise sessions consisted in 1 supervised and 2 self-directed sessions each week. In addition, education sessions of 1 hour were foreseen and covered benefits of exercise, relaxation techniques, managing breathlessness, smoking cessation, anxiety management as well as a group discussion forum.[193]

- Physical health

One study described peak VO_2 and anaerobic threshold to assess the physical health and found no difference between intervention and control groups.[193]

Change between baseline and 3 months post-discharge in 6MWT was analysed in one study.[187] The authors found no significant difference between patients receiving the intervention in comparison with those not receiving post-discharge intervention *(Control group: 185.0 (40.0 to 285.0) vs Intervention group: 140.0 (35.8 to 210.3), p= ns)*.[187] However, both intervention and control group reached the MCID of 35 m walked.[146] In the same study, the ISWT was also used to assess physical health and no significant nor clinically important difference between intervention group and control group was found *(Change between baseline and 3 months post-discharge [median (IQR)] Control group: 170.0 (40.0 to 315.0) vs Intervention group: 115.0 (− 2.5 to 237.5), p= ns)*.[187]

- Mental health

Only one study[187] assessed anxiety and depression and found no significant differences for both. The MCID is 2.5 points in each HADS sub-scale (HADS-A and HADS-D).[148] *Change between baseline and 3 months post-discharge [median (IQR)] in HADS total Control group: − 4.5 (− 13.3 to − 2.5) vs Intervention group: − 6 (− 9.3 to − 2.8), p= ns / in HADS-A Control group: 0.0 (− 7.0 to 0.0) vs Intervention group: − 3.5 (− 5.0 to − 1.3), p= ns / in HADS-D Control group: − 4.5 (− 6.3 to − 1.8) vs Intervention group: − 1.5 (− 3.3 to 2.0), p= ns).*

- Heath related quality of life

HRQoL was assessed by SF-36 scales in both studies.[187, 193]

Physical Function Score (SF-36 PF) at 14-16 weeks post-hospital discharge was reported in one study. A statistical and clinically important difference was found in favour of the intervention group *(mean improvement in SF-36 PF (95% CI) Control group: 14.8 (8.5–23.0) points vs Intervention group: 28.0 (19.4–34.7) points, p= 0.004).*[193]

No significant improvement after 3 months post discharge was observed in Physical Component Summary Score (SF-36 PCS) in one study *(change between baseline and 3 months post discharge (median (IQR) in SF-36 PCS: Control group: 11.0 (4.3 to 28.3) points vs Intervention group: 1.8 (−6.8 to 15.9) points, p= ns)*.[187] The other study focusing on patients with long ventilation[193] (patients invasively ventilated for ≥5 days).found a clinically important improvement in both groups with a significant higher improvement in intervention group *(mean improvement after 14-16 weeks post-hospital discharge (95% CI) Control group: 3.5 (1.6 to 6.7) vs Intervention group: 8.6 (5.4 to 10.6), p= 0.048)*. Stratified analysis based on ventilation duration and adjusted for age showed that improvement was more pronounced in the subgroup ventilated for >14 days *(mean improvement after 14-16 weeks post-hospital discharge (95% CI) in patients ventilated during 5 to 14 days Control group: 3.9 (1.0, 6.8) vs Intervention group: 5.0 (0.9 to 9.1), p = 0.64 / in patients ventilated > 14 days Control group: 3.6 (−0.3 to 7.4) vs Intervention group: 9.5 (6.2 to 12.8), p = 0.024).*[193]

Similarly to the SF-36 PCS, no significant improvement after 3 months post discharge was seen in the Mental Component Summary Score (SF-36 MCS) in one study (change between baseline and 3 months post discharge *(median (IQR) in SF-36 PCS: Control group: − 11.4 (− 19.0 to 19.1) points vs Intervention group: 14.3 (− 3.2 to 26.7) points, p= ns)*.[187] Following the same trend of SF-36 PCS, the second study[193] found a clinically important improvement in SF-36 MCS for both groups with a significant higher improvement in intervention group *(mean improvement after 14-16 weeks post-hospital discharge (95% CI) Control group: 4.3 (0.5 to 7.6) vs Intervention group: 10.2 (6.9 to 14.4), p= 0.017)*. Stratified analysis based on ventilation duration and adjusted for age showed that improvement was also most marked in the subgroup ventilated for >14 days *(mean improvement after 14-16 weeks post-hospital discharge (95% CI) in patients ventilated during 5 to 14 days 3.7 (0.9 to 9.9) vs Intervention group: 10.5 (1.5 to 19.4), p = 0.21 / in patients ventilated > 14 days Control group: 3.9 (−0.6 to 8.4) vs Intervention group: 11.0 (7.0 to 14.9), p = 0.024).*[193]

Physical rehabilitation and nutrition supplements

One RCT reported supervised sessions including physiotherapy and structured exercises during 6 weeks post hospital discharge (PEPSE) and supplement drink taken within 1 hour of physical activity composed of 20-g essential amino acids and 20-g glutamine (EAA).[191] The patients of the control group received the same interventions but the supplement drink was replaced by a placebo supplement drink. Patients were randomly assigned to placebo supplement and no PEPSE (n=17), placebo supplement and PEPSE (n=20), GEAA supplement and no PEPSE (n=18), GEAA supplement and PEPSE (n=17).

- Physical health

The study showed that patients receiving GEAA supplement and PEPSE had the biggest gains in distance walked in 6-minute walking test after 3 months post-discharge in comparison with the other groups (p<0.0001). The patients receiving GEAA supplement and PEPSE showed a progression of 124% in 6MWT after 3 months in comparison with approximately 61% in patients without nutritional supplement nor physical programme (data reported in graph, raw data not shown).

- Mental health

Association of exercises and nutritional supplement seems to significantly reduce the rate of severe depression (HADS-D ≥ 11) after 3 months post-discharge *(proportion of patients score HADS-D ≥ 11 at recruitment vs proportion at 3 months: placebo supplement, no PEPSE 15% vs 7% [p=ns] – placebo supplement, PEPSE 9.5% vs 0% [p=ns] – GEAA supplement, no PEPSE 28% vs 21% [p=ns] – GEAA supplement, PEPSE 30% vs 12% [p=0.009])*.[191] As observed for depression, the association of exercises and nutritional supplement seemed to significantly reduce the rate of severe anxiety (HAD-A ≥ 11). However, the usage of exercises programme alone also showed a decrease in the rate of severe anxiety *(proportion of patients score HADS-A ≥ 11 at recruitment vs proportion at 3 months: placebo supplement, no PEPSE 15% vs 14% [p=ns] – placebo supplement, PEPSE 19% vs 5%[p=0.047] – GEAA supplement, no PEPSE 36% vs 32% [p=ns] – GEAA supplement, PEPSE 31% vs 12% [p=0.036])*.[191]

Physical rehabilitation, cognitive and functional intervention

A three dimensional rehabilitation programme was identified in the literature.[190] The cognitive rehabilitation aimed to improve the patient's executive function and was delivered in his home by a master's level psychology technician supervised by a licensed neuropsychologist. The physical rehabilitation was individually tailored to the patient's functional status level provided by exercise

trainer via telecommunication. During the physical rehabilitation, patients were supported by a trained social worker at their home. Four sessions of functional rehabilitation were provided by an occupational therapist via tele communication and supported by trained social worker at the patient's home. More details about intervention are available in the evidence table (see appendix). Patients included in the control group received physical therapy, occupational therapy, and nursing care, delivered to in-patient, out-patient, or home-health settings but no cognitive therapy nor speech therapy. This study was a pilot RCT and included a low sample size (intervention: n=9 vs control group n=8).

- Physical health

Ambulation ability was assessed by the TUG test. No significant difference was found between control and intervention groups *(median number of seconds [IQR] at 3 months Control group: 10.2 [9.2 -11.7] vs Intervention group: 9.0 [8.5-11.8], p=0.51)*.[190] The difference is below of the MCID described by the authors (MCID assessed for older adults).

Balance was assessed by Activities Balance and Confidence (ABC) Scale. The ABC score rates an individual's confidence in their balance on a 0 to 100% scale on which higher scores reflect greater confidence in balance. No significant difference was found between control and intervention groups *(median number of seconds [IQR] at 3 months Control group: 83 [38- 91] vs Intervention group: 82 [78- 89], p=0.35).*[190]

- Functional ability

Activities of Daily Living (ADL) was assessed by the Katz ADL scale. The scale range from 0 to 18 points and assessed 6 ADL categories. Patients with little to no dependency had no more than partial dependency in 1 of 6 ADL domains and patients with moderate to severe dependency had at least partial dependency in at least 2 of 6 ADL categories. The study reported a similar proportion of patients with moderate to severe dependency in control and intervention groups (proportion of patients with moderate to severe dependency Control group: 2/8 – Intervention group: 0/7, p=0.78).[190]

Instrumental activities of daily living (IADLs) was assessed by a Functional Activities Questionnaire (FAQ). This 10 item self-report measure scores patients from 0 to 30 and higher scores reflect poorer performance. Patients in the control group showed significant poorer performance in IADLs *(median FAQ score [IQR] at 3 months Control group: 8.0 [6.0- 11.8] vs Intervention group: 1.0 [0.0 - 2.5], p=0.04)*.[190]

- Cognitive outcomes

Executive cognitive function was assessed by three different tests: the Tower Test Achievement Score (TOWER test), the Dysexecutive Questionnaire (DEX) and Mini Mental State Examination (MMSE).[190] The Tower Test Achievement Score assesses the patients' overall executive functioning ability on a test of planning and strategy with a scale from 1 to 9, with higher scores reflecting better performance. Normal score range from 7 to 13. The DEX test is a brief self-report measure that rates behavioural markers of executive functioning. It ranges from 0 to 80 and higher scores reflect poorer functioning. The MMSE is a brief objective measure of overall cognitive ability scoring patients from 0 to 30, higher scores reflecting better functioning.

After 3 months, the authors found a statistically significant difference in executive cognitive function between intervention group and control group with the TOWER test while no difference between groups was observed with DEX and MMSE tests *(median TOWER score [IQR] Control group: 7.5 [4.0- 8.5] vs Intervention group: 13.0 [11.5- 14.0], p<0.01 / median DEX score [IQR] Control group: 16.0 [7.8-19.2] vs Intervention group: 8.0 [6.0- 13.5], p=0.74 / median MMSE score [IQR] Control group: 26.5 [24.8-28.5] vs Intervention group: 30.0 [29.0-30.0], p=0.25)*.[190] MICD values were not found for DEX and MMSE for ICU survivors.

4.3.4 Follow-up consultations

Follow-up consultations were studied in 9 publications[188, 192, 194-200] reporting 8 studies. Among those, 4 studies focused on follow-up consultations alone while 4 studies reported interventions combining follow-up consultations with a rehabilitation programme[188, 192] or with diaries.[194, 200] Perceptions of patients regarding the follow-up services are described in chapter 6.

Table 13 – Overview of included studies – Follow-up consultations

Study ID	Design	Patients	Country	Start of intervention	Intervention	Control	Max. follow-up	Tools for outcome assessment
Nurse-led follow consultations								
Jensen 2016[195]	RCT	386 patients ≥18y Ventilation ≥48h	Denmark	1 month post-ICU	3 consultations with nurses. Consultation 1 with relatives (1 to 3 months post-ICU) to construct an illness narrative with photographs of the patient during the ICU-stay and revisiting ICU. Consultations 2 and 3 by telephone at 5 and 10 months post-ICU and tailored to the patient's needs	ICU discharge without follow-up	12 months	SF-36, SOC, HADS, HTQ-IV
Jonasdottir 2018[196]	Quasi-experimental	168 patients ≥18y ICU LOS ≥ 72h acute and elective ICU admissions	Iceland	3 months	1-hour conversation about ICU experience	Unstructured ward visit	12 months	IES, HADS
Multidisciplinary follow-up consultations								
Schandl 2012[197]	Before/after design	410 patients ≥16y ICU LOS > 96h	Sweden	1 week post-ICU	1 ICU visit, 3 follow-up consultations (nurse, physician, physiotherapist)	no ICU follow-up	14 months	IES, HADS, ICU Memory Tool
Schmidt 2016[198] & Schmidt 2020[199]	RCT	291 patients ≥18y survivors of severe sepsis or septic shock	German y	8 days post-ICU	Session by a case manager (nurses with specific training) with patients training on sepsis sequelae, patient symptom monitoring and reporting results to consulting physicians + an evidence-based sepsis aftercare	Usual care from their primary care physician training without additional information or monitoring.	12 months [198] & 24 months [199]	SF-36, MDI, PTSS-10, TICS-M, Mortality, ADL, XSMFA, NSS, GCPS, MUST, BMI, RIS

					training for the patients' primary care physician provided by the consulting physicians			
Follow-up consultations combined with rehabilitation programme								
See Cuthbertson 2009[188] and Jones 2003[192] in Table 12.								
Follow-up consultations combined with diaries								
Akerman 2018[194]	Prospective cohort	441 patients ≥18y ICU LOS ≥ 24h	Sweden	2 months post-ICU discharge	3 follow-up visits to discuss diaries, events at ICU and recovery process	No diary or no follow-up visit	12 months	3-set 4P questionnaire
Svenningsen 2014[200]	Prospective cohort	360 patients >17 y ICU LOS >48h	Denmark	At 1 week post-ICU	Diaries and/or follow-up visits	No diary and/or no follow-up visit	6 months	SF-36

4.3.4.1 Follow-up consultations alone

Nurse-led follow-up consultations

Two studies reported on interventions including only follow-up consultations.[195, 196] One of these studies[195] included 386 adults patients mechanically ventilated ≥48 h. The intervention consisted of 3 consultations. During, the first consultation, one to three months post-ICU, there was a revisit of the ICU and a dialogue to support the patient in constructing an illness narrative. Photographs of the patient during the ICU-stay were used during these consultations conducted in the presence of relatives. The second and third consultations were conducted by phone with patients at 5 and 10 months post-ICU and consisted in a dialogue tailored to the issues of importance to the patients.[195] The other retrieved study[196] analyses in 168 adult patients, with a ICU Los ≥72 hours, the effect of a follow-up performed by a clinical nurse-specialist and consisting in 2 visits of the ICU before hospital discharge, a phone call at the first week after hospital discharge and a 3-month appointment. During the phone call, information about recovery after critical illness was given and patients were interviewed regarding their concerns related to recovery, mobilisation, nutrition and sleep. The 3-month appointment was performed in presence of the closest relative for 1 hour. The consultation included a conversation about ICU experience, a visit to the ICU and referral to psychologist or to GP if IES-R score ≥23, HADS-A≥8 or HADS-D≥8. Patients were invited to contact the clinical nurse-specialist if necessary.

- Mental health

The two studies[195, 196] assessed anxiety and depression separately. Both study assessed depression using HADS-D. One study[195] found no significant difference nor clinical important difference at 12 months post ICU discharge between patients benefiting from follow-up visits compared to those who did not benefit from follow-up visits *(absolute difference in HADS-D scores between standard care and the follow-up visit group (95 % CI) at 12 months: -0.20 (-1.12 to 0.72), p=0.67)*. No increased risk of severe symptoms of depression (HADS-D ≥ 11) was observed in follow-up group *(OR (95% CI) at 3 months 0.66 (0.29 to 1.48), p=0.31 at 12 months 1.10 (0.47 to 2.59), p=0.83)*. The second study[196] found also no difference in the level of depression at different time points between patients attending follow-up visits than those who did not *(mean HADS-D score (SD) at 3 months: Intervention group 3.7 (3.4) vs Control group 3.5 (3.0), p=0.745; at 6 months Intervention group 4.7 (3.9) vs Control group 3.4 (3.2), p=0.053 and at 12 months: Intervention group 3.8 (2.9) vs Control group 3.7 (3.6), p=0.895)*. The same study[196] showed that patients with follow-up visits did not experience more

depression over time than those in the no follow-up group *(mixed effect model estimate 0.362 (SD 0.327, 95% CI -0.280 to 1.00), p=0.280).*

Anxiety was assessed using HADS-A.[195, 196] The first study[195] showed no significant difference nor clinical important difference post ICU discharge between patients benefiting from follow-up visits than those who did not benefit from follow-up visits *(absolute difference in HADS-A scores between standard care and the follow-up visit group (95 % CI) at 3 months -0.16 (-1.15 to 0.82), p=0.75 and at 12 months -0.21 (-1.22 to 0.80), p=0.68)*. No increased risk of severe symptoms of anxiety (HADS-A ≥ 11) was observed in follow-up group *(OR (95% CI) at 3 months 0.50 (0.24 to 1.06), p=0.07 and at 12 months 0.91 (0.40 to 2.07), p=0.82)*. In contrast, the second study[196] found significant differences in favour of patients without follow-up visits. However these differences did not reach the MCID *(mean (SD) HADS-A score at 3 months: follow-up group 4.4 (4.2) vs no follow-up group 2.8 (3.1), p=0.011; at 6 months: follow-up group 3.7 (3.6) vs no follow-up group 2.4 (2.8), p=0.030 and at 12 months: follow-up group (n=54): 4.0 (3.2) vs no follow-up group (n=56): 2.5 (2.8), p=0.005)*. In addition, patients benefiting from follow-up visits experienced more anxiety over time than those without follow-up visits *(mixed effect model estimate 1.07 (SD 0.32, 95% CI 0.442-1.70), p=0.001)*.

PTSD is also assessed in the two studies.[195, 196] The authors of the first study[195] used the Harvard Trauma Questionnaire Part IV (HTQ-IV). This tool provides an evaluation of 3 core symptoms described in DSM-IV (re-experience, avoidance, and arousal), one functional item and 3 items related to stress. This scale has been validated in various trauma populations. Higher scores indicate greater symptoms of PTSD and a cut-off of ≥40 was used as criterium of "positive PTSD".[195] No significant differences were found in the HTQ-IV score at different time points between patients with and patients without follow-up *(absolute difference in HTQ-IV scores between no follow-up group and the follow-up group (95 % CI) at 3 months 0.24 (-2.07 to 2.55), p=0.84 and at 12 months -1.42 (-3.94 to 1.11),p=0.27)*.[195] The Odds Ratio for positive PTSD was not statistical significant *(OR of patients with score ≥ 40 (95% CI) at 3 months 1.23 (0.74 to 2.06), p=0.43 and at 12 months 1.00 (0.58 to 1.73), p=1.00*). No difference in proportion of patients with new onset of PTSD was found during 1 year.[195] The second study[196] assessed symptoms PTSD by the IES-R total score and found no significant difference between patients benefiting from follow-up visits compared to those who did not benefit from follow-up visits *(mean ES-R total score (SD) at 3 months follow-up group 11 (16) vs no follow-up group 12 (14), p=0.157, at 6 months follow-up group 18 (18) vs no follow-up group 13 (16), p=0.097 and at 12 months follow-up group 20 (17) vs no follow-up group 14 (15), p=0.066)*. In this study,[196] the proportion of patients with partial or full PTSD (as defined as an IES-R score ≥ 23–88) was not significantly different between the follow-up group and the no follow-up group at 3 and at 12 months. However, this proportion was significantly different at 6 months and patients attending follow-up visits experienced more symptoms of PTSD over time than those who did not attend follow-up visits *(mixed effect model estimate 4.06 (SD 1.62, 95% CI 0.870 to 7.25), p=0.013).*

- Health related quality of life

HRQoL was studied by the SF-36 survey in 1 publication.[195] No significant nor clinically important differences in the SF-36 PCS were found at 3 and at 12 months[195] *(absolute difference in SF-36PCS scores between no follow-up group and the follow-up group (95 % CI) at 3 months 1.87 (-0.93 to 4.67), p= 0.19 and at 12 months 1.41 (-1.53 to 4.35), p=0.35)*. In addition, no significant nor clinically important differences in the SF-36 MCS were found at 3 and at 12 months *(absolute difference in SF-36 MCS scores between no follow-up group and the follow-up group (95 % CI) at 3 months -0.41 (-3.20 to 2.39), p=0.78 and at 12 months 1.92 (-1.06 to 4.90), p=0.21)*.[195]

- Cognition

No significant difference in 'sense of coherence' was observed between patients with follow-up visits and those without *(absolute difference in scores between no follow-up group and follow-up group (95 % CI) at 3 months: 2.02 (-1.35 to 5.38), p=0.24 and at 12 months: -0.93 (-4.72 to 2.85), p=0.63)*.[195]

Multidisciplinary follow-up consultations

Two studies reported in 3 publications analysed the effect of a multidisciplinary intervention in ICU survivors.[197-199] The first study proposed an intervention on multidisciplinary follow-up including a case manager as core component. The case manager, a nurse with specific training, provided 8 pro-active patient symptom monitoring sessions by phone and one face-to-face patient training on sequelae. The case manager made feedbacks to the consultant physicians. The consultant physicians gave clinical decision support and evidence-based training for the patients' primary care

providers.[198, 199] The proposed intervention in second study[197] started within one week from ICU discharge by visit at the hospital ward by a nurse from the follow-up team to discuss briefly their treatments in ICU and memories. Afterwards, multidisciplinary follow-up consultations with a nurse, a physician and a physiotherapist from the general ICU were offered at 3, 6 and 12 months after ICU discharge. A visit of ICU was offered during the 6-month consultation. Patient referral was considered when patients scored high score in PTSD (IES > 25 points) or in anxiety and depression (HADS > 10 points). Physical training instructions or additional consultation in pain clinic or with patient counsellor, local physiotherapist or other specialists may be offered according to the patients' needs.

- Physical health

The RCT using case managers studied the physical function and the disability assessed by the Short Musculoskeletal Function Assessment (higher scores reflect higher impairment).[198, 199] The authors found a better score in physical function and disability in the intervention compared to the control group at 6 months but no significant effect was observed after 12 and 24 months. *At 6 months, median score [Q1 to Q3] was 31 [12 to 58] in intervention group and 46 [17 to 76] in control group (p=0.04) for physical function and 38 [12 to 69] in intervention group and 56 [25 to 81] in control group (p=0.03) for disability.* Detailed results at 12 and 24 months are reported in the evidence table (see appendix).

- Mental health

A RCT studying an intervention involving nurses, consultant physicians and primary care providers found no significant treatment effect on depression assessed by MDI (Major Depression Inventory) when comparing with usual care at different time points *(a mean difference (95%CI) in MDI at 6 months: -0.0 (-2.8 to 2.8), p=0.99, at 12 months -1.4 (-4.5 to 1.7), p=0.36 and 24 months -1.3 (-5.0 to 2.4), p=0.48)*.[198, 199] The second publication showed no significant difference in depression between patients in intervention group than those in control group *(median HADS-D score at 14 months in women: control group 7 vs intervention group 3, p=0.09 and in men control group 4 vs intervention group 4, p=0.47)*. After adjustment for age, length of intensive care unit stay and previous psychological problems, quantile regression did not show significant nor clinical important difference between intervention and control group unless in 75th percentile in women *(difference in median between control group and follow-up group at 75th percentile -5.4, p<0.05, details results are presented in evidence table in the appendix).*

In the second study[197], anxiety was studied in ICU survivors at 14 months by the HADS-A scale. No significant differences were found in HADS-A score in both women and men *(median HADS-A score at 14 months in women: Control group 6 vs Intervention group 3, p=0.14 and in Control group 3 vs Intervention group 4, p=0.78).* After adjustment for age, length of intensive care unit stay and previous psychological problems, quantile regression in women showed a significant but not clinical important difference at 25th percentile and a non-significant but clinical difference at 75th *percentile (median difference in women between control group and follow-up group at 25th percentile -1.8 (p< 0.05), at 50th percentile -1.2 (ns) and at 75th percentile -3.2 (ns)).* After adjustment no differences were observed in men *(data showed in evidence table in the appendix)*.

The first trial[198, 199] suggested that the increase in late-onset PTSD symptoms in the control group may indicate a possible protective effect of the multidisciplinary intervention, i.e. a follow-up at 24 months post-ICU *(PTSS-10 score mean difference between control and intervention group between baseline and 6 months -1.8 (-4.8 to 1.2), p=0.24, between baseline and 12 months -2.3 (-5.6 to 1.0), p=0.17 and between baseline and 24 months -4.4 (-7.9 to -0.8), p=0.002)*. Finally, gender seemed to influence the onset of PTSD when multidisciplinary ICU follow-up is considered.[197] Indeed, this type of follow-up may significantly reduce the long-term level of stress in women but not in men *(median IES at 14 months in women control group 31 vs intervention group 20, p=0.01 and in men control group 10 vs intervention group 16, p=0.27)*.[197] After adjustment for age, length of ICU stay and previous psychological problems, the 75th percentile for IES in women was lower in the follow-up group than in the control group after 14 months (IES mean difference -17.6 points, p<0.05), suggesting that the incidence of long-term symptoms of posttraumatic stress in female ICU survivors is lower in the follow-up group in comparison with women without multidisciplinary follow-up programme. This was not observed in men (IES mean difference 4.4, ns).[197] However, factual and emotional memories and delusions assessed by ICU Memory Tool at 14 months showed not significant difference in score between patients with a multidisciplinary follow-up and those without *(details results presented in evidence table see appendix)*.[197]

- Health related quality of life

HRQoL was studied in one paper by the SF-36 survey. [198, 199] No differences at 6, 12 and 24 months post discharge between intervention and control groups were found in score for SF-36 MCS, SF-36 PCS, SF-36 vitality, SF-36 PF, SF-36 physical role function, SF-36 bodily pain, SF-36 general health perceptions, SF-36 social role function, SF-36 emotional role function, SF-36 mental health. Detailed results are presented in evidence table (see appendix).

- Cognition

The same publication[198, 199] assessed the cognitive status by the Modified Telephone Interview for Cognitive Status tool (TICS-M). No significant difference was found at 6,12 and 24 months between intervention and control groups *(difference between variation in mean between intervention and control group (95%CI) from baseline and 6 months: -0.3 (-1.3 to 0.8), p=0.63, from baseline and 12 months -0.5 (-1.7 to 0.7), p=0.39 and from baseline and 24 months -0.5 (-2.0 to 1.0), p=0.49)*.

- Activity in daily life

The same RCT[198, 199] assessed the impairment in activities of daily living using a scale ranging 0-11 evaluating the autonomy in activities such as walking, dressing, bathing, eating, getting in/ out of bed, using the toilet getting in/ out of chairs, going outside and taking care of personal needs.[201] The authors found a positive effect of the multidisciplinary follow-up in ADL score after 6 and 12 months. However, the effect did not persist at 24 months post-ICU. The treatment effect at 6 months was 1.0 (0.2 to 1.8), p=0.03. The treatment effect at 12 months was 0.9 (0.0 to 1.7), p=0.05 and the treatment effect at 24 months was 0.1 (-0.7 to 0.9), p=0.94.

- Nutrition

The same trial also evaluated the proportion of patients at risk of malnutrition by the Malnutrition Universal Screening Tool (MUST). The authors found no difference in risk of malnutrition between intervention and control groups (not statistically significant OR at 6, 12 and 24 months; OR (95%CI) at 6 months: 0.8 (0.3 to 2.5), p=0.80, at 12 months 0.7 (0.2 to 3.0), p=0.76 and at 24 months 1.7 (0.3 to 13.1), p=0.67). No difference was found in BMI variation at 6, 12 and 24 months between intervention and control groups.[198, 199]

4.3.4.2 Follow-up consultations combined with other interventions

Follow-up consultations and rehabilitation programme

Two studies associated physical rehabilitation programmes and follow-up consultations.[188, 192] The first study[188] included 286 patients randomly assigned to the control group with no ICU follow-up after hospital discharge or to an intervention group benefiting from a 3-month rehabilitation programme and 2 visits at a nurse led clinic at 3 and 9 months after discharge. During the clinic appointments, the ICU follow-up nurse discussed experiences of intensive care with the patients, formally assessed the patient's requirement for specialist medical or physiotherapist referral, and screened the patient for psychological morbidity related to admission to the ICU. A review letter on the patient's progress was sent to each patient's GP.[188] The second study[192] is also a RCT including 126 patients during which the intervention consisted in a 6-week rehabilitation package combined with 2 follow-up visits at 8 weeks and 6 months after hospital discharge. The results of these two trials are reported at section 0.

Follow-up consultations and diaries

Two other observational studies associated diaries and follow-up consultations.[194, 200] Some patients benefited from diaries and/or follow-up visits. Therefore, the patient groups are not mutually exclusive. The authors presented the results according to of diary handover or according to follow-up visit attendance. The effect of diary on health outcomes are presented at section 4.3.5.1.

- Physical health

Physical limitations and physical condition were assessed in one study with the 3-set 4P questionnaire.[194] The 3-set 4P questionnaire was developed to identify physical and psychosocial problems and the need for the follow-up of ICU survivors. The questionnaire has been psychometrically tested for validity and reliability in mechanically ventilated adult ICU survivors.[202] Thirty-three questions assessed 3 domains: physical set (including physical limitations, physical condition, and change in appearance, psychosocial set (consisting in measurement of mood, memory, social life, sleep and avoidance) and the follow-up set (including questions about the diary, the ICU follow-up clinic and follow-up with other specialists).[202] For the physical dimension, a higher

score indicated fewer problems or fewer limitations. At 6 and 12 months, no significant differences in physical limitations were observed between patients attending follow-up visits and those who did not *(mean score (SD) at 6 months: follow-up visit 2.18 (1.25) vs no follow-up visit 2.20 (1.29), p=ns and at 12 months: follow-up visit 2.33 (1.30) vs no follow-up visit 2.28 (1.32), p=ns).* No significant differences in physical condition were observed (*mean score (SD) at 6 months: follow-up visit 1.20 (0.55) vs no follow-up visit 1.17 (0.56), p=ns and at 12 months: follow-up visit 1.15 (0.56) vs no follow-up visit 1.17 (0.47), p=ns).*

- Mental health

One study[194] showed that patients in the follow-up group reported more problems of mood after 12 months post discharge than those who did not attend follow-up visits. No difference between groups was observed at 6 months (mean score (SD), p-value at 6 months: follow-up visit 4.97 (0.92) vs no follow-up visit 5.15 (0.86), p=ns, at 12 months: follow-up visit 4.79 (1.01) vs no follow-up visit 5.06 (0.98), p<0.05).

The effect of follow-up visits on avoidance is studied by 3-set 4P questionnaire in one study.[194] Higher scores indicated fewer problems of avoidance. No significant difference was observed between patients attending follow-up visits and those who did not attend both at 6 and 12 month post-discharge *(mean score (SD) at 6 months follow-up group 1.85 (0.33) vs no follow-up group 1.86 (0.34), p=ns and at 12 months follow-up group 1.69 (0.50) vs no follow-up group 1.76 (0.47), p=ns)*.

- Health related quality of life

HRQoL is studied by the SF-36 survey in 1 publication.[200] The follow-up visits did not have an impact on SF-36 total scores at six months.[200]

- Social life

Social life was assessed by 3-set 4P questionnaire in 1 paper.[194] Higher scores indicated fewer problems. Patients attending follow-up visits scored better for social life that patients who did not attend follow-up visits at 6 months but the favourable effect of follow-up visits was no longer observed at 12 months *(mean score (SD) at 6 months: follow-up group 0.79 (0.65) vs no follow-up group 0.62 (0.52), p<0.05 and at 12 months: follow-up group 0.90 (0.66) vs no follow-up group 0.77 (0.68), p=ns)*.

The ICU survivors attending follow-up visits did not experience more sleep problems than those who did not attend *(3-set 4P questionnaire score at 6 months: follow-up group 2.42 (0.68) vs no follow-up group 2.40 (0.60), p=ns and 12 months: follow-up group 2.47 (0.62) vs no follow-up group 2.45 (0.58), p=ns).*[194]

- Cognition

When assessed by 3-set 4P questionnaire, patients who did not attend follow-up visits experienced fewer problems in memory than patients attending follow-up visits *(higher scores indicated fewer problems, mean score (SD) at 6 months: follow-up visit 4.15 (1.05) vs no follow-up visit 4.47 (0.79), p<0.05 and at 12 months: follow-up visit 4.14 (1.03) vs no follow-up visit 4.59 (0.71), p<0.001).*[194]

4.3.5 Mental health interventions

The mental health interventions included studies reporting the usage of diaries, mindfulness training and coping skill training (see Table 14). Cognitive interventions and peer support groups are reported in dedicated sections below.

Table 14 – Overview of included studies – Other interventions

Study ID	Design	Patients	Country	Start of intervention	Intervention	Control	Max. follow-up	Tools for outcome assessment
Diaries								
Bäckman 2010 [203]	Non-randomised prospective study	499 patients >17y ICU LOS >24h	Sweden	2–8 weeks after discharge	Diaries discussed during one follow-up visit	No diary	36 months	SF-36
Garroustе-Orgeas 2012[181]	Before-after	143 patients & 136 family members ICU LOS ≥ 4 days	France	During ICU stay	Diary given to the patient at ICU-discharge with a leaflet	No diary	12 months	Peritraumatic dissociation questionnaire, IES, HADS
Garroustе-Orgeas 2019[182]	RCT	657 patients & 325 family members ≥18y Ventilation ≥ 48h	France	Post-ICU discharge	Diary given to the patient without additional support	Usual ICU care without ICU diary	3 months	IES, HADS, ICU memory tool
Jones 2010[204]	RCT	352 patients ≥ 16y ICU LOS ≥ 72h Ventilation ≥ 24h	Denmark, Italy, Norway, Portugal, Sweden and UK	As soon as possible (< 2 months post-ICU)	Diary discussed with the study nurse at 1 month follow-up visit. A second one occurred at 3 months	Same intervention but received their diaries only at 3 months post-ICU	3 months	PTSS-14
Kredentser 2018[205]	RCT	58 dyads patients/ families > 17y ICU LOS >72h Ventilation >24h	Canada	At 1 month post-ICU discharge	Diary reviewed with research team +/- psychoeducation material	No follow-up, psychological support or education	3 months	HADS, IES
Nielsen 2020[150]	RCT	55 patients & 116 relatives ≥18y ICU LOS ≥ 48h Ventilation ≥24 h	Denmark	At discharge to home	Diary given to the patient without additional support	Usual care without diary	3 months	PTSS-14, HADS, SF-36
See also Akerman 2018[194] and Svenningsen 2014[200] in Table 13.								
Mindfulness training								

Cox 2019[206]	RCT	80 patients ≥18y ICU LOS ≥24h Cardiorespiratory failure	USA	1 week post-hospital discharge	Telephone based mindfulness training + mobile app	education information in 6 videos (~10-15 minutes) + handouts + links to contact study team	3 months	PHQ-9, GAD-7, PTSS-10, PHQ-10, QoL VAS, CAMS-R, Brief COPE
Telephone- and Web-based Coping Skills Training								
Cox 2018[180]	RCT	175 patients & 86 relatives ≥18y ventilation >48h	USA	3 week post-hospital discharge	Coping skills training by telephone (6 x ~30 minutes)	6 informational videos with web-based content + 2 phone calls to answer questions	6 months	HADS, IES, PROMIS, EQ-5D, Brief COPE
Zhao 2017[207]	RCT	332 patients	China	Not clear	Learning music playing + learn vocabulary in Spanish + drawing a picture of clock from memories + psychiatrist sessions during 3 months	No cognitive training	3 months	Montreal Cognitive Assessment
See also Jackson 2012[190] in Table 12								
See McWilliams 2016[193] in Table 12								

4.3.5.1 Diaries

In patients discharged from the ICU, factual memories of the stay may be absent or fragmented and many of them report delusional memories.[181] As mentioned in the Introduction, these memory gaps may contribute to anxiety, depression or PTSD. Diaries reporting the ICU events were used from the end of the 20th century to help patients to understand the chain of events during the ICU stay and to fill their memory gaps to avoid as much as possible mental consequences.[144] Patients report that diary had helped them during their recovery process.[150, 204, 205]

ICU diaries may take several forms. In our literature review, we identified diaries written by care providers and close relatives[181-183, 203-205], by providers only,[194] or by close relatives only.[150] The writing of diaries was supervised by guidance for professionals (mostly ICU nurses) and relatives.[181, 183, 194, 203-205] The burden of writing was perceived as low by relatives and healthcare providers.[205] In addition, relatives experienced diary as meaningful and supportive.[150] The diaries often began by a summary including the purpose of the diary and the reason for patient's ICU admission. Photographs were sometime included in the diary after getting the patient's permission.[150, 181, 182, 203-205] While some authors reported to take close-up pictures during care procedures[203, 205], other restricted the photos to the empty ICU room with explanations of the monitoring systems, to the entrance of the ICU, and to the room view as seen from the patient's bed.[181]

Diaries were given to the patients at different moments in the care process either at ICU discharge[150, 181-183, 204] or during follow-up visit.[194, 203, 205] Discussion of the content of the diary with professionals occurred at the hospital,[182] or during face-to-face follow-up visits.[194, 203-205] Sometimes the diaries were read without a health professional.[150, 181, 183] Perceptions of patients are described at chapter 6.

Our literature review retrieved 8 studies, among which 3 publications reported multicentre RCT[150, 182, 204], 1 other reported a monocentric RCT,[205] and 4 last papers reported prospective cohort studies.[181, 194, 200, 203] All retrieved studies were also reported in a previous literature review.[144] Except 1 paper from Canada[205], all the other trials were conducted in Europe (2 in France,[181, 182] 2 in Denmark,[150, 200] 2 Sweden[194, 203] and 1 in UK[204]). Duration of the studies ranged from 12 to 39 months. All studies included adult patients (defined as ≥16y or ≥18y). Except in one study,[205] all studies included more than 100 patients. Duration of mechanical ventilation[150, 182, 204, 205] or LoS[150, 181, 200, 203-205] were used as inclusion criteria in some studies.

Physical health

Akerman et al[194] compared the impact of diary on physical limitation and physical condition scored by patients using the 3-set 4P questionnaire. For the physical dimension, a higher scores indicated fewer problems or fewer limitations. After 6 and 12 months post-ICU, the authors did not find significant differences in score of physical limitation and physical condition between patients who received a diary and those who did not received it *(Physical limitation mean score (SD) at 6 months: diary 2.12 (1.25) vs no diary 2.20 (1.29), p=ns and at 12 months: diary 2.28 (1.31) vs no diary 2.34 (1.30), p=ns – Physical condition mean score (SD) at 6 months: 1.20 (0.55) vs no diary 1.17 (0.56), p=ns and at 12 months diary 31.19 (0.57) vs no diary 1.12 (0.48), p=ns)*.

Mental health

Anxiety and depression are assessed by HADS score in 1 prospective cohort study[181] and 3 RCT.[150, 182, 205] An additional study[194] assessed the level of mood problems by the 3-set 4P questionnaire. This tool scores patients from 0.25 to 6 and higher scores indicated fewer problems.

This study showed that patients benefiting from a diary had significantly fewer mood problems after 12 months that patients without diary. The same effect was however not observed at 6 months (mean score (SD), p-value at 6 months: Diary 4.95 (0.92) vs no diary 5.07 (0.94), p=ns, at 12 months: Diary 4.74 (1.06) vs no diary 5.03 (0.92), p<0.05).

The risk of severe symptoms of anxiety and depression after 3 months post-discharge was assessed through the total HADS score in one study[182] and no significant difference was found between intervention group and control group *(HADS total score > 8, risk difference (95% CI): 0.7 (−9 to 11), p=0.91*).

The risk of severe symptoms of anxiety after 3 months post-discharge was assessed in 4 studies.[150, 181, 182, 205] While 2 studies found no significant difference in the proportion of patients with severe symptoms of anxiety in intervention and control groups, 2 studies showed approximately three time more patients with severe symptoms of anxiety in the group of patients without diary in comparison with those benefiting from a diary *(proportion of patients with HADS-A score >8[181]: diary 10% vs no diary 30%, p=0.09 / Risk difference of HADS-A score >8[182] (95% CI): 0.7 (−9 to 11), p=0.91 / Relative Risk of HADS- A score ≥ 11[150] (95% CI) 1.47 (0.40-5.44), p=0.71 / proportion of patients with HADS-A score ≥8.[205] Diaries 19.2% vs no diaries 63.6%; p = 0.008)*.

Level of anxiety symptoms was assessed after 3 months post-discharge by 2 studies[182, 205] also leading to opposite conclusions. The first study[205] found a significant and clinically lower level of anxiety symptoms in patients benefiting from a diary in comparison with those without diary *(median HADS-A score at 90 days (IQR) diaries 3.0 (2–6.25) vs no diaries 8.0 (7–10), p = 0.01)*, while the second study[182] found no difference between intervention and control groups *(HADS-A score difference (95% CI): −0.36 (−1.22 to 0.50), p=0.72)*.

The effect on severe symptoms of depression after 3 months post-discharge was assessed in 4 studies.[150, 181, 182, 205] While the threshold used to define severe symptoms of depression differed among studies, no more patients with severe depression symptoms were found in patients without diary in comparison with patients with diary *(proportion of patients with HADS-D score >8[181]: diary 15.8% vs no diary 39.4%, p=0.07 / Risk difference of HADS-D score >8[182] (95% CI): 5 (−5 to 13), p=0.35 / Relative Risk of HADS- D score ≥ 11[150] (95% CI) 0.88 (0.14-5.73), p=1.0 / proportion of patients with HADS-D score ≥8[205] diaries 7.7% vs no diaries 27.3%; p = 0.1)*.

Level of depression symptoms was assessed after 3 months post-discharge by 2 studies[182, 205] also leading to opposite conclusions. The first study[205] found significant and clinically lower level of depression symptoms in patients benefiting from a diary in comparison to those without diary *(median HADS-A score at 90 days (IQR) diaries 3.0 (1.75–5.25) vs no diaries 5.0 (4–9), p = 0.04)*, while the

second study[182] found no difference between intervention and control groups *(HADS-A score difference (95% CI): −0.39 (−1.29 to 0.52), p=0.66)*.

Level of PTSS was assessed after 3 months post-ICU discharge by 3 studies.[150, 181, 182] The two RCTs found no difference between intervention and control groups in the mean level of PTSD symptoms at 3 months while a before-after study found a significant lower level of PTSD symptoms at 12 months in the patient group benefiting from a diary in comparison to those who did not *(mean total IES-R score (SD) at 12 months[181] diary 21.0 (12.2) vs no diary 32.1 (15.4), p=0.004 / difference in median IES-R total score (95% CI) at 3 months[182]: −1.47 (−1.93 to 4.87), p=0.38 / total PTSS-14 score, median (range)[150]: diary 21 (14-75) vs no diary 28 (14-75), p=0.44).* The MCID is 0.2 points for the IES-R scale[148] and 4 points for the PTSS-14 scale.[150]

The risk of severe symptoms of posttraumatic stress[d] after 3 months post-discharge was assessed in 3 studies.[150, 181, 182] While the tools and threshold used to define severe symptoms of PTSS differed among studies, no more patients with severe PTSS symptoms were found in patients without diary in comparison with patients with diary *(proportion of patients with IES-R score >22[181]: diary 50.0% vs no diary 69.4%, p=0.02 / Risk difference of IES-R score >22[182] (95% CI): −4 (−15 to 6), p=0.39/ Relative Risk of PTSS-14 score > 31[150] (95% CI) 0.75 (0.35-1.62), p=0.55)*.

The proportion of patients with PTSD was assessed in one study[205] and showed no difference between patients benefiting from diaries and those who did not *(proportion of patients with mean item score of IES-R ≥ 1.6 diaries 11.5% vs no diaries 18.5%; p = 0.6).*

The proportion of patients with a new onset of PTSD at 3 months follow-up was higher in patient group receiving their diaries at 3 months than those receiving it earlier *(proportion of new onset of PTSD: early handover of the diary 5% vs late handover of the diary 13.1%, p=0.02)*.[204] The early handover of the diaries had no impact on change in the PTSS-14 scores between 1 and 3 months but reduced the proportion of patients with severe PTSD symptoms. Among patients scoring PTSS-14 >45 at one month, a significantly larger decrease in PTSS-14 score was observed in those with early handover of the diaries in comparison with those with a late handover (median change in PTSS-14 between 1 month and 3 months: early handover of the diary -23 points versus late handover of the diary -2 points, p=0.04).[204]

Avoidance is studied in three publications.[181, 182, 194] No significant difference in avoidance level were found in 2 studies.[182, 194] The first study[194] assessed avoidance using 3-set 4P questionnaire. No statistically significant differences were found between patients with diaries and those without after 2, 6 and 12 months post-ICU discharge *(mean score (SD): at 2 months: diary 1.87 (0.28) vs no diary 1.87 (0.28), p=ns, at 6 months diary 1.86 (0.32) vs no diary 1.86 (0.35), p=ns and at 12 months diary 1.70 (0.48) vs no diary 1.73 (0.52), p=ns)*. The second study[182] used the avoidance sub-score of IES-R scale and found no difference at 3-month follow-up between patients benefiting from diaries in comparison to those without diary *(median difference (95% CI): −1.01 (−2.35 to 0.33), p=0.08)*. However, the third study[181] found a significant difference in avoidance sub-score of IES-R scale at 12 months between patients with diary in comparison to those without (mean (SD) diary period 6.8 (3.8) vs no diary 11.9 (6.0), p=0.0005).

Intrusion (intrusive thoughts, nightmares, intrusive feelings and imagery, dissociative-like re-experiencing) and hyperarousal (anger, irritability, hypervigilance, difficulty concentrating, heightened startle) were assessed one RCT[182] and one before-after study[181]. No difference in hyperarousal score (measured by IES-R scale) at 3 and 12-month follow-up was found between patients with and patients without diary *(difference in median score at 3 months (95%CI)[182] −0.08 (−1.11 to 0.94), p=0.64, mean hyperarousal score at 12 months (SD)[181]: diary period 5.2 (4.6) vs no diary 7.2 (4.6), p=0.095).* No difference in intrusion score (measured by IES-R scale) at 3-month follow-up[182] *(difference in median score at 3 months (95%CI)[182] −0.25 (−1.64 to 1.12),p=0.74)* but significant difference was found at 12-month follow-up[181] (*mean score at 12 months (SD)[181]: diary period 9.1 (6.1) vs no diary 12.9 (6.1), p=0.0018).*

Peritraumatic dissociation is studied 3 months post-ICU discharge in one study through the peritraumatic dissociative experiences questionnaire.[181] The authors found no significant difference in the level of perceived severity of the traumatic event after 3 months post-ICU discharge between patients with and patients without diaries *(mean score (SD) diary period 22.5 (10.1) vs no diary 27.6 (9.8) vs p=0.12).* In addition, the proportion of patients with high perceived severity of the traumatic

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[d] labelled as such by the studies

event after 3 months post-ICU discharge was also not significant different between intervention and control groups *(diary 66.7% vs no diary 78.1, p=0.3).*[181]

Memory was assessed in two study.[182, 194] The first one[194] used the 3-set 4P questionnaire to assess memory. In this paper, patients receiving a diary scored significantly more unfavourable in Memory score than patients without a diary at 2, 6 or 12 months *(mean score (SD) at 2 months: diary 4.22 (0.98) vs no diary 4.42 (0.85), p<0.05, at 6 months: diary 4.09 (1.06) vs no diary 4.48 (0.82), p<0.001 and at 12 months: diary 4.04 (1.13) vs no diary 4.57 (0.63), p<0.001)*. In contrast, the second study assessed memories from the ICU with the ICU memory tool questionnaire 3 months after ICU discharge.[182] and the authors found no statistically significant risk difference in factual, emotional and delusional memories of the ICU stay between patients with or without diary. Detailed results are available in the appendix. No information about the MICD for both tests was found for ICU survivors.

Health related quality of life

HRQoL is studied in 3 papers using SF-36 subscales.[150, 200, 203]

Physical function score was assessed in the 3 studies.[150, 200, 203] No study found a significant difference between patients who received a diary in comparison with those without diary but two studies[150, 203] reported a MCID in the physical function score *(mean SF-36 PF score (SD) at 6 months[203] diary 64.4 (30.5) vs no diary 59.7 (30.4), p=ns / mean SF-36 PF at 3 months[150] diary 45.8 no diary 38.6, p=0.46)*.

Physical component summary score was measured in 1 publication[203] showing a significant better score in patients with diaries in comparison with those without *(mean SF-36 PCS (SD) at 6 months diary 42.4 (12.1) vs no diary 38.0 (13.0), p<0.05)*. The significant difference between groups did not reach MCID threshold.

Mental component summary score was measured in the same study[203]. No significant nor clinical difference was found between patients who received a diary and those who did not received it *(mean SF-36 MCS (SD) at 6 months diary 47.2 (14.3) vs no diary 44.8 (13.2), p=ns).*

The score of General health perceptions was not significantly different at 3 months in one study[150] but was significant different at 6 months between intervention and control groups in 2 publications[200, 203] *(mean SF-36 General health perceptions score at 3 months[150] diary 53.2 no diary 47.0, p=0.36 / mean SF-36 General health perceptions score (SD) at 6 months diary 66.3 (23.4) vs no diary 52.3 (24.2), p<0.001[203] / data not shown in the last publication[200])*.

The Vitality score was significantly different at 6 months in one study [203] between patients who received a diary and those who did not (*mean SF-36 Vitality score (SD) at 6 months diary 63.2 (24.9) vs no diary 51.7 (24.7), p<0.005).* This result was not confirmed at 3 months[150] nor at 6 months in another study[200] (*SF-36 Vitality score at 3 months[150] diary 48.5 no diary 55.2, p=0.47 / data not shown in the second publication[200]).*

Other SF-36 sub-scores (role physical, bodily pain, social function, role emotional and mental health scores) were not significantly different between patients with and patients without diaries.[150, 200, 203]

Finally, social life and sleep were studied by Akerman et al.[194] using the 3-set 4P questionnaire. No positive impact of diaries was found for these two dimensions at 6 and 12 months post-ICU.

4.3.5.2 Mindfulness training

A pilot RCT[206] tested three interventions post-hospital discharge: a telephone based mindfulness training, mindfulness exercises with a mobile app and education programme using videos. Details on the content of interventions are provided in the evidence table (see appendix). The authors found similar improvement in the three groups in PHQ-9 score for depression and in PHQ-10 for physical symptoms between ICU-discharge and 3 months after hospital discharge. However, no statistically significant improvement was found in quality of life (100-point QoL VAS) and PTSS level (PTSS-10 scale) in the 3 groups during the same period. Anxiety level was significantly improved in the mindfulness app and mindfulness training by phone but not in the education programme group *(difference in GAD-7 scale between baseline and 3 months (95% CI) Education program: −0.6 (−2.5 to1.3); Mobile mindfulness: −2.1 (−3.7 to −0.5) and Telephone mindfulness −1.6 (−3.0 to −0.1)).* However, the reported improvements did not reach the MICD of 4 points.[149]

4.3.5.3 Telephone- and Web-based Coping Skills Training

A multicentre RCT[180] compared telephone- and web-based coping skills training intervention with an education programme provided during 6 weeks in ICU survivors 3 weeks after their hospital discharge. The coping skills training consisted of weekly ~30-minute telephone sessions including mainly relaxation and cognitive restructuration along with web-based material. The education programme consisted in 6 informational videos with accompanying web-based content. More details on interventions are reported in evidence table (see appendix).

The authors failed to demonstrate that a coping skills training improved significantly symptoms of depression, anxiety, PTSD, quality of life or coping response compared with an education program for both patients and family members at 3 and 6 months post-discharge. Stratification analyses showed that in patients with high baseline levels of distress (HADS summary score>14), coping skills training improved symptoms of psychological distress (HADS-summary score and HADS-D) compared with an education program at 6 months, whereas the education program decreased symptoms of psychological distress (HADS-summary score, HADS-D, EQ5-D) at 3 months among those who received ventilation for more than a 1 week. In addition, the education program also improved global mental health among the high level distressed patients at baseline. *In patients with high baseline levels of distress, mean difference at 6 months post-discharge for HADS summary -4.63 (-8.61 to -0.64), p=0.02 stemmed from a HADS-D statistically and clinically significant difference in favour of the coping skills training (mean difference (95% CI)-3.03 (-5.36 to -0.71), p=0.01) and from a HADS-A non-significant and clinically non-important difference (mean difference -1.80 (-4.21 to 0.61), p= 0.14). At 3 months, no statistically and clinically significant difference was observed. In addition global mental health assessed by PROMIS score favoured educational programme (mean difference at 6 months 2.26 (0.47 to 4.06), p=0.01) EQ-5D score is clinically and statistically significantly better in the coping skill training group that in patients benefiting from educational programme after 6 months post-discharge (11.20 (0.02 to 22.37), p=0.0496). No value for MCID and PROMIS (global mental health assessed) was found in ICU survivors. No difference was observed at 3 months in PROMIS and EQ5-D.*
In patient ventilated longer than 1 week, the mean difference (95% CI) at 3 months post-discharge for HADS summary was 4.07 (0.05 to 8.08), p=0.047 stemmed from a HADS-D statistically and clinically significant difference in favour of the education programme (mean difference 2.64 (0.21 to 5.08), p=0.03) and from a HADS-A statistically and clinically non-significant difference (mean difference - 1.29 (-1.11 to 3.69), p=0.29). At 6 months, no statistically and clinically significant difference was observed. At 3 months, a clinically and statistically significant difference in EQ-5D was observed in favour of coping skills training (-15.82 (-28.53 to -3.11), p=0.02). In contrast, global mental health assessed by PROMIS score favoured coping skill training at 3 months but not at 6 months (mean difference at 3 months - 2.18 (-4.21 to 20.15), p=0.04 and at 6 months -1.00 (-3.05 to 1.06), p=0.34).

Global physical health was assessed by PROMIS and no significant differences were found at 3 and 6 months. No value for PROMIS (global physical health assessed) was found in ICU survivors.

4.3.6 Cognitive interventions

Two studies in our review reported cognitive interventions.[190, 207]

The first study[190] was a pilot RCT testing a three dimensional rehabilitation programme associating physical rehabilitation, cognitive and functional intervention in 17 ICU survivors. Physical health, functional ability and executive cognitive function were assessed throughout a range of outcomes previously described in section 0).

The second study reported in 332 Chinese ICU survivors the effect of a cognitive intervention including 4 components (music playing, learning Spanish words, drawing a picture of clock from memory and sessions with a psychiatrist).[207] The intervention was delivered at hospital 4 days a week including 2 sessions by day during 30 minutes during 3 months. Details on the content of sessions are provided in the evidence table (see appendix). The cognition was assessed by the Montreal Cognitive Assessment[151] and showed significant and clinically important positive effects on the intervention in mean total score *(mean total score at 3 months control group 16.47 vs intervention group 25.18, p=0.043)* and also in the subset scores (i.e. executive function, visuospatial ability, short-term memory, attention, language ability and orientation- *results reported in evidence table in appendix*). The younger patients (< 40y) were more likely to recover from acute cognitive

impairments than the older patients. In older patients (60-80y), the intervention only impeded the deterioration of the cognitive function but could not restore it *(results reported in graphs)*.

4.3.7 Peer support groups

We retrieved one systematic review[176] and one additional primary study. None of the studies included in the systematic review meet our inclusion criteria. Only the primary study was retrieved, which included a multimodal intervention mixing physical rehabilitation, education sessions and group discussion forum supervised by physiotherapists.[193] No additional studies describing peer support groups met our inclusion criteria. Peer support is a process of offering advice and sharing stories between ICU survivors. The process acts by building social relationships that influence health and well-being. Peer support for ICU survivors in outpatient setting can take several forms according to the environment (in or outside hospital) or the person facilitating the support group (former patients or care providers). Four models are identified for discharged patients: the community based model, the psychologist-led outpatient model, the model based within an ICU follow-up clinic or the online model.[101] Experiences of peer support groups with ICU survivors are described in the literature.[208]

The study started later (6 weeks post-discharge) but lasted less (7 weeks).[193] This trial focused on 73 patients invasively ventilated for ≥5 days and proposed a multimodal intervention mixing exercise and education sessions supervised by a physiotherapy team. The exercise sessions consisted in 1 supervised and 2 self-directed sessions each week. In addition, education sessions of 1 hour were foreseen and covered benefits of exercise, relaxation techniques, managing breathlessness, smoking cessation, anxiety management as well as a group discussion forum.[193]

The study found a significant and clinical improvement of HRQoL in patients included in the intervention group compared to the control group. Detailed results of this study are reported in section 0.

4.3.8 PICS-F

As mentioned above, PICS-F refers to the psychological effects of ICU stay on the critically ill patients' family or patients' relatives. The symptoms can appear during the ICU stay, after the patient hospital discharge or following the death of the patient.[209] We retrieved one review related to interventions in PICS-F including 11 publications. Among those, 6 did not meet our inclusion criteria. We found 3 additional papers. Finally, 8 publications[150, 178-184] reported health outcomes of patients' relatives. Diaries were the intervention under study in 4 papers.[150, 181-183] Other interventions under study were physical rehabilitation[184], follow-consultations[179], telephone and web-based coping skills training[180] and condolence letter.[178]

Table 15 – Overview of included studies – Interventions for relatives (PICS-F)

Study ID	Design	Patients	Country	Start of intervention	Intervention	Control	Max. follow-up	Tools for outcome assessment
Bohart 2019[179]	RCT	181 relatives of patients included in Jensen 2016[195]	Denmark	1 month post-ICU	3 consultations to construct the illness narrative with photographs and ICU visits at 10 months post-ICU	ICU discharge without follow-up	12 months	SF-36, SOC, HADS, HTQ-IV
Jones 2004[184]	RCT	104 relatives of patients	UK	8 weeks after discharge to home	Material on relaxation and coping with stress for relatives.	Verbal information on the ICU recovery	6 months	HADS, IES
Jones 2012[183]	RCT	36 family members of patients	UK and Sweden	As soon as possible (< 2	Diary discussed with the study nurse at 1 month follow-up	Same intervention but received their diaries	3 months	PTSS-14

		≥ 16y ICU LOS ≥ 72 h Ventilation ≥ 24 h		months post-ICU)	visit. A second one at 3 months	only at 3 months post-ICU		
Kentish-Barnes 2017[178]	RCT	208 relatives of patients ≥18y ICU LOS ≥ 2 days	France	2 weeks after death	Condolence letter written by physicians and nurses	Standard care without condolence letter	6 months	HADS, IES, Inventory of complicated grief

See also Cox 2018[180], Garrouste-Orgeas 2012[181], Garrouste-Orgeas 2019[182] and Nielsen 2020[150] in Table 14.

4.3.8.1 Physical rehabilitation and follow-up consultations

In 2004, Jones et al[184] described the effect on the relatives of ICU survivors of an intervention targeting both patients[192] and relatives (n=104)[184]. The intervention included a textbook covered areas such as nutrition, what to expect when the patient goes home and exercise with sections on relaxation and coping with stress that the relatives were encouraged to use.

Outcomes related to patients are reported above (see section 0)

The authors assessed depression, anxiety and PTSS levels in relatives 6 months post-ICU. They found no difference in anxiety, depression or PTSS level between relatives receiving a ICU rehabilitation manual, and relatives receiving general verbal information about recovery from ICU (*HAD anxiety score [median (range)]: Intervention group 7 (0–20), Control group 8 (0–17), p=0.72) – HAD depression score [median (range)]: Intervention group 3 (0–12), Control group 4 (0–16), p=0.29) – IES scores [median (range)]: Intervention group 16 (0–61), Control group 25 (0–69), p=0.20*). An association was found at 6-months follow-up between psychological distress in the patients and high IES scores in their relatives (*Patients' IES scores at 6 months Spearman's rho 0.40, p=0.0001, Patients' HAD anxiety scores at 6 months Spearman's rho 0.32, p=0.001 and Patients' HAD depression scores at 6 months Spearman's rho 0.23, p=0.015*).[184]

4.3.8.2 Follow-up consultations

One publication assessed the effect of a nurse led follow-up intended for ICU survivors on their relatives (n=181). The patient's outcomes are described above in section **Error! Reference source not found.**). Regarding relatives, the authors concluded that no statistically significant effect of the recovery programme was found on relatives' health related quality of life, sense of coherence, symptoms of anxiety, depression and PTSD at 3 or 12 months post-ICU.[179]

Anxiety

The level of anxiety was assessed by the HADS – A score. No significant difference nor clinically important difference was observed between follow-up group and no follow-up group and no difference in the improvement of anxiety symptoms was found between 3 and 12 months *(mean difference (95% CI) at 3 months after ICU: -0.40 (-1.89 to 1.1), p=0.43 and at 12 months after ICU-0.73 (-2.18–0.72), p=0.99, mean difference of score difference between 3 and 12 months (95% CI): -0.93 (-2.13–0.28), p=0.89)*.

Depression

The level of anxiety was assessed by the HADS – D score. No significant difference nor clinically important difference was observed between follow-up group and no follow-up group and no difference in the improvement of depression symptoms was found between 3 and 12 months *(mean difference (95% CI) at 3 months after ICU: -0.75 (-1.95 to 0.45), p=0.97 and at 12 months after -0.68 (-1.89 to 0.54), p=0.16, mean difference of score difference between 3 and 12 months (95% CI): -0.33 (-1.25 to 0.59), p=0.89)*.

PTSD

Symptoms of PTSD were assessed by HTQ-IV. After 3 and 12 months, no significant difference in HTQ-IV score or in progression of PTSD symptoms were observed between groups *(mean difference (95% CI) at 3 months after ICU: -2.72 (-5.94 to 0.50), p=0.10 and at 12 months after -1.07 (-4.73 to*

1.85), p=0.56, mean difference of score difference between 3 and 12 months (95% CI): -0.25 (-2.05 to 2.55), p=0.83).

Cognitive disorders

Sense of coherence was measured by the Sense of Coherence Scale (SOC-13). The scale ranges from 13 to 91 and higher scores indicate stronger sense of coherence. After 3 and 12 months, no difference in SOC-13 or in progression of coherence were observed between groups *(mean difference (95% CI) at 3 months after ICU: 1.52 (-3.22 to 6.26), p=0.53 and at 12 months after 2.21 (-3.37 to 7.80), p=0.43, mean difference of score difference between 3 and 12 months (95% CI): 1.44 (-3.22 to 6.10), p=0.54)*.

Health related quality of life

HRQoL was assessed by SF-36 scale. No significant difference nor clinically important difference was found in both SF-36 MCS and SF-36 PCS at 3 and 12 months post ICU discharge *(mean difference in SF-36 MCS (95% CI): at 3 months after ICU -0.13 (-4.23 to 3.99), p=0.95 and at 12 months after ICU 1.35 (-3.13 to 5.82), p=0.55, mean difference of score difference between 3 and 12 months -0.73 (-5.16 to 3.70), p=0.75, mean difference in SF-36 PCS (95% CI): at 3 months after ICU 2.85 (-0.63 to 6.32), p=0.11 and at 12 months after ICU 1.86 (-1.88 to 5.59), p=0.33, mean difference of score difference between 3 and 12 months 0.24 (-2.40 to 2.88), p=0.86).*

4.3.8.3 Mental health interventions

Diaries

Four publications[150, 181-183] analysed the impact of diary on the relatives of former ICU patients. The patients' health outcomes are discussed in a previous section 4.3.5.1

- Anxiety

Three publications assessed anxiety in relatives of former ICU patients using the HADS- A scale.[150, 181, 182] No significant risk of anxiety in relatives of patients receiving a diary was found after 3 months *(RR of HADS- A score ≥ 11 (95% CI) 0.80 (0.28-2.33), p=0.76).*[150] One before-after study in 136 relatives found a significant higher proportion of anxious relatives in the no diary group *(proportion of relatives with HADS-A score >8 at 3 months post discharge: diary group 38.3% vs no diary group 59.6%, p=0.08)*.[181] Later, the same first author conducted a larger scale RCT in 281 family members and found no significant difference in anxiety level and risk of anxiety in relatives of patients receiving a diary *(HADS-A score median difference (95% CI): 0.28 (−0.47 to 1.04), p=0.65, risk difference of HADS- A score > 8 (95% CI): 2 (−6 to 11), p=0.56).*[182] The MCID was not reached for anxiety. Moreover, the same trial found no significant difference in HADS total score between intervention and control groups *(median HADS total score (IQR) (95% CI): 0.33 (−0.96 to 1.63), p=0.45).*[182]

- Depression

The same 3 publications assessed depression in relatives of former ICU patients.[150, 181, 182] All authors used the HADS-D scale and found no significant nor clinically important difference in depression level (HADS-D median score difference (95% CI): 0.05 (−0.67 to 0.78), p=0.96)[182], no significant difference in proportion of relatives with severe symptoms of depression *(proportion of relatives with HADS-A score >8 at 3 months post discharge: diary group 22.0% vs no diary group 21.7%, p=0.8)*[181] and no significant difference in risk of depression *(RR of HADS- A score ≥ 11 (95% CI) 0.67 (0.17-2.64), p=0.72*[150] *and , risk difference of HADS- A score > 8 (95% CI): 0.05 (−0.67 to 0.78), p=0.96).*[182]

- PTSS & PTSD[e]

Four papers studied posttraumatic stress related symptoms in patients' relatives.[150, 181-183]

Two studies used PTSS-14 score to assess posttraumatic stress related symptoms in relatives of patients.[150, 183] One study[150] found a significant lower score and a clinically important difference in relatives of patients with diary in comparison with relatives of patients without diary *(median PTSS-14 total score (range) at 3 months: diary group 26 (14-64) vs no diary group 32 (14-77), p=0.01)*. The same study did not find a higher risk of severe symptoms of PTSD in relatives of patients with diary in comparison with relatives of patients without diary *(RR of PTSS-14 score > 31 (95% CI) 0.65 (0.39-*

[e] labelled as such by the studies

1.09), p=0.13).[150] In addition, another study showed a significant and clinically important improvement of PTSS-14 score in relatives of the diary group in comparison with relatives in the no diary group *(median change in the PTSS-14 scores between 1 and 3 months: diary group -5 vs no diary group +5 vs, p=0.03)*.[183] Two other studies[181, 182] assessed PTSD symptoms in patients' relatives by IER-S score. The first one is a before-after study and found significantly higher scores of PTSS in patients' relatives without handover of diary *(mean IER-S score (SD) at 12 months no-diary group 31.4 (13.6) vs diary group 21.6 (10.7), p=0.0003)*.[181] The MICD was reached. Intrusion and avoidance score were also significantly higher in relatives of patients without diary *(detailed results shown in evidence table in appendix)*. In addition, the proportion of PTSD in patients' relatives without diary was significantly higher in comparison to those with diary *(proportion of patients' relatives with IES-R score >22 at 12 months diary group 31.7% vs no diary group 74.3%, p<0.0001)*.[181] In contrast, a RCT of the same author[182] found no significant difference but a clinical important difference in IES-R score *(median IES-R total score difference at 12 months (95% CI): 0.48 (−2.51 to 3.47), p=0.87)*. Sub-scores for intrusion, avoidance, hyperarousal were not significantly different between intervention and control groups. The risk difference for the presence of PTSD symptoms (defined as IES-R score>22) was not significantly different *(risk difference at 12 months (95% CI): 3 (−6 to 11), p=0.53)*.[182]

Peritraumatic dissociation was assessed in one paper.[181] The authors found no significant difference in level of peritraumatic dissociation between diary and no diary groups *(mean score at 3 months (SD): diary group 16.8 (9.1) vs no diary group 19.0 (7.9), p=0.3)* nor a significant difference in the proportion of relatives with peritraumatic dissociation *(proportion of relatives with score >15 at 3 months: diary group 37.0% vs no diary group 58.9, p=0.07)*.

- Health related quality of life

Nielsen et al[150] found no significant difference in SF-36 subscales at 3 months in relative who received a diary in comparison with those who did not. Detailed results reported in appendix for physical function, role physical, bodily pain, global health, vitality, social function, role emotional and mental health.

Telephone and web-based coping skills training

A multicentre RCT[180] studied the effect on 76 relatives of telephone- and web-based coping skills training intervention with an education programme. Details on intervention can be found above (see section 0) and in the evidence table in the appendix.

- Anxiety

No significant difference nor clinically important difference was found in anxiety level assessed by HADS-A *(difference between groups in HADS-A score (95% CI) at 3 months 0.8 (-0.6 to 2.2), p=0.27 and at 6 months 0.8 (-0.6 to 2.2), p=0.26)*. In addition, the global HADS score was also not significant nor clinically different *(difference between groups in HADS score (95% CI) at 3 months 1.4 (-0.9 to 3.7), p=0.23 and at 6 months 1.1 (-0.9 to 3.2), p=0.26).*

- Depression

No significant difference nor clinically important difference was found in depression level assessed by HADS-D (*difference between groups in HADS-D score (95% CI) at 3 months 0.7 (-0.7 to 2.1), p=0.31 and at 6 months 0.5 (-1.0 to 1.9), p=0.52).*

- PTSD

No significant difference was found in IES-R score between patients' relatives in intervention and control groups *(difference in IES-R score between groups (95% CI) at 3 months -0.5 (-8.0 to 7.0), p=0.89 and 6 months 3.8 (-4.4 to 12.0), p=0.36)*. However, MCID was reached (see Box 7).

- Global physical and mental health

Global physical and mental health were assessed by PROMIS (Patient-Reported Outcomes Measurement Information System). Higher scores reflect better global health. No significant difference between intervention and control group was found for both global physical health and global mental health *(difference in PROMIS score between groups for global physical health (95% CI): at 3 months -0.1 (-1.0 to 0.8), p=0.79 and at 6 months -0.2 (-1.0 to 0.7), p=0.71/ difference in PROMIS score between groups for global mental health (95% CI): at 3 months -0.03 (-1.2 to 1.1), p=0.96 and at 6 months -0.7 (-1.8 to 0.4), p=0.20)*.

- Coping responses

In this trial, coping responses were evaluated with the Brief COPE score. Once again, no significant differences were found between intervention and control groups *(difference in Brief COPE score between groups (95% CI): at 3 months 1.1 (-2.0 to 4.2), p=0.47 and at 6 months -1.0 (-4.8 to 2.8), p=0.61).*

- Self-efficacy

Finally, self-efficacy in patients' relative was studied with a four-item scale in which higher scores reflect better self-efficacy. No significant difference in relatives' self-efficacy was found between intervention and control groups *(difference in score between groups (95% CI): at 3 months 0.3 (-0.5 to 1.0), p=0.48 and at 6 months 0.3 (-1.2 to 0.6), p=0.47).*

4.3.8.4 Condolence letter

One RCT performed in 22 ICUs in France studied the impact on mental health of a handwritten condolence letter sent to the 208 relatives of patients who died in the ICU.[178] The findings did not support a condolence letter as a tool to alleviate grief symptoms. No significant difference in the proportion of relatives at high risk for complicated grief was found between relatives receiving a condolence letter compared to those who did not *(Intervention group 37.6% Control group 27.0%, p=0. 11)*. Moreover, the authors found that the condolence letter may have worsened depression and PTSD-related symptoms. After 6 months, a statistically and clinically significantly higher score for anxiety and depression symptoms was observed in the intervention group *(HADS summary score [median score (IQR)]: Intervention group 13 (6–19) Control group 9 (4–17), p=0.04)*. The proportion of relatives with PTSD-related symptoms (defined as IES-R ≥26) was significantly higher in relatives with condolence letter in comparison with those who did not received it (*Intervention group 52.4% Control group 37.1%, p=0.03)*. The clinicians writing the letter assessed the task as easy, not difficult and not time consuming. They perceived the letter as helpful for the relatives but not helpful for themselves. The authors concluded that a condolence letter alone may have been insufficient to provide benefits to relatives.

4.4 Discussion

Since 2012, the wide range of long-lasting problems that may occur post-ICU discharge is grouped under the term of PICS. Unfortunately this term is not yet listed as a Mesh-term by NCBI.[210] Until now, efforts in the scientific community were focused on the epidemiology, the prevention and the risk factors of PICS. However, treatment interventions for PICS-related outcomes are less studied and less understood.[210] Our literature research with search date up to May 2020 did not identify studies dedicated to the treatment of PICS in COVID patients. We focused our search on interventions that address the typical health problems of ICU survivors with PICS syndrome such as ICU-acquired weakness, depression, anxiety, PTSD or cognitive impairments that are occurring or persisting at 3 months or later. We did not take into consideration interventions studies that measured these outcomes in the short term only, i.e. before 3 months post-ICU discharge.

We identified 31 primary studies reporting five main types of interventions i.e. physical rehabilitation programmes (11 studies), follow-up consultations (8 studies) mental health interventions (10 studies); cognitive interventions[190, 207] and interventions for PICS-F (8 studies).

Box 8 – Overview of the most frequently found post-ICU interventions targeting ICU survivors

Physical rehabilitation programmes can include supervised and/or self-directed exercises. The supervision can occur online or face-to-face, at home or at hospital gymnasium, and can be provided by a physiotherapist, a trainer or a nurse. Rehabilitation programmes can start as early as during the ICU stay or after ICU discharge or after hospital discharge. During the rehabilitation, other interventions such as educational material or sessions, follow-up consultations, cognitive interventions or nutritional supplements may be added to exercises.

Mental health interventions may encompass ICU diaries, referral to mental health professionals (e.g. psychologists), mindfulness training or coping skills training. Some aspects are also included in the follow-up consultation.

Follow-up consultations often take place at the hospital and can include one of the following elements: discussion related to the recovery after an ICU stay, nutrition or ICU memories with or without the support of an ICU diary, assessment of health problems with sometimes referral when problems are detected or a feedback letter to the GP. These consultations are provided by either nurses, physicians or a multidisciplinary team. This later can be made up of nurses, physicians, physiotherapist or GP.

ICU diaries aim to fill the ICU survivors' memory gaps due to absent or fragmented factual memories and to support ICU survivors to cope with delusional memories. Diaries help patients to understand the chain of events during the ICU stay to avoid as much as possible mental consequences of thisstay. ICU diaries may take several forms. They can be written by care providers, by close relatives or by both. Photographs of the ICU stay are sometimes included in it. Diaries can be handed over to the patients either at ICU discharge or during a follow-up visit. The reading of the diary can be supervised or not by a health professional (mainly ICU nurses) during the hospital stay (post ICU discharge) or during face-to-face follow-up visits after hospital discharge. The content of the diary is discussed with the patients, eventually in presence of the relatives.

Educational material can take different forms such as paper textbook, digital handouts, online webpages or videos. The content of educational material covers various issues faced by ICU survivors such as ICU recovery process, nutrition advices, psychological or psychosocial problems, physical limitations (e.g. breathlessness), benefits of physical exercises, PICS-F… Educational material allows a passive transmission of information.

Educational sessions allow a face-to-face transmission by a health professional of information similar to that reported in educational material (see above).

Peer support is a process of offering advice and sharing stories between ICU survivors. The process acts by building social relationships that influence health and well-being. Peer support for ICU survivors in outpatient setting can take several forms according the environment (in or outside hospital) or the person facilitating the support group (former patients or care providers). Four models are identified for discharged patients: the community based model, the psychologist-led outpatient model, the model based within an ICU follow-up clinic or the online model.[101]

These studies are characterised by a large range of intervention content (alone or in combination) and heterogeneity in study populations, study design, timing and tools of outcome assessment. Outcomes of published studies were physical health, mood disorders (including depression and anxiety), PTSS and PTSD, quality of life, cognition, ADL, memories, social support and nutrition. Table 16 presents on overview of the evidence of the effect of included interventions, defined as a statistically significant effect, on these outcomes.

Table 16 – Overview of the retrieved interventions on a set of outcomes

Intervention / Outcomes	Physical rehabilitation	Follow-up consultations	Diaries	Cognitive intervention	Mindfulness training	Coping Skills Training
Physical health	No evidence of improvement in 6 studies[146, 152, 187, 189, 190] but improvement in 6MWT*[191] in 1 study and in balance (Berg Balance test) in 1 study[186]	No evidence of improvement in 1 study[194] but evidence in improvement in 1 study at 6 months (not later at long term, 12 and 24 months) [198, 199]	No evidence of improvement (1 study)[194]		No evidence of improvement in 1 study[206]	

Mood		No evidence of improvement in mood in 1 study at 6 months. At 12 months negative effect was observed (3 set-4P questionnaire) [194]	Evidence of fewer mood problems after 12 months (3 set-4P questionnaire) [194]		No evidence of improvement in 1 study[180] but improvement in patients with high baseline levels of distress. Unfavourable effect for global mental health of the same patient subgroup at 6 months. In patients ventilated >7days, evidence of improvement at 3 months.
Depression	No evidence of improvement in 4 studies[185-188] but 1 study[191] combining exercises and nutrition found a reduction of depression at 3 months (HADS-A≥11)	No evidence of improvement in 5 studies [188, 195-199]	No evidence of improvement in 2 studies [150, 182] and evidence of improvement in 2 studies [181, 205] (HADS-D*)	No evidence of improvement in 1 study[206]	No evidence of improvement in 1 study[180] but improvement in patients with high baseline levels of distress at 6 months and unfavourable effect in patients ventilated >7days in the same study at 3 months
Anxiety	No evidence of improvement in 5 studies[185, 187, 188, 191, 192] but 1 study[186] found a positive effect on depression level at 12 months (HADS-A*) and 1 study[191] combining	No evidence in 4 studies [188, 192, 195, 197]. In addition unfavourable effect in level of anxiety in 1 study (HADS-A)[196]	No evidence of improvement in 3 studies[150, 181, 182] and evidence of improvement in 1 study[205] (HADS-A*)	Evidence of improvement but MCID not reached in one study[206]	No evidence of improvement in 1 study[180] but improvement observed in patients with high baseline levels of distress in the same study

	exercises and nutrition found a reduction of depression at 3 months (HADS-A≥11)				
PTSD	No evidence of improvement in 2 study [188, 192]	No evidence in 3 study[188, 192, 196]	No evidence of improvement in 3 studies[150, 182, 205] but evidence of improvement in 1 study[181] (IES-R*)		
Quality of life	No evidence of improvement in 5 studies[152, 185, 187-189] but 1 study found improvement at 3 months (SF-36 PF*)[146]. Improvement in patients ventilated > 14 days in 1 study (SF-36 PCS*, SF-36 MCS*)[193].	No evidence no improvement in 4 studies[188, 195, 198-200]	No evidence of improvement in 2 studies[150, 200] and evidence of improvement in 1 study[203] (SF-36 PCS*)		No evidence of improvement in 1 study[180] but improvement in patients with high baseline levels of distress in the same study
Cognitive outcomes	Improvement in cognitive performance and functional outcomes in 1 study combining cognitive, physical, and functional training[190]	No evidence of improvement of sense of coherence in 2 studies[194, 198, 199]		Evidence of improvement in 1 study[207] especially in younger patients	
ADL	Improvement of instrumental ADL but not in ADL (1 study) [190]	Evidence of improvement at 6 and 12 months (1 study) [198] but not in 24 months (1 study)[199]			
Social support	No evidence of improvement.[192]				

PICS-F	No evidence of improvement for anxiety, depression and PTSS (1 study) [184]	No evidence of improvement for anxiety, depression, PTSD, HR QoL and cognition (1 study) [179]	Evidence of improvement for PTSD (4 studies*) [150, 181-183] No evidence of improvement for anxiety (2 studies) [150, 181, 182] and evidence of improvement in 1 study[181] No evidence of improvement for depression (3 studies) [150, 181, 182] and HR QoL (1 study) [150]		No evidence of improvement for anxiety, depression and PTSD (1 study) [180]

** indicates that clinically important effect was found*

Many methodological challenges were faced by the investigators of studies dealing with long-term consequences of critical illness such as defining the target population (overall ICU patient population or one critical illness specific population), computing the adequate sample size, managing the attrition rate (or rate of patients lost to follow-up during the study) in a context of high mortality, standardizing of outcome assessment and evaluating the effect of co-variates on outcomes.[211] The studies included in this review all face these challenges. The risk of bias in retrieved evidence is overall high (see appendix).

Interventions

Some interventions are a mixture of interventions precluding to distinguish the effect of a single intervention from the effect of the intervention combination. In addition, the content and the time to initiate an intervention varied widely (from ICU stay to discharge to home).

Outcome assessment

Overall, the number of studies by outcome is low. In addition, no standardisation between studies was observed in term of definition of outcomes (e.g. some publications studied PTSD and other PTSS), of tools and scales used to assess these outcomes and of assessment timing. Finally, statistical reporting of the outcome was very poor in some studies.

Heterogeneity in study populations

In this review, one of the inclusion criteria was the population who had to represent an overall case mix of ICU population. While some studies included a low proportion of neurological diagnoses, one study[207] included 22% patients with neurological intensive problems. This high proportion of patients with neurological care may affect the effect of interventions on cognitive outcomes. In addition, a long mean of ICU stay duration (28 days) and relatively young patients *(Age [mean (SD)]: Control group 52y (31) Intervention group 50y (29), p=0.82)* may also preclude the inference to our population of interest.

Sample size

The sample size in a RCT is important to evaluate the ability of the trial to detect difference between intervention and control groups. Among the 23 retrieved RCT, 4 trials were pilot RCT and, by definition, their main objective is to test the feasibility of the trial and no to test the effect of an intervention.[187, 190, 205, 206] A small sample size was thus observed in all these trials.

Twelve publications[146, 150, 182, 184, 189, 192, 193, 195, 197-199, 204] reported a sample size calculation of which only 4 achieved the calculated sample size.[195, 198, 199, 204]

Three studies[146, 186, 187] testing the effect of rehabilitation programs on patients' outcomes found no statistically significant difference between intervention and control groups for the studied outcomes (6MWT[186, 187], SF-36 PF[146], SF-36 PCS[146, 187], HADS-A and HADS-D[187]) but this difference reached the MCID threshold. This is explained by a sample size issue (62 patients in a first publication[186], 20 patients in the second (a pilot RCT[187]) and 150 patients in the last paper that did not reach the minimum sample size calculation[146]). SF-36 PF was also assessed in one RCT[150] assessing the effect of diaries among ICU survivors. This trial found also a non-statistically significant difference between intervention and control groups but reached the MCID threshold. Once more, the trial was underpowered. Large scale studies are needed to confirm the findings of these studies. In contrast, some studies found significant differences in some outcomes between intervention and control groups but these differences did not reach the MCID. In this case, the effect of the intervention must also be considered from patients' perceptive (i.e. the effect experienced by the patients) and additional researches are needed to confirm that MCID is not reached and the potential low added value of the intervention for patients.

Pooling of study results

To address the sample size issue, some authors[144, 156, 165, 172, 174] performed a meta-analysis to gain in power in analyses. An overview of these meta-analyses is shown in appendix. However, we decided not to perform or report meta-analyses because of critical methodological issues due to the large heterogeneity in intervention content, the long recruitment periods leading to possible variations in routine care, the variation in study populations, the study design, the timing and the tools of outcome assessment, the small number of studies and, the low quality. For similar methodological reasons, authors of Cochrane reviews in the topic [171, 175, 187] did not pooled the study results.

Because of the inability to combine data, it was impossible to estimate the average effect of physical rehabilitation on the studied outcomes. It was also impossible to favour directed exercises over self-directed exercises or combination of physical rehabilitation with other interventions such as follow-up consultations, educational sessions, nutritional supplement or cognitive intervention.

In addition, our review retrieved insufficient evidence to determine whether ICU follow-up services are effective. Based on the retrieved evidence, we cannot draw any conclusion on the organisation of such follow-up services (nurse-led follow-up clinics versus multidisciplinary clinics) or amount, timing and content of sessions. However, we anticipate that follow-up services will continue to be developed in a response to an increasing number of ICU survivors with PICS-related outcomes due to COVID. Cost-benefit analysis of such follow-up services has to be studied before large generalisation.

While high satisfaction was observed in patients who received an ICU diary and the burden to write of diary has been rated as low by ICU practitioners, the effectiveness of diaries in improving patients' and relatives' psychological recovery after an ICU stay is supported by insufficient evidence. In addition the best way to deliver the intervention (inclusion of patient photographs during the care or handover of diaries without any support of care givers) raises questions. Finally, there is insufficient evidence for other interventions to draw conclusions regarding their efficacy in ICU-survivors in COVID patients or in overall context.

In conclusion, there is insufficient evidence to recommend one intervention rather than another intervention. However, it is also important to note that no adverse events were reported in all interventions except for condolence letter that is associated with a negative impact on mental health of the ICU survivors' relatives. In this context of absence of evidence (in contrast with evidence of absence), initiatives to develop interventions to prevent or to treat PICS in ICU survivors have to be supported especially in the context of the COVID crises.

4.5 Conclusions

Key points

- **Because PICS is a relatively new concept, we focused our literature research on interventions that address the typical health problems of ICU survivors with PICS syndrome such as ICU-acquired weakness, depression, anxiety, PTSD or cognitive impairments that are occurring or persisting at 3 months or later. In addition, we searched also interventions targeting PICS-F.**
- **We identified 31 primary studies reporting five main types of interventions i.e. physical rehabilitation programmes (11 studies), follow-up consultations (8 studies)188, 192, 194-200 mental health interventions (10 studies); cognitive interventions (2 studies) and interventions for PICS-F (8 studies).**
- **The small number of studies, their low quality and large heterogeneity in intervention content, the long recruitment period leading to possible variations in routine care, the variation in study populations, study design, timing and tools of outcome assessment prevented us from any pooling of results.**
- **A large number of studies are underpowered and therefore, would not have the sufficient power to detect a potential effect of the interventions. Larger scale RCTs are needed to shine a light on the potential effect of these interventions.**
- **We found limited evidence of the effectiveness of interventions on PICS-related outcomes that were statistically significant and clinically important.**
  - **Among 11 studies reporting physical health outcomes[146, 152, 186, 187, 189-191, 194, 206, 212, 213], 1 study on physical rehabilitation found statistically significant and clinically important improvement in 6MWT.**
  - **Depression was studied in 15 studies. One stud combining exercises and nutrition found a reduction in depression at 3 months and 2 studies using diaries found a statistically significant and clinically important improvement in the level of depression.**
  - **Anxiety was reported in 15 studies. One study found a significant and clinically positive effect on depression level at 12 months. Another study combining exercises and nutrition found a reduction in anxiety at 3 months. A last study[205] using diaries found statistically a significant and clinically important improvement in the level of anxiety.**
  - **PTSD was studied in 7 publications. Among those, 1 study reporting the effect of diaries found a statistically significant and clinically important difference in PTSD score (IES-R).**
  - **Cognitive outcomes were reported in 5 studies. Improvement was found in 2 studies involving cognitive training alone or a combination of cognitive, physical and functional training.**
  - **HRQoL was assessed in 13 studies. One 1 study reporting physical rehabilitation rehabilitation found a statistically significant and clinically important improvement in SF-36 PF at 3 months. Another study combining physical rehabilitation with educational sessions found a statistically significant and clinically important improvement in SF-36 PCS, SF-36 MCS but only in patients ventilated > 14 days. A last study on diaries found a statistically significant and clinically important improvement in SF-36 PCS.**
- **Some studies also found statistically significant but not clinically important effect of the intervention under study. Additional research is needed to further assess the added value of these interventions for the patients.**
- **The effect of rehabilitation programs, follow-up consultations, diaries and coping skill training on mental health of ICU survivors' relatives was assessed in 7 studies. No improvement was found for anxiety, depression and HRQoL. A statistically significant**

and clinically important improvement in posttraumatic stress related symptoms was found in 4 studies reporting interventions using ICU diaries.

- **The low level of evidence makes it impossible to recommend one intervention rather than another one (physical rehabilitation, follow-up consultations, diaries or other mental health intervention) neither a combination of interventions.**
- **Overall no side effect of interventions were reported. However, some interventions may have a detrimental effect, as was observed in one study reporting the effect of a handwritten condolence letter.**
- **In this context of absence of evidence (in contrast with evidence of absence), initiatives to develop and study interventions to prevent or to treat PICS in ICU survivors and their family members have to be supported, especially in the context of the COVID pandemic. Currently, 21 trials are ongoing on PICS. Among those, 5 are focusing on PICS in COVID patients and 2 on PICS-F. Two others trials are targeting PICS and PICS-F. The full list of these trials is available in appendix.**

5 CHAPTER 5 : PRISE EN CHARGE DES PROBLÈMES LIÉS AU PICS EN BELGIQUE : ÉTAT DES LIEUX DES INITIATIVES EXISTANTES

Si la Belgique ne compte que quelques unités spécifiquement dédiées à la prise en charge des PICS à l'heure de la rédaction de ce rapport, il apparait néanmoins que certains aspects du PICS sont susceptibles d'être déjà pris – au moins partiellement – en charge via des programmes et services de soins existants, soit parce que les patients présentent un tableau clinique similaire aux patients soignés dans ces services, soit parce que l'offre thérapeutique est susceptible de couvrir leurs besoins. Cette section vise à identifier les initiatives existantes dans le paysage sanitaire belge qui permettent d'offrir une réponse partielle ou complète aux besoins des patients souffrant d'un PICS ainsi qu'à leurs proches (PICS-F). La revalidation respiratoire n'a pas été incluse dans le présent rapport : sans nier leur caractère invalidant, les complications de type respiratoire apparaissent généralement dès le séjour aux soins intensifs et font rarement l'objet d'une première détection par le médecin généraliste (voir Introduction).

Les informations de ce chapitre reflètent la situation en Belgique de mai à juillet 2020, sur base des informations recueillies auprès des sources décrites ci-dessous. Il faut toutefois souligner que les initiatives sont susceptibles d'évoluer dans le temps, en particulier les règles de remboursement ou les services de prise en charge des patients COVID. Celles postérieures à juillet 2020 n'ont donc pu être inclues. À noter également, concernant le COVID, l'INAMI a mis en place une cellule spécifique susceptible de répondre aux questions des différents professionnels de santé. Le praticien désireux d'obtenir des informations plus récentes est donc invité à consulter le site de l'INAMI et/ou à prendre contact avec la cellule COVID de l'INAMI.

Ce chapitre ne fait donc pas un inventaire des structures et services existant en Belgique, mais présente, à l'intention des médecins généralistes, les options de prise en charge des différents problèmes de santé liés au PICS. Certains services disponibles en Belgique sont décrits à titre d'exemple. Les soins donnés au sein de ces services ne font pas l'objet d'une description détaillée : le public-cible de ce chapitre étant les médecins généralistes, les informations reprises dans ce chapitre sont les informations estimées comme les plus pertinentes à l'exercice de leur pratique.

De même, ce rapport se centre sur les services s'adressant aux patients sortis de l'hôpital et susceptibles de consulter leur médecin généraliste. Les services hospitaliers ne sont donc pas couverts (à l'exception des services de revalidation).

Dans ce rapport, nous désignerons par l'appellation générique de « revalidation » les services et/ou soins multidisciplinaires relevant de la médecine physique et de la réadaptation, ainsi que les services et soins proposant de la rééducation.

5.1 Méthode de travail

En l'absence de centralisation des informations, nous avons opté pour une démarche exploratoire par boule-de-neige. Nous avons d'abord parcouru la nomenclature des soins de santé et le site web de l'INAMI pour avoir une vue globale de l'offre en matière de revalidation correspondant aux différentes dimensions du PICS. Nous nous sommes particulièrement intéressés aux conventions établies par l'INAMI, en raison de leur aspect multidisciplinaire, du soutien au partage d'expertise qu'elles permettent, de l'accent mis sur l'éducation thérapeutique du patient et sur le soutien psychosocial, et du rôle donné au médecin généraliste qui, dans bien des cas, est la première porte d'entrée vers une convention.

En parallèle, nous avons pris contact avec des experts et/ou des acteurs de terrain susceptibles d'apporter des éclairages concrets sur une ou plusieurs dimensions des PICS. Ces personnes ont été identifiées soit par leur participation à un projet antérieur du KCE, soit via le réseau de contacts personnels de l'équipe, ou encore par recommandation d'une personne préalablement contactée. Comme souligné en préambule de ce rapport, bien que les PICS fassent de plus en plus l'objet d'études et d'interventions cliniques, celles-ci restent encore dispersées et peu connues, ce qui limite l'identification d'experts. Le caractère polymorphe des PICS nécessite par ailleurs des compétences cliniques larges, compliquant encore le recrutement de ces experts. De plus, la situation sanitaire particulière liée au COVID-19 et les délais de travail ne nous ont pas permis d'organiser une réunion d'experts. Par conséquent quelques-unes des informations présentées dans ce rapport reposent sur l'expérience et l'expertise d'une seule personne.

Ont accepté de répondre à nos questions : l'INAMI (plus particulièrement le centre d'expertise sur les incapacités de travail, la cellule COVID19, les sections Kinésithérapie et Psychologie du service des soins de santé, la section rééducation fonctionnelle de la Direction établissements de soins), les mutuelles, les responsables des cliniques post-soins intensifs du CHU de Liège et de l'Hôpital Erasme[f], un psychologue spécialisé dans le traitement du PTSD, trois kinésithérapeutes (en milieu hospitalier, indépendant et en maison médicale), le Centre Hospitalier de Wallonie Picarde (CHwapi) à Tournai, le centre de revalidation Inkendaal à Vlezenbeek, le centre neurologique et de réadaptation fonctionnelle de Fraiture, la clinique de la mémoire du CHU de Liège, et les services sociaux du CHU Saint-Pierre (Bruxelles) et des Cliniques Universitaires Saint-Luc. Tous les noms des personnes contactées sont mentionnés dans le Colophon du présent rapport.

Pour guider la discussion, nous avons préétabli une liste commune de questions, que nous avons amendées en fonction du champ d'expertise de la personne contactée. Le participant avait la possibilité de répondre soit par retour de mail, soit au cours d'un entretien par vidéo-conférence.

Tous les contacts ont été pris durant les mois de mai et juillet 2020.

Les informations recueillies ont été intégrées dans une synthèse narrative.

AVERTISSEMENT : Les informations reprises dans ce chapitre proviennent du terrain et des sites Internet des différentes organisations et services. Elles reflètent la situation en Belgique en juillet 2020 et sont susceptibles d'évoluer dans le temps et selon les contextes particuliers des institutions de soins.

L'efficacité des interventions, les échelles de mesure, l'expérience des patients, les facteurs prédictifs et le développement du syndrome PICS sont discutés dans d'autres chapitres de ce rapport scientifique.

5.2 Dimension locomotrice

Cette section est structurée d'après le parcours d'un patient nécessitant une revalidation locomotrice dès sa sortie d'une unité de soins intensifs, depuis les formes les plus génériques de revalidation vers les formes les plus spécialisées.

Trois formes de revalidation sont couvertes par l'assurance maladie-invalidité :

- les soins dispensés par des kinésithérapeutes (nomenclature M) ;
- les soins dispensés sous la supervision d'un médecin spécialiste en médecine physique et réadaptation (nomenclature K) ;
- les soins dispensés dans le cadre des conventions de revalidation passées avec l'INAMI.

Comme nous le présenterons dans la section ci-après, ces trois formes de soins de revalidation peuvent être dispensées dans différents contextes de soins : en ambulatoire, dans un centre de revalidation (lits Sp), dans un établissement hospitalier aigu, etc. Les rapports KCE 57B et 87B se sont précédemment penchés sur la kinésithérapie et la médecine physique et de réadaptation[g] ainsi que la réadaptation locomotrice et neurologique[h] en Belgique.[214, 215]

5.2.1 Soins dispensés par des kinésithérapeutes relevant de la nomenclature M i

Dès la sortie des soins intensifs, la nomenclature M prévoit des séances de kinésithérapie suite à un séjour aux soins intensifs, à raison de maximum deux séances par jour dans les 30 jours suivant le séjour aux soins intensifs, avec un maximum de 14 x 2 sessions sur une même journée. Ces

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f D'autres cliniques post soins intensifs existent probablement mais ne sont pas – au moment de rédiger ce document – manifestées comme étant des « PICS clinics »

g https://kce.fgov.be/fr/consommation-de-kin%C3%A9sith%C3%A9rapie-et-de-m%C3%A9decine-physique-et-de-r%C3%A9adaptation-en-belgique

h https://kce.fgov.be/fr/organisation-et-financement-de-la-r%C3%A9adaptation-locomotrice-et-neurologique-en-belgique

i https://www.inami.fgov.be/fr/covid19/Pages/reeducation-pluridisciplinaire-soins-intensifs.aspx

sessions peuvent avoir lieu à domicile, dans un cabinet privé ou dans un service de médecine physique et réadaptation. Elles doivent être prescrites par un médecin.

En l'absence d'une pathologie des listes E, Fa ou Fb, ou d'autres catégories de prestations spécifiques[j] (voir infra) pour lesquelles un remboursement spécifique est prévu, un patient peut bénéficier de maximum **18 séances en ambulatoire** par année civile et par pathologie **au meilleur taux de remboursement**, que ces séances soient dispensés au cabinet privé du kinésithérapeute, dans un service de médecine physique et réadaptation d'un hôpital ou au domicile du patient (prestations 560011, 560114, 560210, 560313, 560416, 564395, 560534, 560571)[k]. Une dérogation peut être introduite auprès du médecin conseil de la mutuelle, donnant lieu à une nouvelle prescription de 18 séances (maximum 3 x 18 séances pour 3 pathologies différentes). La même limitation s'applique pour les prestations effectuées dans des **centres de rééducation fonctionnelle conventionnés** (prestations 560534 (ambulatoire)-560545 (hospitalisé)) soit des séances individuelles de kinésithérapie dans laquelle l'apport personnel du kinésithérapeute par bénéficiaire atteint une durée globale moyenne de 30 minutes (valeur M 24).

Pour les patients dont l'état de santé nécessite un **traitement de kinésithérapie plus intensif**, l'INAMI a établi des listes de situations et pathologies pouvant donner lieu à un nombre plus élevé de séances de kinésithérapie et/ou à un remboursement majoré dans le cadre d'un suivi ambulatoire, que les séances soient effectuées à domicile, au cabinet privé ou dans un établissement de soins (tout en restant hors nomenclature K – voir infra). Ces pathologies sont définies comme suit :

- Pathologies de la **liste E** : **pathologies lourdes** pouvant donner lieu à un remboursement majoré des séances de kinésithérapie dispensées en ambulatoire[l]. Par exemple, certains patients COVID19 ont dû être amputés en tout ou en partie d'un membre suite à un évènement ischémique ; dans ce cas, ils sont éligibles pour la liste E du fait de l'amputation. La demande d'accord pour une pathologie de la liste E se fait via le médecin spécialiste : le médecin généraliste peut introduire la demande de prolongation. La demande d'accord doit inclure un bilan par un médecin spécialiste, en ce compris le bilan de kinésithérapie. Le remboursement dans le cadre de la liste E n'est pas dégressif.
- Pathologies de la **liste Fa** (F aiguës - art. 7, §14, 5°, A) : cette liste reprend notamment les patients qui ont séjourné aux soins intensifs (code 490). De ce fait, **tous les patients à risque de faire un PICS peuvent bénéficier des prestations de la liste Fa**. Ces patients peuvent bénéficier d'un maximum de **60 séances** de kinésithérapie remboursées au meilleur taux de remboursement, pendant une période d'un an (365 jours à partir de la date de la 1re séance effectuée). Le médecin généraliste peut prescrire ces séances si un rapport a été établi au préalable par le médecin spécialiste : ce rapport sera joint à la demande faite par le médecin généraliste auprès de la mutuelle du patient. Pour les patients ayant séjourné aux soins intensifs, le kinésithérapeute doit envoyer une notification au médecin-conseil de la mutuelle du patient. Dans ce cas de figure, il n'est pas nécessaire de disposer d'un rapport de médecin spécialiste.
- Pathologies de la **liste Fb** (F chroniques - art. 7, §14, 5°, B) : cette liste reprend les **pathologies qui nécessitent un traitement régulier de kinésithérapie pouvant durer plusieurs années** (p.ex. en cas de polyneuropathie dans les suites d'un séjour en soins intensifs). Dans ce cas, un maximum de **60 séances** est remboursé au meilleur taux de remboursement par année civile pendant une période allant de la 1re séance effectuée au 31 décembre de la 2e année civile qui suit l'année de cette 1re séance (**renouvellement possible** en fonction de l'état de santé pour le patient). Il est à noter que le remboursement des séances est dégressif à partir de la 61ème séance, bien que le remboursement reste préférentiel par rapport à des séances de kinésithérapies hors listes. Pour les pathologies de la liste Fb, le ticket modérateur reste le même pour les séances 1- 80 dans une année calendrier

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j Entre autres catégories spécifiques, on peut noter les patients en soins palliatifs, les soins de kinésithérapie en période périnatale, les soins dispensés dans le cadre de l'hôpital de jour, etc.

k Sur base d'une prescription, le patient peut toujours excéder le nombre de séances mentionnés mais le remboursement sera moindre.

l https://www.inami.fgov.be/fr/professionnels/sante/kinesitherapeutes/Pages/pathologies-lourdes-liste-payer-moins-cher.aspx

5.2.2 Prestations dans le cadre de la médecine physique et réadaptation

Dans le cadre d'une revalidation, les patients peuvent également bénéficier de séances de rééducation dispensées sous la supervision d'un spécialiste en médecine physique et réadaptation (MPR) dont la présence physique est requise dans l'institution. Il s'agit alors d'une nomenclature K. Les différents honoraires varient des prestations K15 (les moins remboursées) jusqu'aux prestations K60 (les mieux remboursées). Le remboursement K20 est prévu pour les traitements associant une ou plusieurs techniques monodisciplinaires (au maximum 48 séances). Certaines pathologies spécifiques peuvent bénéficier de séances de réadaptation fonctionnelle pluridisciplinaires (K30 et K60), le nombre de séances (60 ou 120) étant fonction de la pathologie. Après une première série de séances K20 (18 séances), K30 (30 séances) ou K60, les séances suivantes ne peuvent plus être facturées qu'en K15, ou le patient peut passer à un traitement de kinésithérapie, facturé en M (voir supra).[m]

La nomenclature K s'applique aussi bien pour des prestations en ambulatoire qu'en décours d'hospitalisation. Ci-après, nous vous détaillons différents types de services dans lesquels cette nomenclature est en vigueur.

Encadré : Application spécifique de la nomenclature K dans le contexte COVID-19 durant le séjour hospitalier

Spécifiquement pour les patients COVID-19 durant le séjour hospitalier (aux soins intensifs ou non), depuis le 14 mars 2020, avec effet rétroactif, les médecins spécialistes hospitaliers peuvent facturer certaines prestations pluridisciplinaires de la nomenclature K, complétées par des prestations supplémentaires pour les patients hospitalisés en unité de soins intensifs ou qui l'ont été (cf. ci-dessus). Toujours dans le cadre hospitalier, une 2e séance quotidienne de kinésithérapie est destinée aux patients COVID-19 hospitalisés après un séjour aux soins intensifs, et ce, pendant le reste de la durée de leur hospitalisation.

5.2.2.1 Revalidation en service Sp1 – Sp2 – Sp3 ou G

Le séjour en unité Sp est destiné en priorité à des patients **pour lesquels un programme de revalidation ambulatoire n'est pas possible en première intention**, soit du fait de leur état de santé, soit du fait de leur situation sociale et familiale. Les services Sp exercent une activité de revalidation active et multidisciplinaire. Ils peuvent être spécialisés dans le traitement et la réadaptation des patients atteints d'affections cardio-pulmonaires (Sp1), locomotrices (Sp2), neurologiques (Sp3), psycho-gériatriques (Sp6) et chroniques (Sp5). Les patients doivent être stabilisés sur le plan médical mais requièrent soit un complément de mise au point médicale, soit un suivi médical ou une prise en charge constante. Ces services hospitaliers ne sont toutefois pas des services de longue durée.

Le séjour en service Sp peut s'inscrire dans la continuité directe d'un séjour hospitalier, que ce soit aux soins intensifs ou non, et se fait donc sur demande du médecin hospitalier traitant. Il est également possible que le patient retourne à domicile mais qu'il s'avère ensuite que sa situation nécessite un séjour en centre de revalidation : dans ce cas, le médecin généraliste peut introduire la demande pour ce séjour. Cependant, le médecin spécialiste en revalidation devra donner son accord définitif quant à l'admission du patient.

Les services de revalidation s'organisent autour d'une équipe pluridisciplinaire associant médecins, infirmiers, kinésithérapeutes, ergothérapeutes, thérapeutes du sport, psychologues, logopèdes et travailleurs sociaux. Selon les services, il est possible de proposer un retour à domicile à l'essai pour s'assurer de l'adaptation du patient à son nouvel état de santé.

La revalidation dans le cadre d'un **service G** est destinée aux patients âgés de 75 ans et plus, avec une attention accrue pour le déclin fonctionnel lié à l'âge. En plus de l'unité de revalidation proprement dite, la revalidation en service G peut également s'appuyer sur la présence d'une équipe de liaison gériatrique facilitant la transition entre l'hôpital et le domicile.

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[m] Extrait du rapport KCE Consommation de kinésithérapie et de médecine physique et de réadaptation en Belgique KCE reports 87B

Déjà avant la crise du Covid-19, certains centres de revalidation ont développé des trajets de soins spécifiques, à l'instar d'Inkendaal qui s'est spécialisé dans la prise en charge des patients présentant des affections respiratoires restrictives (en ce compris l'assistance ventilatoire externe et les trachéotomies).

Encadré : Les unités de revalidation spéciales Covid-19

Lors de la pandémie de Covid-19, un certain nombre **d'unités de revalidation spécifiques** ont fait leur apparition. La spécificité de ces unités tient essentiellement au **risque de contagiosité** des patients : en effet, les patients Covid-19 sortis des unités de soins intensifs ne pouvaient pas être hospitalisés en unités de soins classiques, ni être directement envoyés dans une unité de revalidation. Dès lors, certains hôpitaux (p.ex. le Chwapi à Tournai) ont pris l'initiative de dédier des unités de soins spécifiques à la revalidation de ces patients. Ce type d'unité a permis de poursuivre le **travail de revalidation précoce** initié aux soins intensifs, sans passer par un séjour en unité de soins classique avant l'orientation vers la revalidation.

5.2.2.2 Centres de rééducation fonctionnelle généraux pour affections locomotrices et neurologiques (établissements 950)

Certains centres de rééducation fonctionnelle généraux pour affections locomotrices et neurologiques proposent également une **offre thérapeutique multidisciplinaire intensive** pour une **durée limitée dans le temps**, la durée de la prise en charge étant déterminée par la pathologie du patient[n]. Ils sont alors couverts par la convention 950. Certaines affections spécifiques (décrites dans le texte de la convention[o]) donnent accès à ce type de centre, après leur phase aigüe ou immédiatement après une poussée.

Le patient peut être envoyé par son médecin traitant mais seul le médecin spécialisé en rééducation est habilité à prescrire le traitement. Le médecin spécialiste établit un **programme individuel de rééducation fonctionnelle** et le communique au médecin-conseil de la mutuelle du patient, qui doit donner son accord pour que le programme soit mis en place et inclus dans la convention. L'équipe inclut des médecins, kinésithérapeutes, psychologues, ergothérapeutes et travailleurs sociaux. La convention prévoit des temps de concertation en équipe mais également avec la famille et le médecin généraliste.

La convention 950 n'est pas compatible avec certaines autres prestations. Ainsi, si le patient a déjà suivi soit une rééducation fonctionnelle pour une maladie ou un trouble dans un établissement de rééducation fonctionnelle lié par une convention avec le Comité de l'assurance, soit a bénéficié pour la même maladie ou le même trouble de prestations de rééducation fonctionnelle K30-K60 (voir supra), la durée totale de la rééducation sous convention 950 ne peut excéder la durée maximale prévue pour la pathologie (article 5§5). Un centre "convention 950" ayant déjà dispensé des séances K30 ou K60 doit soustraire celles-ci du nombre de séances auxquels peut prendre le patient.

La convention 950 comprend des **forfaits R30** (ambulatoire ou hospitalisé) ou **R60** (ambulatoire ou hospitalisé)[p] en fonction des pathologies. Les règles de remboursement qui s'appliquent sont les mêmes que pour les forfaits K30-K60 (Circulaire OA n° 2020/25 du 28 janvier 2020), en ce compris la dégressivité du remboursement. En dehors de ces prestations R30-R60, les centres de rééducation du secteur 950[q] peuvent également porter en compte des forfaits spécifiques pour certaines pathologies déterminées.

Les établissements de rééducation pour troubles locomoteurs et neurologiques (951) proposent des programmes de soins similaires aux centres couverts par les conventions 950 et 771 (voir infra), mais avec une durée plus courte.

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[n] https://www.inami.fgov.be/SiteCollectionDocuments/convention_troubles_locomoteurs.pdf

[o] voir note précédente

[p] Prestations de type R60 (2h de traitement – min. 2 prestataires – codes 776171 (ambulatoire) – 776182 (hospitalisé)) ou R30 (1h de traitement – min. 2 prestataires – codes 776156 (ambulatoire) 776160 (hospitalisé).

[q] La convention type de rééducation fonctionnelle locomotrice et neurologique

5.2.2.3 Centres de rééducation fonctionnelle spécifiques (établissements 771r)

Le site internet de l'INAMI liste également un certain nombre d'établissements de rééducation fonctionnelle spécifiques (dits 771), qui proposent de la **rééducation locomotrice et neurologique** aux patients souffrant de problèmes déterminés. Citons, par exemple, le centre neurologique William Lennox, qui s'est spécialisé dans les troubles neurologiques (épilepsie, accident vasculaire cérébral, traumatisme crânien, troubles cognitifs développementaux, états de conscience altérés (tels que réveils de coma), troubles envahissants du développement, etc.). Tout comme dans les centres de rééducation fonctionnelle généraux, un programme de soins individualisé et interdisciplinaire est établi pour chaque patient.

L'admission dans ces établissements se fait sur **présentation d'un dossier médical** ainsi que, selon les établissements, sur base d'un **bilan réalisé** par l'équipe interdisciplinaire. Le séjour ou les soins ambulatoires sont également soumis à l'approbation du médecin-conseil.

5.2.2.4 Prestations d'ergothérapie

À côté des traitements pluridisciplinaires décrits ci-dessus, l'intervention d'un ergothérapeute peut également se faire (en tout ou en partie) dans le lieu habituel de vie du patient. Elle doit être prescrite par un médecin attaché à l'établissement de rééducation[s] où le patient a préalablement reçu des soins, et est soumise à l'accord du médecin-conseil de la mutuelle[t].

Le patient peut bénéficier des prestations suivantes (d'une durée de 180 minutes, déplacement compris) :

- une prestation de bilan d'observation – le patient peut être encore hospitalisé en revalidation ;
- 7 prestations de séances de mise en situation : réservées à des patients ambulatoires qui ont déjà eu un bilan ;
- 2 prestations de séances d'information, de conseil et d'apprentissage réservées à des patients ambulatoires qui ont déjà eu un bilan ;
- 1 prestation de bilan fonctionnel final : réservées à des patients ambulatoires qui ont déjà eu un bilan.

Dans le cadre de leurs avantages particuliers, certaines mutuelles proposent le passage à domicile d'ergothérapeutes **en vue de l'adaptation du domicile**.[uv] Ces prestations sont le plus souvent destinées aux personnes âgées et/ou handicapées.

5.2.3 Conventions de revalidation

Une convention est un moyen de financement utilisé dans le système de soins de santé belge ; elle permet de financer certains soins au moyen d'un forfait unique lié à une affection/problème spécifique. Les conventions sont conclues entre l'Institut national d'assurance maladie-invalidité (INAMI) et les établissements de soins, qui doivent respecter certaines conditions. Elles sont élaborées, conclues et gérées par le conseil d'administration de l'INAMI, où siègent les médecins-directeurs de toutes les mutualités.

Le contenu des conventions peut varier, mais elles comprennent toutes des conditions relatives à leur durée, à leur gestion, à l'équipe multidisciplinaire, aux patients, aux moyens financiers, ainsi que des critères d'évaluation de plus en plus clairs.

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r https://www.inami.fgov.be/SiteCollectionDocuments/liste_centre_reeducation_conventionne_771_fr.pdf

s Il doit s'agir d'un établissement de rééducation fonctionnelle conventionné pour troubles locomoteurs (950), pour troubles neuro-locomoteurs (771) ou locomoteurs et neurologiques (951)

t https://www.inami.fgov.be/fr/themes/cout-remboursement/par-mutualite/centres-reeducation/Pages/ergotherapie-intervention-couts-prestations-ergotherapie.aspx

u https://www.fmsb.be/news/faites-de-votre-domicile-un-endroit-sur-ou-l-on-se-sent-bien

v http://www.solival.be/

Nous avons identifié deux conventions couvrant des syndromes dont la symptomatologie s'approche du PICS par certains aspects, bien que ne le couvrant pas entièrement. Nous les citons ici à titre d'exemple : **la convention Troubles locomoteurs et la convention Syndrome de fatigue chronique**. Il est à noter que les patients PICS ne sont répertoriés comme groupe cible dans aucune de ces conventions, mais que certains patients PICS répondent à une partie des critères de l'une ou l'autre.

Certaines autres conventions ne couvrent pas les symptômes des patients PICS, mais présentent néanmoins une philosophie qui pourrait se révéler pertinente pour eux. Citons par exemple la **convention Cliniques de la mémoire**, qui propose une offre thérapeutique interdisciplinaire susceptible d'aider les patients à améliorer leurs fonctions cognitives. De même, la **convention HIV/SIDA** qui met un accent fort sur la réinsertion professionnelle et sociale, ce qui peut s'avérer crucial dans le cas des patients PICS.

Des **restrictions de cumul** sont incluses dans chaque convention. Le médecin-conseil a néanmoins la liberté d'autoriser le cumul lorsque les conventions ne couvrent pas les mêmes domaines pathologiques : par exemple, il serait envisageable de cumuler un programme de rééducation locomotrice / neurologique avec un programme d'oxygénothérapie ou d'assistance respiratoire. L'accord de rééducation respiratoire (qui n'a été conclu qu'avec 4 hôpitaux) exclut, dans chaque cas, le cumul avec les accords de rééducation locomotrice / neurologique.

Le rapport KCE 299 présente plus en détails les conventions.[w216]

À retenir :

- **Le médecin généraliste peut prescrire jusqu'à 3 x 18 séances de kinésithérapie par année civile, avec un maximum de 3 pathologies, dans le cadre des soins courants (nomenclature M).**
- **Les patients ayant séjourné aux soins intensifs peuvent bénéficier de 60 séances de kinésithérapie par an (liste Fa), avec possiblité de prolongation au-delà de 60.**
- **Les patients qui ont développé des séquelles de polyneuropathie chronique motrice ou mixte sont susceptibles d'être éligibles pour les prestations de la liste Fb.**
- **Le médecin généraliste peut orienter son patient vers un service de médecine physique et réadaptation pour un suivi en ambulatoire dans le cadre de la nomenclature K.**
- **Le médecin généraliste peut faire une demande auprès du médecin spécialiste d'admission en service Sp / service G pour une revalidation plus intense.**
- **Le médecin généraliste peut aider à la constitution du dossier d'admission dans un centre de rééducation fonctionnelle générique (950-951) ou spécifique (771) couvert par la convention troubles locomoteurs.**
- **Si le patient a été soigné dans un service de revalidation (Sp ou G) ou de rééducation fonctionnelle (950 - 951 - 771), il peut bénéficier de l'intervention d'un ergothérapeute à son domicile. Dans les autres cas, le patient peut solliciter sa mutuelle pour l'adaptation de son domicile par un ergothérapeute.**
- **À l'heure actuelle, aucune convention INAMI ne couvre spécifiquement les besoins liés au PICS mais certaines d'entre elles présentent des caractéristiques qui pourraient leur être utile.**

5.3 Dimension cognitive

5.3.1 Bilan des fonctions cognitives

Le patient atteint de PICS qui présente des troubles d'ordre cognitif peut être orienté par son médecin généraliste vers un neurologue, psychiatre ou gériatre. Ces spécialistes sont habilités à prescrire un

[w] https://kce.fgov.be/fr/protocole-d%E2%80%99%C3%A9valuation-pour-les-conventions-avec-l%E2%80%99inami

bilan logopédique ou un « **bilan réalisé par un neuropsychologue** ». Ce dernier est partiellement pris en charge par l'INAMI en cas de « démence débutante », selon les termes de l'INAMI[x]. Ce bilan comprend l'examen neuropsychologique validé et détaillé (durée minimum de 45 minutes) des fonctions cognitives importantes atteintes dans le syndrome démentiel (selon DSM IV) : la mémoire, l'aptitude langagière, l'aptitude visuo-spatiale, les fonctions de l'attention et les fonctions exécutives. Les bilans peuvent également être intégrés à une revalidation logopédique ou neuropsychologique de pathologie « focale » si un accord est obtenu auprès du médecin-conseil de la mutuelle du patient. D'autres examens, comme une IRM, un scanner, voire un PET-scan, peuvent être prescrits par le spécialiste en vue d'objectiver les lésions cérébrales.

Les patients peuvent également se rendre **chez un neuropsychologue de leur propre initiative** ou sur le conseil de leur médecin généraliste, pour un bilan de leurs fonctions cognitives. Ce bilan (moins approfondi) n'est pas remboursé par l'INAMI mais certaines mutuelles interviennent en partie, dans le cadre de leur couverture complémentaire.

5.3.2 Revalidation cognitive

Selon les résultats du bilan et la problématique d'origine du patient, un **programme individualisé de revalidation cognitive** est établi. Ce programme peut faire intervenir des logopèdes, ergothérapeutes, psychologues ou neuropsychologues. Il peut être dispensé dans différentes types de centres.

5.3.2.1 Convention 950

Les centres et programmes de revalidation mentionnés dans la section consacrée à la dimension locomotrice offrent également une prise en charge globale, incluant celle des troubles cognitifs : ces prises en charge interdisciplinaires sont couvertes par la **convention 950 conclue avec les établissements de rééducation locomotrice et neurologique** (voir section précédente). Toutes les conventions 950 reprennent les mêmes termes, ce qui n'exclut pas la spécialisation de certains centres autour des troubles neuropsychologiques. Incluant une équipe multidisciplinaire, dont des neuropsychologues, sous la supervision d'un spécialiste en médecine physique et revalidation, ces centres offrent des soins en résidentiel ou en ambulatoire, avec des séances de 2h de soins. La durée journalière des prestations de rééducation fonctionnelle cognitive n'est pas clairement définie dans le texte des conventions 950 : il y est question d'un forfait journalier, sans précision de durée, ce qui permet aux équipes soignantes d'adapter la prise en charge aux besoins des patients. L'admission du patient dans ce type de programme est conditionnée par le dépôt d'un dossier, incluant des preuves de la présence de lésions cognitives (imagerie), et soumise à l'accord du médecin-conseil. Tout comme dans le cadre d'une revalidation locomotrice, le médecin généraliste peut contribuer à l'élaboration du dossier d'admission.

5.3.2.2 Centres de rééducation ambulatoire (CRA)

Dépendant des entités fédérées depuis la 6ème réforme de l'Etat[y], **les centres de rééducation ambulatoire de type 953 et 965** sont indiqués pour les soins aux personnes souffrant de troubles de santé mentale, de l'audition, de la parole ou de troubles neurologiques. Ils accueillent principalement des enfants (jusqu'à leur 19ème anniversaire) mais pas exclusivement.

Parmi ces différents centres, certains accueillent des patients du groupe 1, soit les enfants ou adultes, ayant une lésion cérébrale d'origine vasculaire, toxique, tumorale, infectieuse ou traumatique, sans symptômes de démence. Au moment de la prise en charge par l'établissement, les patients doivent présenter *des **troubles au niveau des fonctions neuro-psychologiques** (fonctions cognitives, fonctions liées à la communication, fonctions liées à la maîtrise des émotions, fonctions liées au comportement social, fonctions liées au vécu des sentiments et à la personnalité) **allant éventuellement de pair avec des troubles physiques** (lésions motrices, perte des sens)*

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[x] https://www.inami.fgov.be/fr/professionnels/sante/medecins/soins/Pages/bilan-neurologique-neuropsychologue.aspx

[y] Ces établissements sont gérés par l'Agentschap Zorg en Gezondheid en région flamande, par l'AVIQ en région wallonne, par la CoCom ou la CoCof en région wallonne, par la communauté française pour les centres liés à des hôpitaux universitaires et par la communauté germanophone pour les centres situés en Ostbelgien.

***qui entraînent pour la personne des perturbations dans sa vie au quotidien**, que ce soit au niveau affectif, familial, social, professionnel, récréatif,….*

L'orientation vers un CRA se fait **après une rééducation fonctionnelle en milieu hospitalier dans un service Sp**, dans les 3 ans suivant l'événement déclencheur. Les patients sont orientés vers un CRA soit sur prescription du médecin traitant spécialiste de l'hôpital où les patients ont déjà été hospitalisés pour le traitement de la lésion cérébrale, soit par un spécialiste en neurologie, en neurochirurgie, en neuropsychiatrie, en psychiatrie. Le traitement ne peut toutefois pas commencer tant que l'accord du médecin-conseil de la mutuelle n'a pas été donné. Le programme inclut à la fois le bilan initial et le traitement multidisciplinaire.

À retenir :

- **Le médecin généraliste peut orienter son patient pour un bilan cognitif chez un neurologue / gériatre / psychiatre ; ce dernier a la possiblité de confier le bilan à un neuropsychologue ou à un logopède.**
- **Le patient peut aussi se rendre librement chez un neuropsychologue pour un bilan cognitif.**
- **Le patient peut recevoir des soins soit en ambulatoire, soit en résidentiel, selon ses besoins.**
- **Le médecin généraliste peut aider à la constitution du dossier d'admission en centre de revalidation neurocognitive.**
- **Les centres de rééducation ambulatoires (CRA) sont gérés par les entités fédérées depuis la 6ème réforme de l'Etat.**

5.4 Dimension santé mentale et psychiatrie[z]

Les aspects santé mentale du PICS et du PICS-F incluent **l'anxiété, la dépression et le syndrome de stress post-traumatique.** Pour une description plus complète de l'organisation des soins de santé mentale en Belgique, nous vous invitons à consulter le rapport KCE 318.[217aa] Le Conseil Supérieur de la Santé (CSS) a par ailleurs publié un avis concernant la prise en charge psychosociale pendant la pandémie COVID-19[bbcc]. La mise en œuvre de ces recommandations reste à la discrétion des professionnels de santé.

5.4.1 Anxiété et dépression

Les **soins psychologiques de première ligne** sont accessibles à tous les patients, sur prescription par un médecin généraliste, (pédo)psychiatre, gériatre, pédiatre, médecin du travail, médecin de CPMS/PSE ou de l'ONE. Le remboursement couvre 8 séances, soit 2 x 4 séances, la prescription devant être renouvelée après les 4 premières séances[dd].

Destinées aux problèmes modérément sévères pouvant être traités en un nombre limité de séances[ee], ces consultations sont dédiées à certains problèmes bien définis, dont l'anxiété ou la

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z https://www.inami.fgov.be/fr/themes/cout-remboursement/par-mutualite/sante-mentale/Pages/traitement-psychologique-courte-duree-adultes.aspx

aa https://kce.fgov.be/fr/organisation-des-soins-de-sant%C3%A9-mentale-pour-les-adultes-en-belgique

bb https://www.health.belgium.be/fr/avis-9589-sante-mentale-et-covid-19

cc https://www.health.belgium.be/nl/advies-9589-geestelijke-gezondheid-en-covid-19

dd Plus d'informations : https://www.inami.fgov.be/fr/professionnels/sante/psychologue-clinicien/Pages/default.aspx#Prestations_dispens%C3%A9es_par_un_psychologue_clinicien,_tarifs_et_interventions

ee Dans le contexte particulier du COVID-19, un remboursement spécifique est prévu pour les consultations par vidéoconférence pour les patients souffrant d'anxiété et de panique en lien avec la pandémie et pour assurer le traitement des personnes qui ont déjà reçu des soins psychologiques de première ligne, sans que ces personnes ne doivent se déplacer. Cette mesure est d'application jusqu'au 30 juin 2020 (sous réserve de prolongation). Au 21 septembre 2020, aucune date de prolongation n'est mentionnée sur le site de l'INAMI.

dépression. Les séances de soins psychologiques de première ligne sont axées sur : 1) évaluation des problèmes présents ; 2) soins de psychologie généraux ; 3) traitement orienté solution, auto-assistance accompagnée, psychoéducation ; 4) promotion de l'autonomie ; 5) renvoi vers la seconde ligne en cas de problématique complexe. La séance de psychologie est toujours une séance individuelle. Les autres formes de thérapies ne sont pas couvertes dans le cadre de ce remboursement.

Par ailleurs, les patients ont la possibilité de **se rendre chez un psychiatre** sans être référés par leur médecin généraliste. La prestation sera remboursée selon les règles en vigueur à l'INAMI, sur remise de l'attestation de soins à la mutuelle.

Les mêmes dispositions sont d'application pour les proches de patients PICS qui nécessiteraient des soins psychologiques et/ou psychiatriques.

Les patients peuvent également se rendre **librement chez un psychologue** : dans ce cas, en l'absence de prescription, ces soins ne seront pas remboursés par l'INAMI mais peuvent être partiellement pris en charge par la mutuelle dans le cadre d'une assurance de santé complémentaire.

Domus Medica[ff] et la Société Scientifique de Médecine Générale (SSMG)[gg] ont publié un **guide de pratique clinique pour la prise en charge de la dépression** (voir aussi Chapitre 3 pour les outils de détection du PICS).

5.4.2 Syndrome de stress post-traumatique

Le syndrome de stress post-traumatique (Post-Traumatic Stress Disorder ou PTSD en anglais) peut se déclarer **3 à 6 mois après l'événement traumatique**, voire davantage (voir Chapitre 1). Il nécessite une **prise en charge spécialisée** qui s'inscrit dans la durée. En 2017, le Conseil Supérieur de la Santé a publié des recommandations pour la prévention et de gestion des séquelles psycho-sociales dans le cadre de situations d'urgences individuelles ou collectives (CSS 9403)[hh], dont le PTSD mais, à l'heure actuelle, les principales initiatives ne sont pas le fait de la santé publique mais bien de la Défense, des pompiers ou encore la police.

Au niveau de la Défense, le **centre de psychologie de crise** de l'Hôpital Militaire a développé une expertise spécifique pour l'accompagnement des militaires de retour d'opérations et offre, de façon ponctuelle, un soutien aux civils.

Chez les pompiers, les **Fire Stress Teams (FiST)** sont des équipes composées de pompiers ayant suivi une formation courte en soutien psychologique. Ils interviennent – bénévolement – auprès de collègues confrontés à des situations éprouvantes dans l'exercice de leur profession[ii]. Le même type de dispositif existe au sein de la police.

En dehors des forces armées et des pompiers, certains psychiatres et psychologues se sont spécialisés, à titre personnel, dans des thérapies permettant de prendre en charge des PTSD, mais aucune base de données ne permet de les identifier à l'heure actuelle.

Enfin, il est à souligner que l'Hôpital Erasme teste actuellement **l'hypnose** en prévention du PTSD suite à un séjour aux soins intensifs. Un projet Interreg[jj] visant à utiliser les **nouvelles technologies** dans la gestion de l'anxiété et du PTSD est également en cours.[kk]

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ff https://www.domusmedica.be/richtlijnen/depressie-bij-volwassenen

gg https://www.ssmg.be/wp-content/uploads/RBP/RBP-Depression.pdf

hh https://www.health.belgium.be/fr/avis-9403-sequelles-psycho-sociales

ii https://www.prevent.be/fr/banque_de_connaissance/aider-ses-coll%C3%A8gues-%C3%A0-surmonter-une-exp%C3%A9rience-traumatique

jj Les projets Interreg sont des projets de coopération transfrontalière avec le soutien du Fonds européen de développement régional. https://www.interreg-fwvl.eu/.

kk https://www.nweurope.eu/projects/project-search/it4anxiety-managing-anxiety-via-innovative-technologies-for-better-mental-health/

5.4.3 Groupes de parole en unités de soins intensifs et associations de patients

Certaines unités de soins intensifs (UZ Gent depuis 2018[ll], ChWaPi depuis 2020) ont pris l'initiative de proposer des **groupes de parole** aux patients ayant séjourné aux soins intensifs et à leurs proches. Le choix d'y participer ou pas est laissé à la libre appréciation des patients et de leurs proches ; selon les intervenants interrogés, beaucoup de patients préfèrent cependant un entretien individuel ou familial. Ces initiatives restent cependant très locales et sont encore peu connues. L'efficacité des groupes de paroles est discutée au Chapitre 4.

Encadré : l'expérience de UZ Intens

Depuis 2017, le groupe de soutien UZIntens[mm] organise des "drop-in meetings", quatre fois par an, où d'anciens patients et leurs proches sont invités. Ces rencontres prennent place hors de l'hôpital, dans la cafeteria d'un hall sportif. Les rencontres sont animées par l'équipe des soins intensifs (un médecin spécialiste en soins intensifs, deux psychologues et d'autres membres de l'équipe comme des infirmiers ou kinésithérapeutes). Elles rassemblent 15 à 20 participants. Durant ces conversations informelles, les patients évoquent leurs symptômes et souvenirs des soins intensifs, posent des questions aux professionnels de santé – parfois des souvenirs et questions dont ils n'osent pas parler ouvertement –, racontent leur histoire, partagent leurs préoccupations, ou simplement écoutent et apprennent de leurs pairs. Les patients rapportent souvent à quel point ils trouvent rassurant de savoir qu'ils ne sont pas seuls à ressentir ces sentiments ou problèmes. Si des problèmes sérieux sont détectés (par les professionnels présents), les patients recevront des conseils de l'équipe soignante quant à la recherche d'un soutien plus structurel. De leur côté, les professionnels de santé estiment que ces séances leur apportent également des informations précieuses par rapport à l'expérience et au vécu des patients et de leurs proches. Cependant, à l'heure actuelle, aucune évaluation formelle de l'impact de ce groupe de parole n'a été menée. L'équipe soignante le perçoit néanmoins comme soutenant pour les patients, ce qui encourage la poursuite de cette initiative en dehors d'un financement structurel.

En l'absence de groupes de parole organisés, le médecin généraliste peut proposer aux patients de reprendre contact avec l'unité de soins intensifs pour rencontrer l'équipe, visiter les lieux ou toute autre action jugée nécessaire pour soutenir la santé mentale du patient et de ses proches (voir aussi la section sur la consultation post soins intensifs).

Il existe par ailleurs de nombreux **groupes d'entraide**[nn] pour les patients, pour les proches endeuillés ou pour les proches de personnes dans le coma[oo]. Cependant, à notre connaissance, il n'existe pas de groupe d'entraide pour un soutien par les pairs après un séjour aux soins intensifs. Certaines **associations** peuvent soutenir les patients et leurs proches comme Altéo[pp] ou l'ASBL Aidants proches[qq]. Certaines de ces associations sont soutenues et/ou organisées par les mutuelles. De même, dans le cadre de l'assurance complémentaire, certaines mutuelles mettent en place une offre de répit pour les proches, soit sous forme d'une garde à domicile, soit sous forme de court séjour.

À retenir

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ll https://uzintens.be/

mm https://uzintens.be/

nn Les groupes d'entraide sont, généralement, des groupes relativement informels où les professionnels de santé sont peu, voire pas présents, à la différence des groupes de parole où les professionnels participent aux échanges.

oo http://www.soinspalliatifs.be/associations-de-suivi-de-deuil-groupes-specifiques.html

pp http://www.alteoasbl.be/

qq http://www.aidants-proches.be/

- **Le médecin généraliste peut prescrire 2 x 4 séances chez un psychologue clinicien pour des symptomes d'anxiété et de dépression ou un bilan de la santé mentale de son patient.**
- **En cas de besoin, le patient peut se rendre librement chez un psychothérapeute, un coach, un psychiatre ou un psychologue, sans passer par son médecin généraliste.**
- **La SSMG et Domus Medica proposent des recommandations pour la prise en charge des problèmes de dépression sur leurs sites internet respectifs.**
- **Certains psychiatres et psychologues se sont spécialisés dans la prise en charge du stress post-traumatique (PTSD), mais il n'existe pas de prise en charge structurée de ce type de problème.**
- **Le médecin généraliste peut inviter le patient à (re)prendre contact avec l'unité de soins intensifs où il a séjourné pour qu'il puisse, par exemple, rencontrer l'équipe soignante et visiter les lieux afin de les démystifier.**
- **Les groupes de parole organisés par les hôpitaux, les groupes d'entraide et les associations de patients sont des ressources que le médecin généraliste peut recommander à ses patients et leurs proches.**

5.5 Dimension sociale

Les séjours aux soins intensifs à cause du COVID sont souvent des séjours de longue durée non-prévus : ils sont donc plus susceptibles que d'autres d'avoir un impact sur la dimension sociale. **L'aide apportée par les services sociaux hospitaliers est gratuite et inconditionnelle**, dans la limite de leurs compétences.

La prise en charge sociale commence dès le séjour du patient aux soins intensifs, à l'initiative du personnel soignant. Il est possible que le **service social de l'hôpital** contacte pro-activement le patient ou ses proches. En fonction de la situation du patient, le service social peut intervenir dans les démarches auprès de la mutuelle ou du CPAS (aspects de solvabilité et d'assurabilité) et dans l'orientation et la préparation du séjour post-hospitalier : services d'aides à domicile, transfert vers un centre de revalidation ou une maison de repos et de soins, etc. Il n'existe pas de service spécifique pour les proches mais ces derniers peuvent également appeler le service social hospitalier. Durant la crise du COVID, les services sociaux ont joué un rôle majeur dans le lien entre les familles et les patients hospitalisés, du fait des restrictions concernant les visites. Le service social peut également accompagner les proches en cas de décès.

Dès la sortie du patient de l'hôpital, c'est la mutuelle du patient qui prend le relais du service social ; celui-ci envoie un avis de fin d'hospitalisation au médecin-conseil. En général, le patient reçoit, de la part de sa mutuelle, la liste des services auxquels il a accès suite à son hospitalisation, et peut donc prendre contact avec sa mutuelle pour en bénéficier. En fonction de la mutuelle, **d'autres services** peuvent être proposés aux patients et à ses proches en sus de la couverture d'assurance maladie invalidité classique (donc dans l'assurance complémentaire) : aide et soins à domicile, location ou prêt de matériel sanitaire, aide à l'adaptation du domicile, séjours de répit pour les aidants, séjours de convalescence, etc.

En ce qui concerne le retour au travail, les patients et les médecins généralistes peuvent faire appel à différentes ressources. La première est le **médecin du travail**. La récente réforme de la médecine du travail a mis le focus sur l'aide au retour au travail et à l'adaptation des milieux professionnels pour faciliter la réintégration des patients. La médecine du travail propose un regard complémentaire à la démarche du médecin généraliste dans le sens où elle examine les **compétences fonctionnelles**. Il est également possible de solliciter, via le SPF Emploi, une **visite de pré-reprise du travail** pour veiller à l'adéquation du poste de travail[rr]. Un outil supplémentaire est le **trajet de réintégration professionnelle** qui permet au travailleur qui n'est plus en état d'effectuer son travail, temporairement ou définitivement, de retrouver un travail qui lui convient et dans les meilleures

[rr] Voir à ce propos la brochure : https://emploi.belgique.be/fr/publications/retour-au-travail-apres-une-absence-longue-duree-pour-raison-medicale-prevention-et

conditions possibles. Ce mécanisme est cependant très formel[ss] ; une démarche plus informelle avec le soutien du médecin généraliste, du médecin du travail et du médecin-conseil est aussi possible. Un projet est en cours au sein de Domus Medica et de la SSMG pour améliorer la collaboration entre médecins généralistes, médecins-conseils et médecins du travail[tt].

La **cellule santé et bien-être au travail de la SSMG** propose par ailleurs une aide et un soutien aux médecins généralistes devant prendre en charge des situations de reprise du travail, dont une permanence pour les questions directes et des ressources documentaires[uuvv].

Déjà mentionnées comme des ressources pour la santé mentale, les associations de patients et les groupes d'entraide peuvent également apporter une aide aux patients pour les démarches administratives, sociales, voire un soutien matériel. Le médecin généraliste peut dès lors proposer aux patients de prendre contact à la mutuelle ou à l'une des trois coupoles (Ligue des Usagers des Services de Santé LUSS, Vlaams Patienten Plateform VPP, ou Patienten Rat und Treft PRT).

À retenir :

- **Le médecin généraliste peut recommander / aider à son patient de (à (re)contacter le service social de l'hôpital pour connaître les démarches à effectuer et veiller à ce qu'un relais soit organisé avec l'organisme compétent (mutuelle, CPAS, autre service social…).**
- **En cas de visite chez un médecin-conseil, le médecin généraliste peut communiquer au patient la brochure de la LUSS « Se préparer à une visite chez le médecin conseil »ww ou la brochure de la VPP « Wie is wie? De expertiseartsen en hun opdracht" xx.**
- **En cas de reprise du travail, le médecin généraliste peut se concerter avec le médecin du travail et le médecin-conseil pour faciliter le retour au travail.**
- **Le SPF Emploi a édité une brochure informative pour la reprise du travail, accessible en téléchargement.**
- **Le médecin généraliste peut proposer au patient et à ses proches de prendre contact avec sa mutuelle ou la LUSS/VPP/PRT pour entrer en contact avec une association de patients ou un groupe d'entraide.**

5.6 Consultations post-soins intensifs

Depuis quelques années, certains hôpitaux pionniers (à l'étranger mais aussi en Belgique) ont mis en place des consultations post-soins intensifs avec l'objectif de détecter d'éventuels symptômes de PICS et de proposer au patient une prise en charge adéquate. Déjà présentes avant la crise COVID-19, ces consultations ont vu leur développement s'accélérer depuis cette crise, même si leur pérennité n'est pas encore assurée. Elles constituent un outil encore peu connu permettant d'amorcer le parcours de revalidation pour les patients à risque de développer un PICS. Le Chapitre 4 sur les interventions discute l'efficacité de ces consultations de suivi.

En 2019, une étude recensait six centres belges de soins intensifs organisant **une consultation post-soins intensifs,** sur un total de 36 centres investigués.[12] Nous avons contacté trois centres qui organisent actuellement un programme de suivi dédié à certains patients sortant des soins

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ss https://emploi.belgique.be/fr/themes/bien-etre-au-travail/la-surveillance-de-la-sante-des-travailleurs/reintegration-des

tt https://www.ssmg.be/sebt2/

uu Il n'existe pas d'équivalence au niveau de Domus Medica

vv https://www.ssmg.be/avada_portfolio/sante-et-bien-etre-au-travail/

ww https://www.luss.be/classement/fiches-pratiques/

xx http://vlaamspatientenplatform.be/uploads/documents/brochure_vpp_wieiswie_v2020_web.pdf

intensifs : le Chwapi (Tournai), le CHU de Liège et l'Hôpital Erasme[yy].Certains autres hôpitaux envisagent également de le faire dans un horizon plus ou moins proche.

La consultation post-soins intensifs est une consultation **interdisciplinaire** visant à évaluer et (ré)orienter – si nécessaire – le patient vers le ou les services appropriés à sa situation. Les critères varient selon les centres, mais sont surtout basés sur deux des principaux facteurs de risque de PICS : la durée de séjour aux soins intensifs (par ex. 5 jours pour l'Hôpital Erasme, 7 jours pour le CHwapi) et la durée du maintien sous respirateur.[12] Les équipes peuvent être constituées de médecins, infirmiers, kinésithérapeutes, ergothérapeutes, travailleurs sociaux et psychologues, et évaluent le patient à l'aide d'échelles validées. La fréquence varie entre 1 et 3 visites (à 1, 3, 6 et 12 mois selon les centres) pour suivre la progression du patient.[12] Cette consultation permet également d'avoir un feedback de la part du patient sur son vécu des soins intensifs, de discuter de ses émotions et de son ressenti avec un spécialiste et, le cas échéant, de démystifier certains aspects du séjour ou d'aider à reconstituer ses souvenirs. En ce sens, selon l'expérience des intervenants, la discussion autour d'un éventuel journal de bord (avec ou sans photos) et/ou la visite de l'unité de soins intensifs sont des initiatives qui visent à aider le patient à surmonter cette expérience.[zz].La consultation post-soins intensifs n'a théoriquement **pas de visée thérapeutique** : les différents intervenants en profitent néanmoins pour suggérer des pistes de traitement dans leur rapport à l'attention des médecins généralistes, parties prenantes indispensables dans le suivi des patients. Ils peuvent aussi référer le patient à un autre professionnel de santé, si nécessaire, le plus souvent un psychologue.

À l'heure actuelle, cette longue consultation (de 1 à 2 heures selon les centres et les intervenants) est financée, selon les institutions, par le remboursement d'une simple consultation, les fonds de l'hôpital et/ou une fondation privée.[12] Certaines institutions demandent une participation financière au patient, d'autres non.

A retenir

- **Les consultations post soins intensifs permettent de faire un bilan d'orientation afin de faire des recommandations de suivi au généraliste et éventuellement proposer des soins adaptés aux besoins du patient.**
- **Les médecins généralistes peuvent informer leurs patients de l'existence des consultations post soins intensifs et les motiver à s'y rendre.**
- **Les consultations post soins intensifs ne sont pas encore généralisées.**

[yy] https://www.erasme.ulb.ac.be/fr/infos-pratiques/depliants-et-brochures/le-syndrome-post-soins-intensifs

[zz] Même si la littérature ne démontre pas encore l'efficacité de ce type de pratique, le journal de bord est néanmoins reporté par les intervenants comme une pratique intéressante (voir les chapitres XX et XX).

6 CHAPTER 6: WHAT IS THE PERSPECTIVE OF PICS PATIENTS IN BELGIUM AND IN SIMILAR SETTINGS, ACCORDING TO THE LITÉRATURE?

6.1 Introduction

> "*Levensveranderend. Er is een leven vóór en een periode na de ic, voor zowel de patiënt als zijn naaste familieleden*." (Marianne Brackel, president of the Dutch patient's organisation IC-Connect for patients after an ICU stay)[218]
>
> *"Op het moment dat je het bericht krijgt dat je naar de ic moet, besef je dat er een grote kans is om te overlijden. Dan word je verteld: we gaan u in slaap brengen, neem voor de zekerheid alvast maar afscheid van uw familie. Je hoopt dat je wakker wordt. Wie het overleeft, ontwaakt in een soort schemertoestand. Met allerlei piepjes, geluiden en maanmannetjes om zich heen. Vaak treden er hallucinaties op: een compleet vertekend beeld van de werkelijkheid."* Dr Mark van den Boogaard, Verplegingswetenschapper IC Verpleegkundige Radboud UMC Nijmegen.[218]

This chapter intends to assess the perspective of PICS patients, and in particular their experience along the critical illness trajectory and their preferences in terms of support and care for their PICS-related problem. A great part of PICS symptoms originate from events and experiences of the patients during the ICU stay. As these perceptions may be difficult for caregivers to imagine, patient testimonies may also help health care workers to better understand the patient history and state of mind.

6.2 Method

For this rapid report, it was not possible to organize an interview survey of (former) ICU patients. We opted for a review of the qualitative literature focused on studies from Belgium and similar countries, published testimonies from patients and interviews with a small numbers of key informants (mostly ICU staff) on the subject. The broad rapid literature search done for the other chapters (see search terms in Appendix 1) was used to retrieve peer-reviewed articles on patient experiences and perspectives, with some additional papers retrieved by snowballing. All qualitative studies using interviews or focus groups were retained and screened for quotes of patients. We also screened websites from patients' associations for testimonies in English, Dutch and French. All selected quotes were then clustered according to converging themes.

6.3 Patients' experiences of the ICU stay

From the literature relating patients' experiences of ICU according to qualitative methods, we identified 8 themes in the perceptions and remembrances, as described in 2013 by Cutler et al.[219] in a critical review of 26 qualitative studies classifying patients' quotes and experiences of ICU.

The eight themes of this typology are as follows:

- transformation of perceptions: unreal experiences and dreams
- proximity to death
- transformation and perception of the body in illness
- transformation and perception of time
- dependence on the critical care environment and technology
- care, communication and relationships with healthcare professionals
- support of family and friends and desire for contact
- transfer from critical care and recovery from critical illness

6.3.1 Transformations of perception: unreal experiences and dreams

> *"There were puffin birds jumping out of the curtains with toy guns, firing blood at me. I kept wiping my face…There were loads of birds jumping on the next bed, laughing at each other. Completely crazy. I was really scared. I didn't say anything to anyone."* [220]

Patients lying in ICU often report to experience the reality as diffuse and unreal. It often goes along with **hallucinations and dreams** whose content is strongly influenced by their distorted perception of the reality surrounding them. This disturbance of consciousness and cognition is called **delirium** and its relation with PICS is described in Chapter 1. This appellation itself may be misleading because the patients experience terror and panic as 'real' but the health care professionals recognise them as 'unreal' since they name it 'delirium'.[221]

These experiences are remembered as distressing and sometimes terrifying. The hallucinations seem to arise from elements of the ICU environment: the clothing of the staff, the beeps and buzz of the machines, the tubes and lines they are tied to, etc. Not unfrequently, they have a paranoiac connotation, with feelings of being trapped, tortured and trying to escape. Some of the hallucinations, however, are pleasant experiences, such as a friendly dog in the ICU.[222] These memories – often called "**delusional and/or intrusive memories**" – may influence the risk of later occurrence of a PTSD as described in Chapter 1 and 2. **Not knowing whether these memories are real or delusive** is a problem many patients retrospectively have to fight with, even months after they left the hospital: "*I have all these images in my head that are totally false, that never existed …*"; "*I dreamed it or maybe it actually happened, I don't know …*"; "*I ask myself, did it really happen or did I just dream it?*"[223] Of note that it is sometimes difficult to distinguish hallucinations from true nightmares that also happen very frequently.

Box 9 – Experiences of hallucinations and dreams

"One of the strangest things that happens to you physically and mentally are hallucinations (…); until you've actually been through it you do not really realise the intensity of the experience."[224]

"The reason I attacked all the nurses and doctors and pulled out my feeding tube was because I believed it was the only chance I had to escape from the hospital… I couldn't trust anyone that worked there. Every sound I could hear (machinery) and people speaking to me was misinterpreted.''[225]

"Suddenly, crowds of people in yellow suits gathered around me."[226]

"When I awoke I saw my husband who I knew to be in Australia hovering at the end of the bed like a hologram and assumed it was some new Skype phone development where he could send me his picture whilst telephoning from Australia! He was unable to convince me that he was actually in the UK." (Barbara)[227]

"Ik zie ze sjouwen met dozen. Lopen allemaal in blauwe operatiekleren met mutsen en mondkapjes voor. Ik weet het zeker: in die dozen zijn er organen. Ik word hier gevangen gehouden voor mijn organen. Straks ben ik aan de beurt en komen ze er alles uit halen. Of hebben ze er al iets uitgehaald. Ik voel geen wonden, nee nog niet dus. Weg wil ik en wild sla ik om me heen. Ik zit vast aan slangen. Mijn handen vastgebonden. Ik kan niet weg. Ik raak in paniek. En dan staan ze ineens allemaal om me heen. Nu gaat het dus gebeuren. Ik roep mijn dochter, maar ze komt niet."[228]

"Endless days and nights filled with strange broken sleep. A sea of fragmented menacing faces and shadows swimming through erratic beeps and bells. A large cackling face floating over me, constantly morphing and changing shape. The staring old lady in the bed opposite, her sallow skin disintegrating, eyeballs disappearing to reveal deep dark holes from which cockroaches crawled. Her weary face melting like wax into a big grey smudge. Deafening, haunting laughter filling every space. Blood seeping through holes and cracks in my skin, forming a puddle of red around me. Small insects scuttling up my arms and legs. My chest locked to the bed with wires and straps, as a plastic mask repeatedly smothered me. A strangling sensation around my neck. A warm metallic taste. An invisible force pinning my body down as a dark curtain was drawn closed. These are my memories of intensive care. They formed the fabric of reality that I would take forward and recall vividly in my dreams for many months afterwards. Such fragmented delusional memories made it extremely difficult to understand and make sense of what really happened to me. This prevented my psychological recovery and led to the development of post-traumatic stress disorder." (Sarah Wake, patient and medical doctor, Cardiff, UK)[229]

About the memories, a French study noted that the 20 participating patients spontaneously first responded that they could not remember anything of their stay in the ICU (*"black hole"; "I don't know what happened to me*"), but that fragmentary and confused memories resurfaced during the interview. For a majority of them, it was their family who recounted the events of the ICU stay: *"I have no recollection"; "It's a blank"; "All I know is what my family told me, I don't remember myself".*[223] In a Swedish study[230], some patients reported to find it difficult to accept that someone else – even next of kin – knew better what had happened to them, which rose a feeling of exclusion.

A British study noticed that the first clear memory for all interviewed patients was a family member at the bedside: *"[my first memory on awakening] was my mother stroking my arm, saying 'Mum's here'… that was some 30 days after my admission"*[222]

Box 10 – The story of Francine

A narrative discourse analysis [231] tried to **give sense to the delusive memories** of a young woman of 27, Francine, who was brought to the ICU in the last trimester of her pregnancy because of severe complications and nearly died. Her baby was born prematurely. During her treatment in ICU, Francine experienced severe anxiety, hallucinations and awareness that were beyond her comprehension. "Some of the prominent memories were about a small, bloody, purple thing in a plastic bag and huge, poisonous frogs in her room. The frogs then became crocodiles that constantly made a suctioning and blowing sound. There was spaghetti hanging from the ceiling that would rot if it is too warm. (…) After discharge, she recovered but had an urge to go back to the ICU in an attempt to understand what had happened to her. The nursing staff reconstructed the ICU room where Francine was treated to look almost the same as it did when she was there. (…) She managed to identify certain sounds, smells and images and asked various questions. The image of a baby in her shirt's pocket was clarified with the nurse's answer that they brought baby Neil to her on a daily basis and placed him on her chest to stimulate his development and improve bonding. The sound of the airplane was similar to the sound of the air conditioner in the room. She also pointed out that the ventilator made the suctioning and blowing sounds that she remembered the crocodiles in her dreams made. (...) All the lines (plastic tubes for intravenous medicine and feeding) that hung above her bed could have looked like spaghetti. In her distorted mind, she interpreted the risk of infection as the spaghetti that would rot in the heat. The white polystyrene pipe and the smoking turned out to be the daily physiotherapy sessions where she had inhalations to loosen the phlegm from her lungs. The constant need to empty her bladder was clarified when the nurse explained that a urinary catheter often causes the sensation of a full bladder."(Herbst, 2012, p 25 [231])

6.3.2 Proximity to death

> *"I woke up. I heard the voice of the people; but, my body was not moving at all. I just felt like I was going to die. You cannot even imagine how terrible it was. The doctor shines a light in my eyes… I was so afraid that they thought I was dead and they would take me to the mortuary. I felt so close to death at that time. Even these days, I keep thinking about it; it is so horrible*."[232]

Facing death is a traumatic event whatever the circumstances; ICU is no exception to this rule. This may give rise to a state of deep anxiety and vulnerability, seeing one's own life literally hanging by a thread, a monitoring screen or a ventilator, and fearing that these technological devices could stop working. [233] This may lead to loss of confidence in one's own body and a long-lasting anxiety of falling ill again.[234]

The fear of dying is not only conscious; it may also influence the content of many hallucinatory and delirious perceptions. This sense of deep fear is a very alienating experience that can last for years and even transform the meaning of life afterwards.[219, 234]

In their qualitative literature review, Cutler et al[219] also mention that facing one's own death is one thing, but that ICU-patients also realise that other patients around are dying or had died. *"I was not aware of others in CCU [Critical Care Unit] at first. As time went by and I became more aware it was more distressing being around other ill people"*.[225]; "*Zoveel geluiden, mensen horen sterven, de dood is zo dichtbij*."[228]

Box 11 – Experiences of fear of dying

"I felt like I was on my way out – I'll never forget it."223

"I had this fear all the time, I felt, like, not a safe place."223

"To witness your body deteriorating and slip into a life threatening condition in only a few hours' time at high speed...It takes much time to gain confidence in your body again. I've played the movie back many times."234

"I was dreaming I passed the border; it was the end and everything turned dark." 226

"I had fantasies and was horrified: the nurses were dangerous. I was attending my own funeral." 226

"They [the nurses] had to prepare so many patients for death. They turned you into a zombie… put you into a shopping trolley and wheeled you into a basement. They got paid according to how many patients they brought down. People were lying round at various stages of dying. I ended up in a trolley with an old boy called George, who was dead. He was leaning on me and there was unbearable heat… Before I knew it, a nurse came upon me. She gave me the injection. There were people there with cloaks like an abbot, I couldn't see their faces. They were families who would take your soul. They would envelop you… suck you up and move on….I jumped out and got away but ended up in a coffin in a chapel of rest." 220

"My particular hallucination was that (…) every time I closed my eyes something descended over my face. And the best way that I could describe it, (…) it was like a bat, you know, like a bat flying with a sort of triangular shape. And in the middle of this triangular shape was something moving, pulsing, which made me think that it was alive, that therefore it was a bat. And it came over my face very slowly, very gently. (…) And I would be looking madly, intensely to see if there was any hole in this thing. Because if there was no hole in it, then I wouldn't be able to breathe through it. And because of that I didn't sleep for four nights."[224]

6.3.3 Transformation and perception of the body in illness

Experiencing that your own body is not completely yours anymore, that you do not have control of it anymore, or that you even do not feel it, may cause deep feelings of vulnerability and anxiety of further deterioration.[233] "The taken for granted aspects of smooth body functioning are disrupted".[219]

In her qualitative (grounded theory) study, Corner et al. explored the experience of physical rehabilitation after critical illness.[222] They elaborated about the discrepancy experienced by patients between "their current self, which incorporates their physical dependency, fatigue, clarity of mind and self-image, and the mental representation of themselves, which is still consistent with their preadmission self. (…) Physical independence and function are core components of the concept of self. When physical ability deteriorates so unexpectedly, rapidly and without obvious causation, it comes as a shock to the patient blurring their sense of self."[222] According to these authors, an important aspect of early physical rehabilitation will be to challenge this self-perception in order to achieve a 'recalibration'. Kang and Jeong make a similar statement when they describe the entire process of recovery as "survivors embracing themselves as vulnerable".[232]

The sensation of not being able to breathe/not getting enough air and being connected to mechanical ventilation is a scary experience that can be panicking: *"It was like putting your head outside the train with your mouth open. It was painful because you have poppers. Keeping the mask airtight…. It was the feeling of panic that I wasn't able to breathe properly with all this air being pushed in so fast… Like sucking in an empty crisp packet… the anxiety, the fear of having the mask on, made my heart go like the clappers… I would try to get my thumb underneath it to let some air out; every time I did that the alarm would go off and I would get into trouble."* [220]

Discomfort and pain are mostly reported in relation with endotracheal tube, drain tubes and catheters, nursing care, but also with pre-existing diseases and/or cause of the ICU-stay (for instance after cardiac surgery). Pain is also reported in combination with other feelings of indignity, fear, and distrust[220] or in the context of delusive dreams in a struggle to understand the reasons for it.[219]

Thirst is another bodily experience that is more and more reported by patients with the use of light sedation protocols – and that might be underestimated by the staff. Indeed, endotracheal tubes, electrolyte disturbances and the use of various medications, especially opioids, can generate a

strong feeling of thirst, and when patients are conscious, they can feel it but are prevented from drinking because of the mechanical ventilation. Besides the deep discomfort of the thirst sensation itself ("a paramount thirst"), the inability to take action on such a basic human need can generate feelings of frustration and powerlessness: *"The worst thing is that you are thirsty, and you just lie there, and you can't tell anyone that you are thirsty".*[235]

6.3.4 Transformation and perception of time

> *"I don't know if it was day or night, I don't know…"*[223]

Patients often report that they lost track of time during their ICU-stay and that they could not distinguish between day and night. This was reported to enhance the feelings of helplessness, confusion and stress:[233] *"I was totally confused …"; "I had lost all notion of time …"*[223]

Some studies also describe how this transformation of patients' perceptions of time may have contributed to the way the situation was (mis)understood or perceived with distorted duration. Being given a posteriori chronological information (by healthcare professionals or by family members) facilitated understanding for the patient of what he/she had been through.[219]

"Het is niet eenvoudig voor die patiënten om te bevatten dat ze soms weken in slaap geweest zijn. Dat is vaak traumatiserend. (…) Geregeld moeten we herhalen welke dag het is. Of er hangt een grote kalender op, zo kunnen patiënten zien welke dag het is." (Interview of an intensivist during the Covid crisis - [236])

One consequence of this blurring of the time passing by are the sleep disturbances, though these were also caused by the discomfort, the strange body experiences and nightmares, the fact of being regularly flipped around and the permanent noise in the ICU.

"It was noisy, you're woken up all the time and when you try to sleep or rest, there are all these alarms going off, and you're woken up regularly for care." [223]

6.3.5 Dependence on the critical care environment and technology

> *"I didn't think of anything. No. I put up with it… I just let them decide... I wasn't really aware of what they did at first."*[237]

Lying in an Intensive Care unit is an **experience of total dependency** to the technology and to the health professionals, which may also cause feelings of helplessness and frustration. Passivity can be experienced as being a burden for the professionals; for example, not being able to go to the toilet can be particularly humiliating.[233]

Memories of being tied down are also painful: *"I couldn't move and I would get upset …"; "It really affected me, I strained my fists to try to untie myself but I was powerless."*[223]

A Swedish study about patients' experiences of autonomy in intensive care noted that the forced passivity of the patients and the focus of the carers on the biological body can create a risk that "ICU staff not only take command of the patient's vital functions but also their decision-making, leaving the patients without control of their own body and mind".[237] Another Scandinavian (Danish) study also reported that involving the patients in their own care 'made them feel human, fight for survival and experience control. It gave them a sense of caring from the staff.'[233]

Box 12 – Experiences of passivity, dependence and wishes for autonomy

''In the beginning I was so sick. I felt grateful that there was someone to make the decisions for me! Waking up in the morning and being shaved, we bathed, I mean, it was incredibly nice.''237

''I was very dependent, especially on the ventilator. It was my lifeline… I was grateful for it after having traumatically experienced, little by little, the loss of breathing… Finally you sort of die, before you are connected… Scared to death that something would happen to it (the ventilator)''237

''It was consent, as they asked if I wanted to get rid of it (the feeding tube) and I said yes.''237

"I could also exert more influence as time passed, as I became more and more healthy. Then it was not such an acute phase as it was at the beginning. Besides, I was affected less and less by strong medication and that caused me to have reason to actually make decisions and have opinions about things.'' 237

‘‘I think that my attitude is very important for my care and I believe that to recover you also need the desire to desire to recover… you need to show them that you have…You have to decide!’’[237]

The dependency to highly technological environment also appears at the moment of the transfer to a less technological environment and less technologically based care (see further).

6.3.6 Care, communication and relationships with healthcare professionals

The experiences of **the staff being present around** and of **not being able to communicate with them** were the two most frequently reported experiences in the nine studies included in the metasynthesis of Baumgarten.[233]

In a critical review of 26 qualitative studies, patients mostly perceived healthcare professionals as competent and caring and their presence was generally positively associated with safety and security[219]: “*I felt in good hands because the ICU team acted decisively, they radiated routine and expertise*” [234] ; ‘‘*I felt protected, safe and very well cared for, both night and day.*’’ [225]

However, not being able to communicate was perceived as a strikingly difficult experience. Another common complaint is patients hearing their case being discussed by healthcare professionals within earshot but not being involved in the discussion.[219]

Box 13 – Experiences of not being able to communicate

“Losing the ability to talk was really difficult for me.”[223]

“I couldn’t move, couldn’t move my head or talk or anything, but I could hear everything.”[223]

“Je wilt zo graag wat zeggen en vertellen hoe jij je voelt maar dat kan niet.”[228]

“Vooral ook het besef dat je gewoon absoluut niet wakker kunt worden en geen enkel contact kunt maken, heeft heel veel impact op mij gehad.”[228]

“Iemand die je kan horen, niemand die beseft dat jij dat wel kan.”[228]

“Ik probeer hem duidelijk te maken dat ik wakker ben, maar ik kan niet praten en ik ben vastgebonden”. [228]

“My experience is that it is quite awful to be mechanically ventilated. You can’t speak, you can’t have anything, you feel thirsty… In the beginning, all kinds of communication are confusing. You are totally beside yourself”[235]

In such a frightening environment, patients often report to be **eager for any form of human contact**, attention, verbal or non-verbal communication and reassurance. All small signs of attention are welcome and go straight to the heart. “A remark that pays attention to your fear, and assures you that you will be cared for can help a lot. Intention and intonation can make the difference.”[234]

“The one most important thing was to have eye contact with the nurse. Some of them only needed a glance to understand what I wanted.” [226]

“A woman came in and asked if I would like to hear some music. They brought guitars into my room and played music. I found it to be incredibly uplifting.”[238]

Another communication need expressed by the patients is the **need to receive information** from healthcare professionals about their illness and treatment. Patients left without information about their situation report strong feelings of powerlessness and/or anger.

Box 14 – Experiences of being left without understanding of what you’re going through

“No one took care of me”[223]

“I didn’t get any explanations”[223]

“No one told me what happened”[223]

"Someone from the unit came to see me and I asked him why I was hooked up and he explained to me; after that, I think everything calmed down, and went ok."[223]

"I think, if they could have explained things in simpler terms, instead of so many doctor language you know...so that the layman could understand".[239]

This lack of understanding about what is going on may reinforce the sense of fear and anxiety caused by the frightening environment and influence the dreadful delusions: *"I remember being petrified one night....crying to my mother...I couldn't sleep...I was so scared they were going to come and stab me with needles...One nurse...very nice...said we will not stab you when you're asleep...made me feel better."*[239]

On the contrary, when patients were informed about their care and about what is going to happen, they felt safer and accepting.[233]

(Former) ICU-patients reported how important they felt the role of their **family members** in receiving information from members of the healthcare team: "*They were talking to my family about everything. It does help that the family gets all the information, if the patient can't think...*" [239]; "*In the ICU, they treated my wife like one of the team. That was very important to me. They often invited her to rounds."*[238]

6.3.7 Support of family and friends and desire for contact

"*Ik vond het fijn dat er iemand naast me zat, het bood afleiding en ik was dan niet alleen*" [228]

The high **importance of having a loved one close by** during the ICU stay is underlined in several studies. Patients associated the presence of their families and relatives with a feeling of security, support and comfort. Family members were considered like 'an anchor in a strange environment' whose presence could reduce feelings of restlessness, fear and agitation.[234]

Ik ben juist zo blij dat mijn broer en zus er zijn. Bij hen kan ik gewoon gaan slapen, dan voel ik hun handen in de mijne voordat ik in slaap val."[228]

"I always felt that there was someone there for me."[223]

"My wife looked after me, and that was great because … well, I could see her".[223]

A consistent finding reported in a meta-synthesis [233] was that the patients themselves felt concerned for their loved ones, for instance about how they were coping with the situation at home and how far they had to travel to come and visit them. But visits could also be exhausting for some patients, especially when the relatives did not understand their attempts to communicate with them.

Also **family and relatives are exposed to considerable stress** during this period, sometimes even more than the patient self (who is not always aware of his/her situation). A Norwegian study reports that relatives say they often have to neglect their own feelings because they have to stay strong and remain in control, but that this can have consequences later on, because these feelings will have to be processed: *"You have to be strong, and thus you end up neglecting much of your own feelings; what is bothering you is neglected. I have put it away, and I have to deal with it little by little."* (wife of a patient, 6 months after discharge)[240]

Some relatives try to make themselves useful in any way they can[234] and they are very thankful when they are allowed to take part in care: *"As the time and days went by the nurses started to let me help with the suction from her mouth when she coughed up mucus, give her water on her lips from a sponge and wipe her brow when she was clammy (…) they started to call me Nurse Colin which was nice as I felt I contributed to her recovery."* (Colin)[227]

Box 15 – Testimony of 'warm care' in the ICU (Ghent- UZ-Intens)

"In november vorig jaar heeft mijn man een hartaanval gekregen. (…) De artsen hebben hem zeven weken in een kunstmatige coma gehouden omdat hij te veel pijn had. Uiteindelijk hebben we hem moeten laten gaan.

In die zeven weken zijn we amper van zijn zijde geweken. Elke dag zaten we aan zijn ziekbed. Hoewel er op Intensieve Zorg strikte regels gelden voor bezoek, mocht dat. Het team begreep hoe

belangrijk het voor ons was om dicht bij hem te zijn. Ik heb in de ziekenhuiskamer ook foto's mogen hangen van Bart. Want ik wilde dat mensen hem zagen zoals hij echt was, niet als de hulpeloze man die daar lag.

De zorg op de afdeling was heel menselijk. We voelden ons er warm omringd. Als we op de gang stonden te wachten, kwam er altijd wel iemand horen hoe het ging. We konden ook altijd bij de psychologe van de dienst terecht om ons hart te luchten. Die grote betrokkenheid van heel het medische team had ik niet verwacht. Op geen enkel moment heb ik mij daar een nummer gevoeld. Bij het overlijden van Bart heb ik op de rouwbrief gezet: breng geen bloemen mee, doe een gift aan vzw UZ Intens. Met dat geld gaan we nu de kale wachtkamer van de afdeling gezelliger maken zodat familieleden van patiënten een fijne plek hebben om even tot rust te komen. Zo eindigt die donkere periode toch nog met een positieve noot. En voor mij is het een manier om Bart een beetje te doen voortleven." [241]

6.3.8 Transfer from critical care and recovery from critical illness

6.3.8.1 Transfer from ICU to the ward

"I was horrified by the ward…no-one seemed prepared for my needs…" [225]

Although many patients felt being transferred from ICU to the ward as a positive step towards recovery, they also remember being struck by the huge difference between critical care and the ward. The presence of fewer healthcare professionals was felt as strikingly contrasting with the constant presence of the critical care nurses, leading to **feelings of vulnerability and anxiety**.[219] Patients also had a feeling that healthcare professionals outside the ICU had little knowledge of the symptoms that could occur following a critical illness, like swallowing problems or extreme weakness or even not being able to push a button to call the nurse.[242]

Family and relatives also experience mixed emotions of relief and uncertainty[243].

Box 16 – Experiences of feeling vulnerable when transferred to the ward

"Transition to the ward is huge…..no 24/7 observation anymore....and the feeling not to be safe anymore....Nurses on the general ward did not have any idea of what I had been through."[234]

"It was scarier on the floor...I was in a room and there was no one else in the room...I felt less people monitoring me...I was more left alone and ...it was more a psychological thing."[239]

"Op de IC vertrouwde ik erop dat ze meteen bij me waren als het nodig was. Het was een grote overgang toen ik na een week van deze IC naar een verpleegafdeling ging. Ik lag niet meer aan de bewakingsapparatuur en de verpleegkundigen hadden niet zo vaak tijd om te komen kijken. Ik voelde me de eerste nacht erg eenzaam en onrustig. Mijn bloeddruk en de hartslag gingen enorm omhoog, ik raakte in paniek. Die volgende nacht heeft mijn moeder bij mij op de kamer geslapen zodat ik me veilig voelde en kon rusten."[244]

"Er was geen nazorg en wat me heel erg opviel was het enorme contrast in de overgang naar de 'gewone afdeling'. Eerst word je 24 uur per dag bewaakt en vervolgens loopt er 'af en toe' een verpleegkundige binnen. Ik voelde me erg kwetsbaar en was bang dat er toch weer iets mis zou gaan."[245]

"She is very weak, the step from ICU to the general ward, it was surprising, oh, it's such as big step. It's positive she has left the ICU, but, on the other side, I ask myself, is it safe?"[243]

Patients, as well as family and relatives, also expect that the time in the ward should be a **transition before discharge**. They start realising that they will soon have to go back to everyday life and that a lot of things will have changed, which can be emotionally challenging. They have many questions about what would happen afterwards: will the patient be able to walk again? Will we need a wheelchair? Will we have to move to another residential home? Will I have to quit my job to look after him? etc.

But family and relatives also claim for **more help and support in the preparation of their returning home**. They expect to become informal caregivers after the patient is discharged – as more than half of the relatives do[243] – so they think it would be natural for them to be involved in the treatment or

care plan, but they often feel that they are not acknowledged in that role by the staff.[243] This need for acknowledgment and information will be further developed in the next section.

Box 17 – Experiences of lack of information and involvement

"I started to realize what had really happened to me, like the whole self-realization about oh well, I can't quite walk, we needed more support like about, like when I had to go to other places, we need support so the wheelchair taxis and wheelchair services and more about it...kind of now starting to look beyond the hospital, and ....so it's the needs for support, and information definitely greater, because I was more lucid and we were looking at the future"[239]

“In the last weeks we all lived on adrenalin. Now we try to process and carry on. We hope and assume that the situation will continue to improve.”[243]

“Yes, we want to have a conversation with someone, what is the follow-up? (…)[we would like to meet] someone who gives us guides and advice in how to continue from here.”[243]

“The government expects us to provide care and live independently, but we are not facilitated by the nursing staff. They have the knowledge, so I would say: do not let us walk in the dark, show us the way.”[243]

6.3.8.2 Discharge from hospital

The feelings of vulnerability and abandonment that prevail at the moment of transfer from ICU to a ward are also reported at the moment of discharge from hospital, but combined with feelings of relief:

“*That was the hardest thing because when you’re in hospital you’re very safe, or you feel like you are because you’ve got your buzzer, and when you’re in intensive care you don’t realise at the time but you’ve got the safety net of all the doctors and nurses around you.”* [246]

“Being in your own home is nice, your own bed, family, but I was worried. I guess with technology, they knew everything was fine, so they let you go. Still in the back of your mind you worry. Is it healed? Will anything go wrong? Because in the hospital, the nurses are there. You push a button and they’re there. But here, there is no button to push!”[247]

Some patients report having had a **bad experience of their discharge**; they felt like they were being ‘thrown out to the wolves’, as discharge happened in a rush and was not accompanied with information on how to get effective care and nursing support at home, nor communication with the first line professionals in their community.*[247]*

Some patients also report that they would have liked to have more to say in the decision to leave:*"I would like to have had people talk to me a little bit more...about what to expect, like my choices, ...to go to a rehab home, go to a home, or stay a little longer".*[239]

Box 18 – Experiences of frustrating discharge

“There is a need for hospitals to modify release procedures so you’re not just thrown to the wolves when you’re released, there’s somebody who is going to keep track of you (…) They’re prescribing stuff in the hospital, throwing it to the family doctor to monitor.”[247]

“It felt like they just wanted a bed and had to throw me out… I just felt like… sort of abandoned really” [248]

“It was a rush to get rid of me. They should have a little more ample time to explain. As I say, you are on so much drugs, you really can’t remember. As a matter of fact, they took me out of the ward to a TV room. I waited for my family. Anything could have happened to me and nobody was there. I guess the rush was just to get the room empty to place somebody else in.”[247]

“Dumped at home from a taxi with two sticks… I was just a number then.”[248]

“The discharge information is really vague. I wish people would spend more time going over it with patients.”[238]

"We were kept in the dark… just to get put back into your home. No guidance for your family as to how to take care of you".[248]

"I think it's just starting to hit me now how difficult the future is going to be. (…) Whilst our time when he [my husband] was on a ventilator was a complete hell, I realise the hard work starts when he comes home so any preparatory information for this is really helpful."[227]

6.3.9 Key messages about patients' experiences of ICU

- **A great part of PICS symptoms originate from events and experiences of the patients during the ICU stay.**
- **Patients in ICU often perceive their reality and environment as distorted. They can experience hallucinations and terrifying dreams (delirium). Memories of this can last very long after discharge. Not knowing whether these memories are real or delusive can also be a long lasting problem.**
- **Proximity to death can be a very alienating experience, giving rise to deep feelings of anxiety and vulnerability. The same goes for the total dependency to the technological environment.**
- **Not being able to communicate (intubation, altered state of consciousness) and being tied down are difficult and frightening experiences.**
- **Patients in ICU are eager for human contact, reassurance and all signs of attention to their needs, but they also need to be informed about what is happening to them.**
- **The presence of family and relatives is felt as being of utmost importance for the patients. They highly appreciate when the staff allows it.**
- **The transfer from ICU to the ward often gives rise to feelings of vulnerability and insecurity.**
- **Family and relatives claim for more recognition in their (future) caregiver role and for more information and preparation to return home.**

6.4 Patients' needs in the months following discharge

A recent (2019) scoping review[249] of the qualitative literature categorised patients' support needs framework into four categories, based on House's Social Support Needs.[250]

- informational needs: provision of information to address problems.
- emotional needs: provision of empathy, love, trust and caring.
- instrumental needs: provision of tangible aid and services to directly assist needs. In this context, we will rather call it 'Revalidation needs'.
- appraisal needs: provision of constructive feedback, affirmation and social comparison.

6.4.1 Informational needs

6.4.1.1 Reference information

Patients generally report that they feel too little informed and they express the need for '**permanent' information**, such as booklets or other information supports that they (or their relatives) can go back to when questions arise. [239] The impact of such educational material on PICS is discussed in Chapter 4 on interventions.

6.4.1.2 What did happen? Filling the holes in one's own history

> *"It's a jigsaw and what you remember is not right. I would like to know who was there and what was going on."* [251]

> *"It's hard to believe that it's happened. And everybody else is talking about it and it's as if I wasn't there, but I suppose I wasn't really."*[252]

'Black holes' and blurred memories make it difficult for the patient's personal narrative to achieve temporal coherence. This can be highly disconcerting as this coherence is necessary in order to **make sense of one's own story and regain control of one's life**. In particular, "life-threatening experiences need to be storied and understood if the life threat is to be responded to effectively. Otherwise the individual might become more susceptible to an avoidable repetition of the event."[252] The quest for information on what happened during periods of unconsciousness or blurred consciousness – to get the 'full story' – is thus an essential need. Filling these gaps is the reason for measures such as ICU diaries and return visits to the ICU. These will be analysed in detail further (see 6.5.3 and 6.5.4). The effects of such initiatives on PICS outcomes are discussed in Chapter 4 on interventions.

6.4.1.3 What will happen? Warning on the symptoms that are likely to occur

> *"See, I didn't know that was going to happen to me. When they released me from the hospital I thought everything was perfectly fine...Then slowly things kept creeping up on me....memory loss, trying to read and write,...trying to run a computer,...forgetting things about the kids...really crazy"* [239]

A number of studies underline how **patients and their relatives feel insufficiently prepared about what to expect as changes in their daily life**. Information – be it verbal, written or online – is not always provided. And when verbal information only is provided, it may not be fully understood and/or be forgotten in such a critical moment.

A Canadian study about the discharge's experiences after cardiovascular intensive care concludes that the information given is often 'technologically driven' and does not sufficiently address all the unfamiliar bodily sensations that participants would experience.[247] It suggests that this could lead to anxiety because patients do not know whether the sensations they experience are normal or not. Many testimonies suggest indeed that fatigue, cognitive problems, emotional vulnerability, etc. all seem to fall unexpectedly on them although one would imagine that they would have been warned about it. This situation of not understanding what's going on could last for a long time after discharge.

On the contrary, those who did receive adequate information about the symptoms they would likely encounter said it was hugely reassuring, even when the predictions weren't very optimistic: *"About three months later my hair started falling out but [that booklet] was really good to have because it said one of the things… your [hair] may fall out… And so I thought 'that's OK'"*[246]

Box 19 – Experiences of 'not being warned'

"All I want to know is, is what I'm feeling part of the normal getting over this process? Because it doesn't say anything about that in the [discharge] book, 'cause I've gone back to that book a couple of times." [247]

"Sometimes you need to be told. I'm used to not being sick. It just really never occurred to me that I couldn't just get up and split wood and do the whole nine yards"[239]

"When I am in bed and everything is quiet, I hear my heart beating loudly, it keeps me awake for a long time, it's something I have not gotten used to. I will be seeing the surgeon, I will ask if this is normal."[247]

"Mainly in the first three weeks after my stay in hospital during which I needed mainly to rest and my mail and other things I needed to progress piled up so that I now feel somewhat overwhelmed with what I have to catch up with. Now 6 weeks later, I feel quite battered physically and emotionally and I suppose I am still quite tired and emotionally processing the experience of having had such a serious illness. I still feel quite vulnerable.''[225]

"There wasn't enough explaining of things like hallucinations, so I thought I was mad (…) it went on for such a long time and I did have quite bad flashbacks." [246]

"I could have used an explanation of the hospital stay. I'm still confused about what happened [months after], and that is concerning to me."[238]

6.4.1.4 Better informed first line professionals

> *"To find that the GP doesn't know really much about what you've gone through it's a bit… worrying."*[246]

Along with the lack of information of the patient, the lack of information of the community healthcare professionals that are taking over the care may add to the distress of the patient when leaving the reassuring environment of the hospital. A number of studies report the **lack of (in)formation of first line health professionals** about the specific problems and needs of patients discharged from ICU and how to handle the symptoms likely to occur after an ICU stay.

Box 20 – Experiences of insufficient information of the health care professionals

"Home care nurses are not provided enough information about the hospital stay."[238]

"De huisarts en specialist vertelden dat het normaal is, ik ben immers erg ziek geweest. (…) Ik had sneller en beter aan mijn herstel kunnen beginnen als ik beter geïnformeerd naar huis was gegaan en goed begeleid was thuis.[107]

"I could really have done with a bit more support from professionals who knew. I mean none of those people knew about intensive care. And I think a bit more support from people who have actually worked with people who've been through the intensive care experience would have been really helpful at the time." [13]

6.4.2 Emotional needs

6.4.2.1 Emotional/psychological distress

> "*The emotional side was very difficult to come to terms with... You can cry uncontrollably and there was no reason for it... You don't know when it's going to start. You don't know when it's going to stop. You don't know how long it's going to go on for. I found this one of the worst things to come to terms with..."*[13]

The first few months after hospital discharge are generally felt as a most difficult period. During this time, patients need a lot of **reassurance** and **psychological counselling/support.** Most of them are willing to 'turn the page' and to set all their efforts on their recovery. Some prefer not to think about their ICU stay anymore, and manage to do so. But for others, intrusive feelings of anxiety, distress and depression may arise. They may also be worried about the complexity of their illness and the long duration of their recovery.[249]

In a qualitative study describing former ICU patients' wishes about the support needed to optimise their recovery, the **psychological impact** of critical illness was cited as **the most frequent limiting factor to full recovery**, and **psychological services were the most frequently requested and most urgently prioritized** by most participants.[246] They also pointed out that clinicians and patients did not always have the same views (and outcome measurements) when assessing recovery and quality of survivorship.[246],[221]

A Canadian study which particularly investigated the early phase of 'home adjustment' and the re-integration back into the community underlines how this period can be **emotionally difficult** for many patients and a cause for increased stress and depression. The re-integration into the community was considered as a source of increased stress and depression, and patients expressed their need for more support from community-based healthcare providers in re-building psychological independence and confidence.[239]

Another study focused on the determinants of **self-reported unacceptable outcome of intensive care treatment**, conducted on 1453 survivors of ICU, concludes that "the mental component of PICS, but not the physical and cognitive component, is strongly associated with self-reported unacceptable outcome of ICU treatment 1 year after discharge", especially the symptoms of depression and anxiety.[253] And in several studies, patients report that **their emotional and psychological health had received little attention in comparison to their physical health**.

Box 21 – Experiences of emotional difficulties and need for support

"I guess in hindsight...I didn't feel like I had adequate support...I should have had someone coming in to give me a hand... I just felt scared and helpless" [239]

“I felt like I was never going to be myself again, feeling depressed, I would have liked to have had more support from physicians like psychiatrists to talk to.”[238]

“You could never imagine the emotional side even if you were prepared…emotionally it was a rollercoaster”[225]

"If I had maybe a list of people or something, then, I might have considered calling...there might have been someone...if I had questions I would have called just to have gotten some answers" [239]

"Everyday I was realizing a little bit more how deep the hole was...so every step that I actually learned that oh you don't have hair anymore, oh you only weigh 90 pounds, no you're not eating anymore,...you just fall deeper and deeper, into this big hopeless hole of depression...they didn't have a psychiatrist come and meet my needs,...until the middle of October when I was extremely depressed."[239]

"I definitely would have wanted [a counselor or therapist]...I'm a person that likes to spew. And I think if I would have had somebody to listen other than my husband ...it would have been a real asset to me"[239]

6.4.2.2 Personality and relational changes

> *“It was such a slow process…it was only afterwards that I realised how unsettled my world was as a result of, not the physical… here, but the mental side of it… it took me 3 or 4 years.”* [246]

A French study also reports that patients describe “feelings that **their psychological state has profoundly changed** since ICU stay”, with feelings of not being the same person as before, incomprehension, rejection, irritability, nervousness, sleep disorders, recurrent major anxiousness, depressive symptoms, PTSD.[223]

The lack of understanding of the patient’s difficulties may also lead to **tensions within the couple or the relations,** because everyone often expects the patient to rapidly return to his/her previous level of functioning.[239] Personality changes could also occur without being noticed by the patient himself. For instance some testimonies of relatives indicate that the patient had become more irritable and impatient, but that he/she did not always understand how deeply this could affect the family.[242]

Box 22 – Experiences of psychological/personality changes

“Lots of things that are hard to admit, it’s the fact that you change so much, because well, when you have a big shock like that, well, it’s a big change, it’s important and it’s visible, and that’s hard to accept …”[223]

“Ik zit anders in mijn vel en reageer anders. Toen ik weer op mijn werk verscheen, zeiden collega’s: ‘Jij lijkt wel een ander mens.’ Mijn familie zegt dat ook.”[218]

“Ik heb het gevoel dat ik letterlijk uit de tijd ben gevallen. Er was een Daphne van vóór de IC-opname, en een Daphne van na de opname. Die laatste is vooral op zoek geweest naar wat er al die maanden in het ziekenhuis is gebeurd.[254]”

“I think it took six months to physically recover. I think that the psychological side of it, the experiences that I’ve have had made me realise that they were much deeper experiences than I’d appreciated at the time. I think it’s taken me – five years later I feel well-adjusted – I understand the psychological side much more.”[246]

“I have changed a lot from the past. I used to be the breadwinner; but, now, I need the full help of my wife. I am so sorry for my wife... I used to think that I could do anything before; but, now I wonder what I can do. I wanted to volunteer and do activities against the nuclear power plant... In reality, it

is not easy for me to go out to meet friends now… I do not want to go out. I am not even confident to meet new people." [232]

"I didn't understand... I thought she [my wife] could be kind to me. She wasn't kind anymore. She saved my life, got me out of the hospital, brought me home, and then was mad and angry... maybe it was too much in retrospect to ask of my wife... my wife became my primary caregiver and that probably really ticked her off... she was mad at me.... I was mad at her"[239]

"It has been hard to reconcile the two separate lives that we lived during that time, and neither of us will ever be able to fully comprehend what the other went through. Initially I think this put our relationship under a little bit of a strain. Perhaps we had built our 'reunion' up in our heads to be something more than it could ever be for two emotionally and physically exhausted people. However the old saying 'time heals all wounds' really is true, and we are now moving into a new era of serenity."[227]

"Hij doet alsof er niets gebeurd is. Stapt op zijn fiets, komt later thuis dan gezegd….en ik helemaal in paniek. Ik durf niet te slapen, lig voortdurend te luisteren of ik hem hoor ademen. Als ik erover wil praten, zegt hij dat ik me niet zo druk moet maken. Er is niet over te praten met hem."[244]

''It tends to be embarrassing sometimes. When there is a long queue at the checkout in the supermarket, he becomes annoyed and talks loudly and does not always think about what he says. (The husband replies, ''No, that's not true.') 'Yes, I'm afraid it is.'"[242]

6.4.2.3 Post-traumatic stress disorder

The emotional and psychological distress expressed in the former section may culminate in a genuine post-traumatic stress disorder (PTSD). Intense testimonies refer to known symptoms of this disorder: distressing, unwanted memories, vivid nightmares, flashbacks, depersonalisation feelings, panic attacks, heart palpitations, avoidance of situations that remind of the ICU. These are often accompanied by depressive feelings. Moreover, patients who exhibit avoidant behaviour are less likely to seek help, as help is often linked to reminiscences of the ICU stay.[255]

Box 23: Experiences of symptoms of post-traumatic stress disorder

"Het leven van een patiënt hangt op dat moment [tijdens de ICU opname] aan een zijden draadje. Het vertrouwen in het eigen lichaam is compleet verdwenen. Hij is volledig afhankelijk van de zorgverleners. Dat kan als heel traumatisch worden ervaren. Als gevolg van een geluidje in de omgeving dat herinnert aan deze periode kan iemand dit gaan herbeleven." (Dr Marieke Zegers, ICU in Nijmegen)[218]

"It's been 3 months already but there are sounds that I hear every day, and they often remind me of the ICU noises …"[223]

"There are times when I turn in bed and I think I'm still tied down."[223]

"I slept so badly, I had these awful dreams, really horrible."[223]

"I was having these major panic attacks when I arrived in cardiology and I'm still having them, even now that I'm home, it's often in the evening, every evening I get really panicky."[223]

"It's incredible to wake up all of a sudden only to find that, well, everything's OK, and you wake up anyway just to check…"[223]

"Ik had nachtmerries en sliep slecht. Overdag was ik continu gespannen.[218]"

"Now I have nightmares as if it's happening then and there. My daughter says I'm sweating like anything, really panicking. It takes ages to get my bearings that I'm not in hospital, there's no mask, I'm safe at home."[220]

6.4.3 Revalidation needs

6.4.3.1 Physical revalidation

"*Everything was a challenge. I had no strength to do anything.*" [238]

"J'avais la mobilité d'un ver de terre…"(personal communication)

Patients frequently experience **lack of physical strength** and **extreme fatigue** resulting from ICU-acquired muscle wasting (ICU-AW). They also report shortness of breath, limited mobility and difficulties in performing activities of daily living. These physical problems can last for several months and have repercussions on other areas, sometimes leading to widespread discouragement and a sensation of being a burden to the family and relatives.[249, 256] They may also lead to intense boredom: *"That's the worst thing about coming out of hospital, sitting doing nothing"; "All I had was the telly"; "Just bored all the time…"*[248]

Recovery from ICU-AW is a long and complex process. It requires that the patient explores and adapts to his/her new body and body limits. This phase can be considered as a 'recalibration of the self'. Rehabilitation plays a key role in this recalibration period, helping patients to reconstruct a desirable future.[222]

Box 24 – Experiences of physical weakness and fatigue

"Ik dacht dat ik na een paar maanden wel weer kon werken, maar er komt nog veel op je pad. Ik moest mijn conditie weer vanaf 0 opbouwen."[244]

"Mijn spierkracht was sterk afgenomen. Ik kon bijna niet bewegen, zitten of staan. Dat heeft enkele weken geduurd."[218]

"Het zijn vooral mijn arm en beenspieren. Vooral mijn beenspieren, ondanks dat ik altijd veel heb gefietst, is er niets meer over.[257]

"Ik kon mijn hoofd niet eens optillen, niet praten, niet slikken. Dat heb ik allemaal moeten leren. En ik had overal spierpijn. Mijn conditie was helemaal verdwenen, ook al was ik vier keer per week in het revalidatiecentrum te vinden."[254]

"The muscle wastage I had also impacted greatly on my mental state. I couldn't walk more than a few yards; I couldn't lift the kettle to make a cuppa, the worse one being I couldn't pick up my son."[227]

"I was 34 but I felt 94. (…) None of us think we'll end up in a wheelchair or on a Zimmer frame learning to walk again - until it happens. And even then it's very surreal. I couldn't get up off a floor for about 3 months after I came out of hospital. My core muscles were so destroyed that 4 months after coming home I slipped a disc in my lower back which ultimately required micro-discectomy surgery to fix a year later."[227]

"I get easily tired. I can only do one thing a day. If I had two appointments, I couldn't make it because I would be exhausted even before I finished the first one. I cannot move as much as I did before."[232]

6.4.3.2 Cognitive dysfunctions

"Ik merkte dat ik moeite had met concentratie/focus/dingen tegelijk doen. Ik had het idee dat ik na 32 jaar vervreemd was geraakt van mijn bekende werkzaamheden, alsof je gereset bent. Dit gaf en geeft tot op heden nog onzekerheid. Het duurt een lange tijd om hier weer vertrouwd mee te raken."[258]

The reported cognitive dysfunctions mostly include memory loss, attention deficits, learning difficulties, slowness of understanding, executive dysfunctions (for planning, multitasking, time management, etc.). These types of 'handicap' can be very disabling as well in daily family life as in a professional context. They sometimes appear to last long after the acute illness episode.

Box 25: Experiences of cognitive dysfunction

"[Drie jaren na de ic-opname] een boek lezen, een film kijken of een spel doen lukt me bijna niet. (…) Als mij iets wordt gevraagd, moet ik dat meteen doen, anders vergeet ik het. (…) [In vergadering] duurt het me lang om te verwerken wat er wordt gezegd. Ik bedenk pas een reactie als het onderwerp al is gepasseerd. Al deze klachten zijn puur het gevolg van de ic-opname, niet van de ziekte."[218]

"Niet meer kunnen concentreren, niks kunnen onthouden. In een groep vergaderen of bellen en schrijven tegelijk. Allemaal cognitieve processen die niet meer vanzelfsprekend zijn."[259]

"Toen ik blij huiswaarts keerde was mijn gedachte: dat was het, we zetten er een dikke punt achter en we gaan verder zoals voor juli 2014. Tijdens het IC nazorg gesprek in het ziekenhuis had ik al verklaard nergens last van te hebben. Met goede moed heb ik me 100% hersteld gemeld en ben weer gaan werken. Na een week werd het echter allemaal anders. Ik constateerde concentratie en geheugenproblemen, lusteloosheid en een enorme vermoeidheid. Deze symptomen zijn er nog steeds."[244]

"I feel so close to memory a long time ago; but, I cannot remember what happened just yesterday."[232]

"...extra training is good for me...I was a cook...after the accident, the occupational therapist took me to my workplace...I forgot everything...Chef you know...I had to relearn everything."[239]

"Ik heb geknokt om goed te revalideren. Knokte me door alle pijn heen. Kreeg hoop bij iedere kleine vooruitgang, die ik boekte. Een prachtig gezin, een leuke baan, ik ging ervoor. Ja…die mooie baan bij de politie. Rustig aan begonnen. Dacht dat het allemaal wel zou lukken. Maar als ze twee dingen tegelijk aan me vroegen, was ik de eerste vraag alweer vergeten. Ik raakte geïrriteerd, was prikkelbaar en doodmoe. Er volgde een neuropsychologisch onderzoek en ik werd voor 100% afgekeurd. Deze pijn was niet te beschrijven. Mijn werk…mijn passie. Ik wilde dat het weer was zoals voorheen."[244]

6.4.4 Appraisal needs

Appraisal needs in the post-ICU context integrate and prolong the other types of needs mentioned before in this chapter. The critical illness recovery is a long-lasting process where the patients have to struggle to create existential meaning and coherence about what they have been through and to reconcile with a weak and unfamiliar body that is unable to accomplish life projects as before. Thus, they need **to be supported in the construction of a coherent understanding of what happened, and in changing their life projects**. This entails a much longer duration than the sole initial acute phase, or even the few weeks or months of their physical revalidation.[222, 249]

Some authors specifically studied the coping of patients after an ICU-stay in order to explore ways to optimise their rehabilitation process. A better quality of life seems to be associated with use of **active coping strategies** and positive reframing, optimism, humour, acceptance, leisure activities, and family support. [223] Understanding a patient's coping style may enable healthcare professionals to offer support that best match the patient's needs and situation. Active, task-oriented coping style is classically associated with better quality of life, whereas passive, emotion-oriented and avoidance coping styles are generally associated with lower quality of life. A Dutch study shows that ICU survivors with an emotion-oriented coping style had poorer mental health three months after ICU discharge. These may thus be most in need of **targeted psychoeducational interventions**. [260]

Appraisal needs can also be met in the sharing of experience with other patients who understand the ordeals they've been through. In several studies, patients expressed an overwhelming desire to know that what they are going through is 'normal', and that they should not be concerned with slow progress. [230],[13] We will analyse this further in the peer group section.

6.4.5 Psychological needs by relatives (PICS-F)

> *"I experienced a very strange feeling when Mum was finally home - suddenly everybody's focus was on Mum, how she was feeling, etc, and I was put on the back-boiler - I wanted to shout; ' Hey, what about me, what about what I've been through. Mum's been asleep through most of it, I've had to cope with keeping life normal for my children, racing backwards and forwards to the hospital, plus all the emotional side of it.' I felt extremely guilty for feeling like this, but maybe it's normal."* [227]

The president of the Dutch patients' association IC-Connect describes the situation of family and relatives during the Covid-19 crisis as follows:

"Tijdens de opname zit hij of zij continu in angst dat de dierbare zal overlijden. Een ic-opname is vaak heel acuut, naasten zijn overrompeld en ze worden geconfronteerd met moeilijke beslissingen. Daarbij komt dat de omgeving echt naar is. Denk aan alle apparatuur, de continue piepjes en het felle licht. Bij coronapatiënten is dat nog erger. Artsen lopen met kapjes voor de mond en in beschermend pak door de IC. Naasten mogen vaak niet op bezoek, of de patiënt ligt ver weg in een ander ziekenhuis." Marianne Brackel[218]

Patients' family and relatives are put under intense emotional stress during the ICU-stay of a loved one. But when the time comes to take the patient back home, their stress may change of nature, because relatives often have **to endorse the responsibility of supporting the patient and to adopt a role of caregiver**. As already mentioned, this is a heavy burden of care for which they are often not well prepared, but it may also be **a considerable psychological burden which may require some form of support**. A Norwegian study thoroughly analysed the lived experiences of everyday life of family members after intensive care treatment of a loved one.[240] The author describes how the episode of critical illness of a close relative can turn their lives upside down, eventually requiring support. She identifies various elements in those changes, among which:

- seeing the patient become a person with limited social resources and memory losses, that they have to treat in a completely different way from previously;
- feeling frustration and anger from not understanding the meaning of the patient's treatment;
- feeling uncertain about the patient's mental prognosis, certainly for those who had to fill in the 'holes' caused by memory loss and to repeatedly explain things to the patient;
- more generally feeling uncertain about the future;
- feeling the responsibility for the patient's well-being, having to advocate within the healthcare system to ensure that the patient had sufficient after care.

In a systematic review about outcomes and experiences of patients' relatives discharged home after critical illness, the following feelings were reported: anxiety and intense feelings of fear for the future, anxiety about becoming a caregiver, feelings of isolation, loneliness, and guilt.[261] They may also experience PTSD-like symptoms (sleep disturbances, anxiety or panic arising without particular reason) or cognitive problems (*"I have started wondering if I have become senile…My wording, when I am going to express myself I suddenly feel that I can't find the right words…and that I relate to these experiences [of my husband's illness]."* [240]

Some express aggressive feelings towards the healthcare system (*"I felt like being there or not I was not important to those at work. So actually I felt neglected I feel like aggressive towards that hospital, and especially towards that ICU. I am not able to let it go"*) or feelings of gratitude – even more than from the patient self (*"I feel grateful, but it doesn't seem like my husband does. At the same time, I admit that he didn't know how ill he actually was…so I think: You have received life as a gift, utilise it, do something, learn something new, and get out."*)[240]

6.4.6 Key messages about patients' needs in the months after discharge from the ICU

- **Post-ICU patients frequently experience a deep loss of physical strength and extreme fatigue (ICU-acquired muscle wasting), shortness of breath, limited mobility and difficulties in performing activities of daily living, all of which require intensive revalidation programmes.**
- **Post-ICU patients also frequently report cognitive dysfunctions as include memory loss, attention deficits, learning difficulties, slowness of understanding, and executive dysfunctions. All these cognitive dysfunctions can be very disabling in daily life and in a professional context; they also require intensive revalidation programmes.**
- **The first few months after hospital discharge are generally felt as an emotionally difficult period during which patients need psychological counselling/support. This is often reported by patients to be the main limiting factor to full recovery.**
- **The psychological distress may culminate in a genuine post-traumatic stress disorder (PTSD) requiring specific professional support. It is important to notice that patients who exhibit avoidant behaviour are less likely to seek help, as help is often linked to reminiscences of the ICU stay.**
- **The critical illness recovery is a long-lasting process where the patients have to reconstruct a coherent narrative of their life and regain control of it. They also have to reconcile with a weak and unfamiliar body that is unable to accomplish life projects as before. These achievements require that they receive adequate information and long-lasting support.**

- **Patients sometimes report feelings of 'not being the same person as before'; this can lead to tensions within the couple, the family and their whole social network.**
- **Patients need to be better prepared for discharge, and warned about the changes that could occur in their body and their life. This can be provided through reference booklets or films, but they prefer when information is more personalised.**
- **Patients and relatives need that first line health professionals are better informed on their specific problems and on how to handle the symptoms likely to occur after an ICU stay.**
- **These physical, psychological and cognitive problems can lead to widespread discouragement and a sensation of being a burden to the family, relatives and carers that also may require psychological support.**
- **Family and relatives are also put under intense emotional stress when the patient comes back home. They often have to endorse the role of caregiver. This is a heavy burden for which they are often not well prepared, but it may also be a considerable psychological burden which may require some form of support.**

6.5 Patients' experiences and preferences about PICS prevention and management measures

6.5.1 Physical rehabilitation

> *"Slowly I learned how to use a wheelchair, then a walker, and left on crutches. Every day I had physical therapy in an amazing facility alongside many individuals, be it amputations, accidents, surgery recoveries. It was humbling, a reminder that my illness was not permanent and I would recover. Plus I had so much to look forward to – the kids, my husband, family and friends."*[262]

Physical weakness is the most outspoken symptom right after an ICU-stay, and also the most foreseen one. Patients therefore find it quite natural to follow a physical rehabilitation program after leaving the hospital. Quotes retrieved from testimonies on this topic are thus not specifically related to PICS. It can also be added that participation in these rehabilitation sessions, whatever their location and organisation, may be part of the coping strategies of the patients.

In a qualitative study assessing the quality of life of patients after a post-ICU exercise programme (PIX), several positive aspects were brought forward by participants: **improved fitness levels** with a positive impact on activities of daily living, **emphasis on improvement and recovery** ("*a sense of achievement, every time you went"; "You felt like you were progressing*")[248], **increase in self-reliance** ("*You can end up doing nothing for months so yeah…it was very good for that side, it actually gets you to a point that you did more*")[248] and **better psychological well-being** *("It sort of improved your mind a lot as well"; "It gave you space to think, gave your brain a break, instead of being sat at home thinking about it constantly"*).[248] Walker notices that exercise is often welcome as an alternative to 'sitting doing nothing': "*That's what I liked about coming in to do the exercise group, because they give you something to do"*.[248] Furthermore, these programmes also allow patients to **meet other patients** instead of "*being at home relatively locked up*" and eventually to share experiences with them.

According to the aforementioned 'recalibration' theory, physical rehabilitation "helps patients to challenge and explore their current functional level and reconcile their self-discrepancy, that is, difference between their physical self and the cognitive image of themselves".[222] Or, as Kang puts it: "Survivors gained a new perspective on their normality that adapting to their changed self was recovery itself."[232]

6.5.2 Information support

> *"It feels safe with the information; I can read it in black and white, and the written information can be read and re-read."* [226]

Patients leaving the ICU/the hospital may receive general leaflets and information about recovery. Information about what to expect during the recovery period is aimed to reduce stress levels. Patients also appreciate being able to keep it and to read it again at their leisure.[239]

However, they appreciate when information goes more specifically about them and their personal condition. They also asked for information on tracheotomy scar, MRSA, mobility, weakness, sex, support and making a complete recovery. They are also worried about the probability of becoming critically ill again.[13]

Box 26 – Reflections on the information booklet

"The pamphlet was our 'user manual' after the ICU stay; to answer questions such as: What is happening in my body? Why have I lost my appetite? Why do I have bad dreams? Am I normal?" [226]

"I understood that what I was going though was normal and that I was not going mad. It was the critical illness and the ICU stay that gave me hallucinations and bad dreams." [226]

"The manual is very important to me. It's in the living room. In case I want to look something up. And if I am unsure— I often get it out." [15]

6.5.3 Post-ICU clinics

Some ICU-teams structurally invite patients to ICU follow-up sessions, others don't. However, studies indicate that these follow-up sessions – also named post-ICU clinics – can be very different in their nature, objectives and organisation. For instance, they may rely on the reading of a diary (these are developed in the next section), include a visit to the ICU-ward, or be exclusively oriented towards information and/or evaluation of the patient (eventually for research purposes mainly). Some are nurse-led, others are provided by physicians or professionals from other disciplines. It should be noted that we could only retrieve testimonies from studies evaluating the existing sessions/clinics (from which a certain bias could not be excluded), and that we did not find the opinion of patients not benefitting from or rejecting such follow-up.

The patients interviewed about the follow-up sessions globally said that they were **happy with being invited** to attend, although some reported feeling nervous and tense before going.[230] Some stated that they would not normally have contacted the ICU staff themselves, but that they felt it was nice to be invited.[230] On the other hand, **some declined the invitation**. This was the case of about 45% of ICU patients in a Belgian clinic (personal communication D Prevedello). The most frequently reported reasons for declining were because they felt fine and were recovering well, because they were already accompanied by their GP or by another specialty, because they were afraid of coming to the ICU again, or simply because they had mobility problems and/or were reluctant to travel such a long way, or even to pay for the hospital parking. However, this doesn't allow to identify patients who use avoidance as a coping strategy. Some patients suggested appointments over the telephone to overcome the problem of travel and/or location.[13],[246] The experience in Ghent is that patients are not very enthusiast over coming to the hospital 'just for a talk'. Therefore, the team considers coupling the ICU-follow-up visit with a technical examination or a consultation by the organ specialist. They also mentioned that some Dutch teams visit former patients at home for the follow-up visit.

Some patients considered the principle of being invited to a follow-up session as **a sign of continuity of care** after hospital discharge, which was deemed as very important. Taking tests could give them a feeling that they were **being monitored**, and that eventual problems would be detected. For the patients who were recovering well, one appointment was reported to be sufficient. For others, being referred to other specialists gave them **a feeling that their problem was addressed** and that they would receive more care.[13] Some patients also reported that they felt their feedback would **help ICU staff with research** into service provision and audit, as a way of 'giving something back'. ICU follow-up was also seen as **an opportunity to see staff again and thank them** for the care and support they had provided, or to give them feedback about their experience in order to improve care for future patients.[13] For some patients, the follow-up was deemed **insufficient**: *"Ik heb nadien één gesprek gehad met een intensivist, en ik ben een keer gebeld door een ic-verpleegkundige. Die wist eigenlijk niets af van klachten na een opname en zei dat ik op internet moest zoeken naar informatie. Ik heb zelf een fysiotherapeut en een psycholoog ingeschakeld."*[218]

Studies found that **70-80% patients think the follow-up visit was useful for their recovery** (Akerman et al.: > 75% up to one year after discharge (n=around 125) [194]; Farley et al: 81 % (21/26 patients) thought an ICU follow-up clinic would have been beneficial[263]).

6.5.3.1 About the timing and organisation modalities

Most of the follow-up sessions took place **about 3 months after hospital discharge**, but some patients said they would have needed information and reassurance before that and felt that coming earlier could have saved them from unnecessary anxiety.[242] "*I, of course, wasn't at work, still at home recovering... So you spend far too much time chewing the cud and feeling frustrated that you'd like to kind of do something about it. And that's why it was a good thing that they had a follow up. But the follow-up came far too long after. It needs to be a lot sooner."*[13] Even when nurses had encouraged them to call in case of problems, some reported feeling uncomfortable about doing it because they thought nurses were too busy and likely to have forgotten them.[13]

In some studies, patients asked **for more flexibility in the timing** to adapt for their needs at different stages in their recovery: *"If you'd taken a snapshot of me at three months, and one at six months, it would have been a dramatic difference, and if you'd taken a snapshot at twelve months, you wouldn't have realized I was the same person."*[246]

A Swedish qualitative (small) study[230] about the experiences of patients during follow-up sessions reported that the patients who were not offered a chance to meet with a counsellor during rehabilitation experienced a greater need for a follow-up session.

Patients are usually **accompanied by a relative** for the follow-up session. This accompanying role is reported to be important not only because of the logistic support for the patients (driving them to consultations, keeping track of their appointments, etc.), but also because relatives were 'the patients' eyes and ears' during the period when the patient was unconscious, as he/she usually has no memories of his/her ICU stay. Of note, a Norwegian study about the lived experiences of everyday life of **the relatives** after intensive care[240] points out that some relatives expressed the wish that someone **had also asked *them* about their emotional state** at some point after returning home, even if they usually did not expect the ICU staff to help them after the patient's discharge.

6.5.3.2 Not being alone with those feelings

> ''*People don't know what it's like to be a patient in an ICU*."[242]

In a Danish qualitative study exploring the benefits of follow-up consultations[242], all patients reported feelings of isolation because they felt nobody in their entourage could perceive what they had been through. They were relieved to have **an opportunity to talk openly about it** – and to be listened to by nurses who knew what it really meant. Talking with the carers who were with them when they were critically ill **helped them understand their actual symptoms at the light of what happened during their ICU stay**. Making sense of inexplicable symptoms, such as sensory disturbances, altered eating patterns, difficulty concentrating, irritability, crying without reason, memory loss and anxiety/nightmares was experienced as a **strong relief** by patients because they had spent a considerable amount of time speculating about them. Some authors[242],[221] refer to the concept of '**sense of coherence'**[264] as a key factor enabling people to adapt to stress and resist illness: "the consultation contributes to increased comprehensibility because the patients receive explanations of their symptoms and memories from their hospitalisation. It is easier to handle the challenges and demands that you face as a former intensive care patient when your experiences and memories are normal, and others have experienced the same."[242] The benefit of discussing dreams and hallucinations and learning more about what had been real or delusion is also reported in other studies.[13],[230] Peers-support groups can also fill this need (see further).

Another important finding reported about the follow-up meeting is **the understanding that rehabilitation is a long process** and that it is not something to be concerned about.[230]:

Patients also expressed that, without this consultation, they would have been anxious for longer and less able to move on.[13]

Patients who could not attend follow-up consultations felt that they would have benefitted from a contact with clinical specialists.

Box 27 – Experiences of relief by making sense of symptoms

''…but it turned out that I was normal. It's not just me that's special because I can't drink coffee anymore or eat green jelly beans or whatever. And I lose my hair. Other people do as well…"[242]).

‘‘It was a relief to know. It really was. It was nice to know that I was not the only fool who dreamed such dreadful dreams because it – while it was happening – consumed me completely. It did.”[242]).

‘‘I thought it was nice to know that it could be linked to having been in a coma. Here at the rehabilitation centre, they said it could be because of my type 2 diabetes.”[242]).

‘‘The clarity that arose about my hallucinations and taste disturbances and that I was not alone in having had such experiences. I think that was the biggest eye opener – for me at least.”[242]

“I knew something was wrong when I was sedated but I didn't quite know what it was (...) and I thought I'd been a victim of a sex crime. And apparently what we've talked about, me and the doctors, we think it was because of the personal care you know, touching me in really intimate places. And I'm a very private person that way so they think that was the link and that made sense.”[13]

“There are still days even, what are we six, seven months on now, yeah I just couldn't see the point of anything... in my mind I was thinking ‘Well what's the point of it, we're all going to die anyway?’ And I needed to speak to, I went back and spoke to the nurse consultant on ICU and she explained, and I only saw her the once but she explained it's perfectly normal. And that helped, once she said to me, ‘Loads of people feel like that when they come out of intensive care and you need to be kind and give yourself a bit of time, it will pass.’” [13]

“I would have liked to have had access to a critical care specialist… so I could have said ‘I can’t cope with this; I feel like my lungs aren’t working and I can’t breathe…’ And somebody could have said… ‘this is normal’”.[246]

6.5.3.3 Visiting the ICU

> *"Somebody asked me did I want to go to ICU unit while I was there and I felt that particular time I was asked, yes, it was a good time for me. It would have been, I was trying to piece things together in my mind. I was trying to put right a jigsaw of my life, if that's the best way to describe it. And I needed to put pieces together to complete, as I was before."*[13]

In some cases, the follow-up sessions entail a visit to the ICU, which would confront the patients with how ill they had been. Some patients report a feeling of tension on beforehand: *‘‘And you think, oh now I’m going to be in that environment where I was in such bad shape. But…I didn’t experience it like that when I got there.’’*[230] Other patients prefer not to visit the ICU and have the meeting with the staff in a different place, to avoid reviving unpleasant memories and feelings.[230] Visit to the ICU can also happen quite informally, outside any follow-up consultation, on own free will. Patients then come mainly to thank the team, exchange with the carers about their history and their future. It can even happen that they spontaneously ask to visit the premises.[265]

Visiting the ICU can be experienced as an extension of the process of making sense out of dreams, hallucinations and frightful memories, as described above. But some teams consider this visit to the ICU to be **an outright form of ‘exposure treatment’** as would be used in the treatment of patients suffering from PTSD, like a way of facing the reality, ‘confronting the demons’ to get rid of them.

The effect of follow-up service on PICS outcome is described in Chapter 4 on interventions.

Box 28 – Experiences of visiting the ICU

‘‘What made the biggest impression was the recognition of how sick I had been. I probably wasn’t aware of that myself.”[242]

‘‘When you walked past the rooms and thought you were in there, too, and you realise you could have been dead, it does something to you afterwards, one becomes happier to be alive.”[242]

‘‘The downside of the consultation was that it forced me to face my feelings about having been so sick. I had put a lid on that part of my life.”[242].

‘‘Since I revisited the unit and heard the sounds, my nightmares have stopped. I guess I closed that chapter in my life.”[242].

6.5.4 ICU Diaries

> *"I was very lucky that my nurses wrote in my diary in detail. From the moment I arrived, almost every day was documented, to the point where I could actually picture everything that happened on a particular date when I read my diary months later. Each entry was written with emotion and feeling. Even though I was in a coma, my nurse wrote to ME and it was only months later when reading it back to myself, that I realised how unbelievably significant this was. My nurse had the empathy and compassion to take the time to write these words with such feeling – She didn't have to – she was most likely incredibly busy and could've scribbled just a few words to describe the weather but instead, she painted a picture. (...) The point I'm trying to make is that patient diaries shouldn't be seen as something that 'just gets given' to a patient and written in only when it's thought about. They should be seen as an important tool. Mine, combined with my ICU psychological support, has helped me immensely to understand different parts of my journey but more importantly, it's helped me start to work out what happened in the real world and what happened in Delirium world. For me, my diary exists as a reminder of how far I've come, how I fought and won and more importantly, what I'm capable of achieving in the future."*[266]

In Scandinavia, the Netherlands and England, many ICU-teams write diaries for the patients to relate what happened during their ICU-stay. Some diaries are held by the staff, some by the family and relatives, and some by both altogether. The moment the diary is given to the patient is variable (see Box 30).

Most studies on diaries report positive feedbacks from the patients (Akerman[194]: > 85 % up to one year after discharge, Tavares[267]: 65 % with more than 40 % asking for more pictures.) According to Barreto et al,[144] "patients mostly felt that the diaries helped them to (1) connect their own memories to what actually happened during the ICU admission, (2) connect with their families as a way to confirm information presented on the diary or as a way to understand what they also have been through during ICU admission, and (3) improve perception of ICU care". [144]

Also patients considered that the presence of photos was "'good or very good', leading to a greater understanding of what it looked like in the ICU and how ill they had been."[144] Of note that, in Belgium, taking pictures is generally forbidden – however, this interdiction has been lifted in some hospitals during the COVID-19 crisis, given the impossibility for families and relatives to visit the patients.

6.5.4.1 Filling the gap

> *"Op advies van de verpleegkundige hielden mijn moeder en schoonzus een dagboek bij, wat heel erg waardevol is gebleken. Je mist een stuk en je wilt zoveel mogelijk details horen om te kunnen begrijpen wat er gebeurd is. Er zijn ook heel veel foto's gemaakt. Ook deze had ik niet willen missen, deze geven een beeld om zodoende alles nog beter te kunnen plaatsen."* (Marielle)[244]

Diaries help patients to fill the 'black holes' in their memories and to sort out what was real and what was delirious in their experience. This can be helpful when nightmares and bursts of anxiety poison their daily lives (see in Box 10 – The story of Francine). Another example is the story of a woman who had visions of being trapped under snow during her ICU stay. Things cleared out for her when she read that she had very high fever and that ice packs were stacked on her to help bring the fever down. Llamas (quoted by Kuehn[268]).

However, an Australian study suggests that not all patients want to know more about their ICU experience (47/57 patients found the diary helpful and 10 not helpful).[251] The reluctance could be explained by a willingness to forget about what they have been through, which is a mechanism described in the avoidance coping style (see section 1036.4.4) Others report that they are not interested in reading their diary.

Box 29 – Experiences of the ICU-diary

"The intensive care unit diary is a reality-sorting tool that is effective in aiding patients to connect their flashbacks and delusional memories to actual events." [269]

"Help ground me and bring me back to reality." [251]

"My dreams were really nightmares and not pleasant . . . once I read the diary and got the timeline, I got to understand it." [269]

"My wife kept a diary, and I can now reconcile the actual events in the ICU unit and therefore the stimuli around me, with my dreams. The stimuli included all the ventilator alarms, the other devices keeping you and the other patients around you alive, the conversations around the bed, the phones ringing, and all the blinking monitors and flashing lights. I post-rationalise now (though there is no science behind this) that my nightmares were the result of my pickled brain trying to make sense of the ICU environment and stimuli and the circumstances I found myself in."(Anthony)[227]

"I look back at my time in ICU with a bit of humour as family tell me stories of what I did or what I was like. I still remember bits of it in the small moments I woke and even those moments bring a smile. Whilst seriously ill and very delirious at the time with some awful hallucinations, the pictures and short videos my family had taken, as well as a diary the ICU staff had created for me, for them and family to write in, all helped piece everything together. I am very, very grateful for that." (John)[227]

"I don't really want to know the honest truth. I just want to move on."[251]

"It is something I'd rather move ahead with and put behind me. I don't want to have to dwell on the period of time I spent in there too much. It can be quite stressful and upsetting just depending on what frame of mind you're in at the time." [251]

"It wasn't something I ever tried to remember. I'm not really curious about what happened in ICU." [251]

"It's just something that's never crossed my mind. I've never really cared enough about it. It is just move on, keep going." [251]

6.5.4.2 Acknowledging the role of the family

> *"[It's] helping family deal with stress. Just as a means to kind of record and express their emotions and manage them."*[251]

A systematic review about how diaries written for critically ill influence the relatives reports that writing an ICU-diary can be seen by family and relatives as a **mean to express their love to the patient**.[173] It can also help them cope during the critical illness [251] and help them support the patient after discharge.[173]

The diary is also seen as an active, continuing reference tool to promote communication between healthcare professionals and family: *"So we knew what went on each day. Things changed, then you could look back and go, when did that happen?"* [251]

Reading the diary retrospectively helps the patient **understand how emotional and stressful for the family** the experience was: *"My daughter has only just given me the diary which she kept during my stay in ICU. After reading this my emotions were very high, thinking of the distress that my family went through whilst I remember nothing."*(Peggy) [227]

Moreover, it can **help the patient share his/her actual emotions** and post-traumatic stress: "*Het was erg druk in mijn hoofd. Ik kon maar geen rust vinden. 's Nachts werd ik zwetend wakker. Nachtmerries, beleefde de intensive care opname steeds opnieuw. Samen met mijn vrouw ben ik het dagboekje gaan lezen. We huilden. Goed vond ik dat ze had opgeschreven hoe zij zich voelde toen ik daar zo kritiek ziek lag. We leerden onze, zo verschillende, ervaring met elkaar te delen. Het samen kunnen delen heeft me enorm geholpen.*" [244]

But, similarly to the patients, some family member participants were reluctant to dwell on the past *"Because we want to forget about it rather than remember how it was, because it was a really depressing time."*[251]

6.5.4.3 Acknowledging the role of the nurses

In some ICU-teams, the diaries are exclusively written by nurses. Here is an example of what this looks like: *"You were agitated early last night. You were sweating and grimacing. When I said your name, you opened your eyes. I asked if you were uncomfortable, – you shook your head. // We turned you over so that you could lie on your side for a while. You relaxed right away. // Be assured*

that we are taking good care of you. There is a nurse at your bedside all the time." Or this one, as legend to a picture of the patient with the relatives: "*They were so happy that you were awake and could look at them. This is the first time since the operation, and they have really been looking forward to this moment. It looked like you felt it was very good to have them by your side."* [270]

In the Norwegian study these examples are taken from, patients were really struck by the fact that the nurses took the time to write individual diaries with the purpose of helping them on to recovery (*"The way it is written especially to me, in my language, sort of … without all of those medical terms ..."*) and by the fact that the nurse who writes sees the patient as a person rather than as a medical case among many other medical cases: *"What's most important is that it shows me that they really cared about me as a person in the middle of everything else they had to deal with".* [270]

6.5.4.4 Timing

The moment that the diary is given to the patient can be very variable: when they leave the ICU, or at hospital discharge, or just before the first follow-up appointment. The way patients appreciate this timing is also variable. Patients who did consider the diary to be beneficial generally thought they should receive it a substantial period after ICU discharge, but their opinion regarding this period ranged from weeks to months later. They also felt beneficial to have the content explained to them and questions answered at the time of receiving the diary.[251]

The effect of diaries on PICS outcomes is described in Chapter 4 on interventions.

Box 30 – Reflections on the timing of reading the diary

"It became very emotional, reliving the steps of what I went through. I started reading the diary at [rehabilitation] and I think it was too soon." [269]

"I didn't really read it until I was in [rehabilitation]. My first take on it was that it was so overwhelming for me… I didn't finish reading the whole thing until I was out of [rehabilitation]."[269]

"It took me about five minutes to read. And I read that on the bus going to the park-and-ride [laughs]. And I thought, 'Why on earth was I not given this, if not before I came for my appointment for the follow-up meeting, just five minutes before I went to the follow-up?' Because it was full of stuff that I had no idea... And if that had been given to me the next seven days before, I could speak to anybody in intensive care and get the answers. I wouldn't have needed that anxiety. If that had just been given to me 10 minutes before that meeting, I could have asked the questions and had the answers. Simple things, silly things like that. But that was so important." [13]

"I just didn't feel like I wanted to read the diary right away. I didn't want to find out that maybe what I was thinking or dreaming about somehow played out worse. Once I read the diary, I was able to put those dreams behind me."[269]

6.5.5 Psychological support

> *"I still feel frustrated and I still find it hard... I still have to take something to make me sleep, because I still find that hard... I find it hard to watch hospital things on television, where there's somebody in intensive care with the machines all around them... I feel so guilty. He [GP] said, 'You need to talk to somebody, talk through these feelings.' I've only just now said that I will probably need counselling."*[13]

We found very limited literature about specific psychological support for former critically ill patients. Some studies mention a contact with a counsellor after discharge from the ICU (during the stay in a rehabilitation ward) or after referral from the post-ICU visit. In both cases, patients stated that this contact was beneficial:

''*If I hadn't gotten that help [from the counsellor], it would've felt meaningful to ask questions and straighten things out [at the follow-up session] because anyway it happens that what you remember can be twisted or right, which can be nice to get confirmed.''*[230]

"I also saw a specialist in behavioural medicine who's part of the follow-up team and she was absolutely brilliant... I don't think I could have done it without her... Each time I went to see her she'd sort of say, you know, 'How have you felt this week?' And I'd tell her what had happened and she'd

say, 'Well next week this will probably happen, you'll probably feel like this.' And then when it happened, 'cause she'd prepared me for the anxiety attacks and the panic attacks and then when it happens you don't feel quite that bad because you think, 'She's already told me this might happen. And she told me that might happen.' So I'm not going daft."[13]

However, an external (private) counsellor that has no knowledge of ICU-related problems can be seen as inadequate*: "I saw a counsellor privately and then I was also given a couple of sessions through my GP. But I could really have done with a bit more support from professionals who knew. I mean none of those people knew about intensive care. And I think a bit more support from people who have actually worked with people who've been through the intensive care experience would have been really helpful at the time... They'd [counsellors] never really come across anybody like me or if they had maybe one or two other cases so they didn't really know what to look for."*[13]

6.5.6 Peer support groups

> "*People often come out of life threatening critical illness as somebody different and I think as a group we can support each other through that. (…) It's amazing how much you have in common with the other families. Everyone has a lot of empathy and understanding because they have been through it themselves."* (Tony&Diane) [227]

Peer support (see Box 8) is founded on the principles that both taking and giving support can be healing, if done with mutual respect'. Peer support groups (eventually online) are seen as playing a positive role "by helping patients to be reassured about their feelings and experiences and to adjust their expectations of recovery."[246]

The commonest barrier encountered in their organisation seems to be recruiting participants, which some authors ascribe to the fact that patients do not necessarily see that the problems they encounter are related to their ICU stay, because there is a lack of awareness of PICS and because such patients are not necessarily attending clinical services that might benefit them. There is also a high rate of lost to follow-up and mortality, especially at 1 year.[101]

In Belgium, we only know of one peer support group (UZIntens in Ghent); they organise 'drop-in meetings' four times a year, where former patients and their relatives are invited. These meetings take place outside the hospital, in a sports hall cafeteria. The meetings are held by the ICU-team (an intensivist, two psychologists and other members of the ICU-team (nurse, physiotherapist)) and they gather 15-20 participants.

An interesting initiative in the Netherlands is the "Sepsis en daarna" initiative, set up by a nurse who went through a sepsis episode. She wrote a book about her story, launched a website to gather information and collect patients' testimonies, and now gives workshops for ex-patients to provide information and support.[271]

Box 31 – Experiences of peer support groups

"If I had maybe a list of people or something, then, I might have considered calling...there might have been someone [ARDS survivor group] ...if I had questions I would have called just to have gotten some answers"[239]

"I found the [ICU recovery charity] website and started reading the blog, and I sort of went 'oh, there's other people like me.' And that was the bit where I started to accept that I needed some help." [246]

"The ICU Steps group has been a great help – they are a lifeline. People talk about their experiences and you realise that you are not the only one going through it."[227]

"I'd say it's only now, 10 months on, that I've started to feel like myself. And I credit that to the fact I've spoken about what happened nonstop, at first Id 'stop myself, no wanting to get upset or upset anyone else. (…) I've started a group 'Critical Care Survivors' so far I've only met 2 people through it, but that's 2 people I wouldn't have met so any difference no matter how small is relevant. I hope to help people coming out of the critical care unit, as out of 300+ hospitals in the UK only around 80 offer support after their stay, and although not everyone experiences the hallucinations, paranoia, flashbacks and the mental torture, most people do, and if I can reach any of them and let them know it does get better, it won't ever go away but you'll learn to deal with it, then what I went through wont have been for nothing."[227]

6.5.7 Visit by a case manager

We found one German qualitative study about a structured aftercare programme for sepsis patients in primary care, the SMOOTH project (Sepsis Survivors Monitoring and Coordination in Outpatient Healthcare).[15] This programme included patient and GP education and patient monitoring by ICU-nurses having received a case manager training. Nineteen patients and 13 GPs participated in the evaluation of the project.

The patient education session was moderately appreciated by patients (because it reminded them of their illness) but highly appreciated by GPs (because they thought well-informed patients are more likely to participate in follow-up). Case management was globally appreciated by the patients; however, the visits of the case manager were felt as irritating by some patients who did not want to be remembered about their critical illness episode again and again. A number of patients did not see the benefit of monitoring; on the contrary, they felt that the questioning only occurred to get study data. Some patients also reported that their GP felt the monitoring was unnecessary.

Box 32 – Experiences of case-management

"That was reassuring to me – I felt in good hands."[15]

"Somehow, that was pleasant, as I was still at home, I still was on sick leave, when she phoned and asked whether I had half an hour. That was, well, somehow nice. I would say."[15]

“It was pleasant, that one could talk to someone else, too. As sometimes I, as before Christmas, when sometimes I start again a depressive phase ... that there is another someone. That helped me.”[15]

“As I wanted to get done with it – well, that was always refreshed again, I had that feeling. As I said, I was sometimes so irritated, not with the woman, but as I didn’t want to talk about it anymore.” “It simply was annoying to me. Yes. Let’s be honest. It was annoying to me.” [15]

“The woman, from the study, you could tell her: look, I have a problem since then, yes. And she passed it on and I told her: my hip is aching. She passed that on. But there was nothing that was done.” [15]

“Yes, he told me the lady [case manager] was there. And then he died laughing at the many questions.”[15]

6.5.8 *Key messages about patients' experiences of different interventions for preventing/managing PICS*

- **Patients report that physical revalidation programmes improve their fitness levels, put emphasis on improvement and recovery, increase self-reliance and psychological well-being and allow them to meet other patients and share experiences with them.**
- **Information booklets and films are appreciated by patients because they are permanent and can be looked whenever needed. However, patients don't always find them sufficient. They also appreciate getting more targeted information adapted to their personal case (tracheotomy scar, MRSA, mobility, weakness, sex, etc.) and about their probability of becoming critically ill again.**
- **Follow-up sessions were usually welcome according to the participating patients. They were considered as a sign of continuity of care, they were reassuring as patients felt they were being monitored, or eventually referred to a specialist.**
- **Reported reasons for declining the follow-up visit were because they felt fine and were recovering well, or that were already accompanied by their GP or by another specialty, or that they were afraid of coming to the ICU again, or simply because they had mobility problems and/or were reluctant to travel such a long way.**
- **Studies found that 70-80% patients think the follow-up visit was beneficial for their recovery.**
- **Some patients asked for more flexibility in the timing of the follow-up sessions to adapt for their needs at different stages in their recovery.**
- **Some relatives also expressed the wish that the follow-up session should also consider their own emotional state**.
- **Follow-up sessions and reading ICU-diaries are two ways of helping the patient understand their actual symptoms at the light of what happened during their ICU stay and reconstruct their narrative. Visiting the ICU can also be seen as an extension of that process.**
- **ICU diaries may allow to acknowledge the role of the family and the carers and can be a support for exchange on these topics.**
- **Psychological support was generally appreciated but often difficult to obtain.**
- **Peer support groups offer an interesting way of sharing emotions and feelings with professionals and/or other ex-patients who are able to understand them.**

7 CHAPTER 7: WHAT COULD BE THE ROLE OF GENERAL PRACTITIONERS ACCORDING TO THE LITERATURE?

The transition of care between hospital setting and primary care is a vulnerable and challenging period in which global health of survivors is at stake.[272] In addition, during the period following hospital discharge, physical, mental or cognitive disorders, which developed throughout the ICU stay may persist and new symptoms may arise. Attention must turn to the identification of such complains in order to refer patients for appropriate treatment and to avoid re-hospitalization, often directly related to such ICU-acquired disorders.[273] Back at home, patients and their relatives may feel insufficiently prepared about what has changed in their activities of daily living. They will mainly rely on their general practitioner (GP) for detection of new health problems and for referrals to other healthcare specialists. The Chapter 3 proposes a small set of rapid tools to detect these impairments in an outpatient context. Furthermore, many ICU-survivors have multiple medical comorbidities that are typically managed in primary care and that may have worsened after critical illness. Accordingly, transition back to primary care puts GPs on the frontline of care delivery.

Ensuring an optimal continuum of care is nevertheless still facing several obstacles and GPs are in the first line in the transfer of ongoing responsibility after ICU and hospital discharge. The obstacles for appropriate care in ICU survivors may have multiple causes.[274] A work conducted in the UK aiming at determining what type of information GPs do require, identified several issues. First, GPs reported a delayed and uncomplete overall communication from the ICU or the hospital ward. Second, GP's limited understanding of critical illness sequelae was recognized as a barrier to continuum of care. Third, the absence of information on available resources was also reported as a factor impeding appropriate management.[275]

7.1 Access to information on the ICU stay

GPs need accurate information about the ICU stay (discharge summary) to better support patients recovering from critical illness.[275, 276] The paucity of medical information handoff from the ICU to GPs is one of the most reported impediment that can adversely affects patients' health.[276, 277] It has clearly been identified that information can be missed or can be misinterpreted. A recent systematic review has reported delayed or incomplete transmission of information between hospital and GPs. While discharge summaries included pending test results or medications lists, important information related to the patient condition and follow-up strategies were lacking. [277] We did not identify a study on this issue in Belgium, but an assessment of the relationships between GPs and intensivists has been conducted in a French survey. [278] Globally, GPs were dissatisfied with the quality of information received on admission and at discharge. They were willing to be more active and participative in the decision-making on treatments. Some barriers were identified and included the scarceness of information provided by intensivists, the poor quality of family reception in the ICU and the lack of discharge summaries. Similar results were also described in other countries.[279, 280] A qualitative study analyzing the collaboration of GPs and hospital care physicians emphasized the importance of working collaboratively. GPs preferred a two-way interactive approach along with the development of trustful relationships between both levels of care. They also pointed to the need to familiarize hospital physicians to their family practice. GPs consider that new collaborative models could bring about reciprocal inspiration and new skills.[281] In this regard, systematic communication model strategies, in the setting of critical illness, have been proposed to improve overall communication.[276] Even more so, projects of joint consultations have been investigated but not specifically in the field of post- ICU patients.[282] Such a collaborative approach could provide more skill and expertise to primary care and caregivers.

7.2 Getting experience and skills

Likewise, GPs need to be more familiarized with the consequences of critical illness.[13, 275] Since only few patients globally require ICU in the population, GPs have limited expertise in post-ICU disorders and could dismiss the likelihood that some symptoms or longstanding burdens could be related to critical illness *per se*.[9, 16, 283, 284] Thus, GPs are often not aware of PICS manifestations and this ignorance may jeopardize the ability to help patients and their family. It has been suggested that providing better education among primary care physicians would overcome this barrier.[283] Indeed, complications of critical illness are almost exclusively published in critical care literature. Spreading

this information beyond the intensivist audience could, to some extent, raise awareness about PICS and improve its detection at the primary healthcare level.[275] Post-ICU clinics is an opportunity concept that could help to set up a network between primary and secondary care.

In the same vein, GP should have access to practical tools to screen for PICS-related impairments. The current lack of defined tools for the primary care level represents another barrier for appropriate post-ICU follow-up.[16] As PICS is a relatively new concept, assessment of PICS in primary care settings has not been well defined yet.[119] Furthermore, physical disorders are generally much easier to identify than mental or cognitive ones. Mental and neuro-cognitive problems are poorly recognized and often left behind.[5] For example, ICU-survivors suffering from PTSD symptoms reported that their GP were unacquainted with such symptoms and overlooked their seriousness.[5] Those patients will presumably be more at risk to develop severe PTSD. Since early detection is important, GPs definitely need validated and reliable tools to refer patients in good time for further assessment.[119] Those tools would immediately warn GPs that something wrong is occurring and needs to be investigated. It should be noticed that time constraints are frequent in daily GP practice and that implementing such tools should not increase the GP's workload.

Besides, some studies suggest that GPs should proactively contact a patient discharged home after an ICU admission in order to discuss their experience and assess potential disorders, including those (such as PTSD) that are not expressed by the patient.[5] Indeed, patients can meet difficulties to realize that they have a new problem or even never realize. It is well known that patients with symptoms of PTSD may adopt an avoidant behavior, denying difficulties, and may be reluctant to seek help and may not contact their GP for that problem.[5, 60] Some patients may feel ashamed for their mental problems and would not communicate about them, even to their relatives. So, building up a good and realistic aftercare plan from the hospital discharge, involving the hospital physician, the GP and the patient (and his family) would save time to reach appropriate treatment As GPs care for their patients over many years, they may be the most suited to identify psychological distress in patients who have been discharged following an ICU admission.[5] We only found one study on interventions at GP level for PICS-related outcomes. A German trial evaluated the combination of skilled nurses and GPs on a cohort of patients discharged from ICU after sepsis. Both GPs and nurses were trained in post-sepsis care and patients were systematically checked by appointments or by phone calls. Referrals to other specialists was systematically proposed if necessary. Although they did not show any substantial improvement on global mental health (see Chapter 4), they emphasized that patients benefiting from the intervention showed a trend to display less PTSD symptoms at long-term.[213] This suggests the relevance of a systematic and collaborative healthcare network in which GPs coordinate the aftercare program, in close collaboration with the hospital team. This way of working would benefit to GPs since they would not be alone to set up aftercare strategies.

7.3 Demystify what happened

Regarding mental health disorders, some studies have shown that ICU diaries could decrease the onset of anxiety, depression and PTSD (see Chapter 4). Its effectiveness on GPs' care has not been clearly defined yet. Narration of ICU stay through diaries is thought to help preventing PTSD and facilitate family members to support patients.[285] As such, narration of the ICU events to patients by skilled professionals have been proposed as a therapeutic intervention in primary care for mental recovery.[213] GPs have been caring their patients for many years. Although they are less used to the ICU way of working, they may be the best skilled and suitable caregivers to read and explain these diaries with patients and families.

7.4 Schedule aftercare program and organize resources

Furthermore, GPs need information on resources available to the patient after a hospital stay. The lack of well-structured aftercare programs is reported as a real barrier to implement a high quality follow-up of ICU-survivors at a primary care level.[15] Recovery programs such as cardiac or respiratory rehabilitation are classically much better established in the healthcare system. Regarding people recovering from critical illness, little is known about how to optimize their discharge plan and long-term follow-up. The patient's care pathway is therefore much more intertwined in the setting of critical illness.[286] When leaving the ICU, patients spend most often several weeks in a general ward before going back home or before being temporally transferred to a rehabilitation center. Moreover, the high number of specialists involved in the process complicates the aftercare management.[286] Even if patients have appointments with specific specialists, GPs have frequently to ensure the role of "gatekeeper" for the overall care of patients. Moreover, the impact of PICS components can differ

from patient to patient. GPs can personalize and adapt post-ICU care to their patients and support them in the best way. Since they coordinate the distinct health dimensions, they should be aware of the available healthcare system resources such as rehabilitation services, referrals possibilities (physiotherapists, psychologists, occupational therapy etc.) and their funding. Dissemination of this information is incumbent to the healthcare authorities and should be actualized in the light of advances on PICS components.

A study tried to evaluate the feedbacks of GPs and patients experiencing a structured follow-up program after sepsis[15, 212]. It included visits to patients at their home and call them by phone every 4 weeks for 6 months. Information on problems consecutive to the ICU stay and follow-up were sent to a liaison GP, who provided support to the patient's GP. Patients and GPs were overall satisfied. Patients were more informed and more likely to take part in their follow-up. The need to strengthen resources for mental health disorders was highlighted in the study. First, authors showed that psychological burden precluded some patients from receiving appropriate information and from accepting regular monitoring. Second, some patients were not willing to join the program because it unpleasantly remembered their illness. Besides, GPs reported organisational issues with the availability of psychotherapy.[15]

7.5 Perspectives

After improvements in the understanding of PICS, our healthcare system should lay emphasis on new structural developments of aftercare strategies in order to meet patients and family needs. The stakes are high because effective rehabilitation after critical illness requires a multidisciplinary, coordinated and individualized approach. Furthermore, the efficiency of PICS prevention and management could influence societal costs at long-term.

Since patients may report some of the PICS-related problems only after hospital discharge, GPs will frequently be their first contact for care. In a poorly coordinated healthcare system mainly focusing on organ specific issues, GPs can be under pressure to ensure the leadership of global coordinator. To that end, specific pathways of care for ICU survivors should be standardized in a comprehensive, and customizable approach. Besides, caregivers need to improve the awareness and understanding of critical illness. Since PICS symptoms are generally subtle at the beginning, further research is mandatory to develop validated screening tools and implement them in primary care.

8 GENERAL DISCUSSION

This report, aimed at GPs, describes the long term impairments of PICS and its consequences on the daily life and patient experience, proposes tools to help GPs to detect PICS-related impairments in their patients (and their relatives) and provides information on how these patients can be managed in Belgium. It covers PICS in adults and not the pediatric PICS. It does not provide recommendations but information and proposals for the GPs.

The most frequent physical complication is the ICU- acquired weakness (ICU-AW), which occurs rapidly after admission and is observed in around 40% of patients at ICU discharge. It is the result of damages to both muscular and peripheral nerve systems. Recovery mostly occurs within 12–24 months, but disease persists in a proportion of patients, for up to 5 years in a Belgian study. The mental health problems include mostly anxiety (35% at 1 year), depression (29% at 1 year) and post-traumatic stress disorders (PTSD, at around 20% at 1 year), which often co-exist and do not improve in frequency and severity over time. Cognitive impairments (in 20-40% survivors at 1 year) include loss of verbal fluency and memory, and may aggravate existing cognitive disorders. They may improve in the first year after discharge but not in the following years. At 1 year after ICU discharge, 40% of survivors did not return to work and the other social consequences make these patients more vulnerable. PICS-related disorders are more frequent in some patients, in particular those with pre-existing health problems, with severe disease and with traumatizing ICU experience.

A high proportion of family members of ICU survivors are also affected by mental health impairments (20-50%), including PTSD, which corresponds to the syndrome PICS-F (F for family).

The patients treated in ICU for severe COVID-19 disease are at increased risk of PICS disorders, as well as their family caregivers, because they may cumulate several risk factors for PICS. Some risk factors for PICS that are present before ICU admission (e.g. older age) are also risk factors for severe COVID-19 disease. Factors that are related to the ICU stay, such as ICU delirium, are more frequent in ventilated patients with long ICU stay – which was the profile of most severe COVID-19 cases during the first wave. In addition the isolation and lack of contact with families and friends in the ICU may aggravate the delusional and traumatic memories of the ICU stay.

A major rationale for this rapid report is that PICS and PICS-F are so far largely unknown among health care professionals. Some PICS disorders may be unrecognized because health professionals are not aware of that complication, but also because patients surviving from ICU meet difficulties to report their psychological distress. This is especially the case for PTSD cases with a strong avoidance component as these may deny the problem and not look for assistance. We also expect that mental impairments in family members of the patient (PICS-F) may be unrecognized when the medical attention is more focused on the ICU survivor.

Patients discharged from the ICU are cared and followed-up by their hospital organ specialist. However, some PICS disorders may be noticed only when the patient returns home. The first visit to the GP after hospital discharge may be the first opportunity to detect them. This is why we also propose simple detection tools that are easy and rapid to conduct at the GP practice, and a standalone sheet is provided on our website. There are currently no specific clinical guidelines or services for the management of these patients in Belgium. This is why we provide information for GPs on the services and resources that are already available for these health problems at the time of writing this report (August 2020), as well as the effectiveness of interventions. But now that other post-COVID complications are increasingly reported, other resources and services may become available after the publication of this report.

The selection of the detection tools that we propose at GP level was mainly based on recent research performed by a German team of clinical experts to develop a set of outcome measurement tools in outpatient care settings (Spies et al, 2020).[119] The process combined several steps of consensus with medical experts and several feasibility assessments with health care workers and ICU survivors. These feasibility tests, in combination with our own selection criteria, convinced us of the applicability of the set of tools to detect PICS-related disorders by the GP.

Some interventions that we identified in the literature, such as ICU diaries, post-ICU consultations and peer-support groups, are not common in Belgium, with some exceptions due to the initiative of health care professionals. Their effect on PICS-related disorders is not well described so far in the literature but they may bring support to the patients who feel isolated with their lasting impairments.

This report has a number of limitations. As our objective was to rapidly provide information to GPs, we had to focus on systematic reviews of the literature, could not conduct large expert and stakeholder consultations as we do in classical KCE studies, nor direct patient and GP interviews. We could also not conduct validation and feasibility studies of the proposed rapid tool among GPs, and we are aware that the overload of the clinical work at GP level may impede the assessment proposed here. However we consulted more than 40 experts from the different PICS-related fields, and one or several chapters were revised by 10 different external experts, including GPs.

We also based our data on the effectiveness of interventions on primary studies, and retrieved patient experiences from existing sources to understand the patient point of view and difficulties. We hope that this report may be useful to help GPs and their patients to recognize these health problems and address them.

This work on the management of PICS as well as our current work on PICS prevention highlight the need to enhance the relationship between GP and the ICU team. Since GPs are frequently the first contact for support after hospital discharge, the need for receiving information from ICU is essential to allow them to ensure the transition of care.

This report also highlights that most PICS-related disorders do not improve with time and that the effectiveness of interventions is limited - or not demonstrated yet. This is why a focus of current research, as well as KCE work, should be on how to prevent the occurrence of PICS by an improved management at ICU level.

Table 17 – Findings of studies on predictors for PICS-related outcomes after ICU stay

Author, study period, country	Outcome predicted and time post-ICU	Number patients	Method	Risk factors	Predictive values
Milton 2020[114] 2016, Sweden, Denmark, the Netherlands	New-onset physical disability at 3 months (Barthel I 10 reduction of 10)	404 included at 3 months	Area under ROC curve (AUROC)	Physical status at ICU discharge (CPAx ≤18) Length of stay ≥72h alone	AUC 0.68. Se 73%, Sp 60%. For low risk CPAx >18: NPV 88% For high risk CPAx ≤18: PPV 32% AUC 0.57, Se 48%, Sp 59%, PPV 22%, NPV 82%
Schandl 2014[115] 2011, Sweden	New-onset physical disability at 2 months (reduction ADL or sick leave)	148 included at 2 months	AUROC	Set of 4 predictors: low educational level, inability to sit without support in ICU, fractures in ICU and ICU length of stay >2 days ICU length of stay >2 days alone	AUC 0.82 AUC 0.70
Milton 2018[108] 2016, Sweden, Denmark, the Netherlands	Psychological problems at 3 months post-ICU (PTSS-14 and/or HADS)	404 included at 3 months	AUROC, multivariate analysis	Set of 4 predictors at ICU discharge: depression (PHQ-2), traumatic memories (PTSS-14 Part A), reported lack of social support at hospital discharge and age (peak risk 49-65 years). Previous psychological problems	Area under the curve (AUC): 0.76 For low risk <30%: PPV 10% NPV 84% For risk 30-60%: PPV 37% NPV 58% For high risk >60%: PPV 83% NPV 17% Previous problems did not improve prediction
Milton 2017[113] 2012-13, Sweden	PTSD (PTSS-10 >34), anxiety/depression (HADS-A and D >7) at 3 months post-ICU	82 included at 3 months	AUROC	Mental outcomes 1 week after ICU discharge:* PTSD: PTSS-10 part B score >34 or >29 Anxiety: HADS-A >7 or >5 Depression: HADS-D >7 or >4	Outcomes at 3 months:* PTSD: Se 91%, Sp 86%, PPV 50% NPV 98% Anxiety: Se 77%, Sp 75%, PPV 37% NPV 95% Depress. Se 76%, Sp 66%, PPV 37% NPV 91%
Schandl 2013[111] 2011, Sweden	Psychological problems at 2 months post-ICU (PTSS-10 and/or HADS)	150 included at 2 months	AUROC	Set of 6 predictors at ICU or at discharge: major pre-existing diseases (Charlson >3), having children <18 years, previous psychological problems, ICU agitation, being unemployed at ICU admission, depressed at ICU	Outcome at 2 months : AUC: 0.77 ICU length of stay was poor predictor
Oeyen 2018,[116] Belgium	Quality of life (QoL), global at 1 year, using EuroQoL-5D and utility indices	1831	R square of model, no predictive values	Set of 12 factors: QoL at baseline, age, activity of daily living, imaging, APACHE II-score (P=0.001), ≥80 years, mechanical ventilation, hematological patient, SOFA-score, tracheotomy, surgical admission and comorbidity (Charlson - CCI)	Adjusted R^2 0.39
Hodgson 2017,[112] 20-15 Australia	Disability (WHODAS II) moderate/severe i.e. score 25–95% at 6 months post-ICU	262	AUROC	Set of 4 predictors: history of anxiety / depression, being separated or divorced, duration of mechanical ventilation and not being discharged to home	AUC 0.71

*ROC: receiver operating characteristic; AUC: area under the curve; QoL: quality of life; CCI: Charlson comorbidity index ; *: predictive values are those with the lower threshold; AUROC in the text are those with higher threshold*

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Colophon

Title: Post intensive care syndrome in the aftermath of COVID-19

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Disclaimer: This document is a rapid review of scientific literature retrieved from several publicly funded COVID-19 resource collections. The literature included in these repositories is not always peer-reviewed or externally validated. KCE synthesised the evidence in short time frames to respond to urgent questions and could therefore not follow its regular methodological procedures. This work is used to inform guidance of other governmental agencies (like Sciensano, CSS/HGR, AFMPS/FAGG and SPF/FOD).

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