Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

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COVID 19 – KCE CONTRIBUTIONS

POST INTENSIVE CARE SYNDROME IN THE AFTERMATH OF COVID-19: APPENDICES

GERMAINE HANQUET, NADIA BENAHMED, DIEGO CASTANARES- ZAPATERO, MARIE DAUVRIN, ANJA DESOMER, KARIN RONDIA

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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APPENDIX 1. SEARCH STRATEGY FOR LITERATURE REVIEW

Appendix 1.1. Search terms for systematic literature reviews on prevalence and risk factors

(("ICU"[Title/Abstract] OR "i c u"[Title/Abstract] OR "IC"[Title/Abstract] OR "CCU"[Title/Abstract] OR "intensive care"[Title/Abstract] OR "intensive therapy"[Title/Abstract] OR "critical illness"[Title/Abstract] OR "critical ill"[Title/Abstract] OR "critically ill"[Title/Abstract] OR "ARDS"[Title/Abstract] OR "adult respiratory distress syndrome"[Title/Abstract] OR "a r d s"[Title/Abstract] OR "respiratory distress syndrome, adult"[MeSH Terms] OR "acute respiratory distress syndrome"[Title/Abstract] OR "Critical Care"[Title/Abstract] OR "high dependency"[Title/Abstract] OR "Intensive Care Units"[MeSH Terms] OR "Critical Care"[MeSH Terms] OR "Critical Care Nursing"[MeSH Terms]) NOT ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn"[All Fields] OR "newborn infant"[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonates"[All Fields] OR "neonatality"[All Fields] OR "neonatals"[All Fields] OR "neonate s"[All Fields] OR "intensive care units, neonatal"[MeSH Terms] OR "neonatal intensive care units"[All Fields] OR "nicu"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn infant"[All Fields]) OR "newborns"[All Fields] OR ("intensive"[All Fields] AND "care"[All Fields] AND "units"[All Fields] AND "neonatal"[All Fields])) **AND** ((("Mental Disorders"[MeSH Terms] OR "Cognitive Dysfunction"[MeSH Terms] OR “Cognitive decline”[Title/Abstract] OR "stress disorders, post-traumatic"[MeSH Terms] OR “psychological symptoms”[Title/Abstract] OR "Anxiety"[MeSH Terms] OR "Depression"[MeSH Terms] OR "Depressive Disorder"[MeSH Terms] OR "post-sepsis syndrome"[Title/Abstract) OR "post-sepsis syndrome"[Title/Abstract] OR "cipsm"[Title/Abstract] OR "cipn"[Title/Abstract] OR "critical illness neuromyopathy"[Title/Abstract] OR "critical illness myopathy"[Title/Abstract] OR "critical illness polyneuropathy"[Title/Abstract] OR "ICU-AW"[Title/Abstract] OR "icuaw"[Title/Abstract] OR "ICU-acquired paresis"[Title/Abstract]) OR (("Critical Care"[MeSH Terms] OR ("critical"[Title/Abstract] AND "care"[Title/Abstract]) OR "Critical Care"[Title/Abstract] OR ("intensive"[Title/Abstract] AND "care"[Title/Abstract]) OR "intensive care"[Title/Abstract]) AND ("acquirable"[Title/Abstract] OR "acquire"[Title/Abstract] OR "acquired"[Title/Abstract] OR "acquirement"[Title/Abstract] OR "acquirements"[Title/Abstract] OR "acquires"[Title/Abstract] OR "acquiring"[Title/Abstract]) AND ("paresis"[MeSH Terms] OR "paresis"[Title/Abstract] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "muscle weakness"[Title/Abstract] OR "muscle weakness"[MeSH Terms] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "intensive care acquired weakness"[Title/Abstract] OR "Intensive Care Unit-Acquired Weakness"[Title/Abstract] OR "ICU-acquired weakness"[Title/Abstract] OR "muscle wasting"[Title/Abstract]) OR ("post-intensive care syndrome"[Title/Abstract] OR "post-ICU syndrome"[Title/Abstract] OR "critical care illness"[Title/Abstract] OR "post critical illness"[Title/Abstract] OR "postintensive care syndrome"[Title/Abstract] OR "post-intensive care syndrome"[Title/Abstract] OR "p s s"[Title/Abstract] OR "pics"[Title/Abstract]))) AND ((“Treatment”[Title/Abstract] OR “Approach”[Title/Abstract] OR “Therapy”[Title/Abstract] OR “Mobilisation”[Title/Abstract] OR “reorientation”[Title/Abstract] OR “recovery”[Title/Abstract] OR “Convalescence”[Title/Abstract] OR "Therapeutics"[Mesh] OR "therapy"[Subheading] OR "Rehabilitation"[Mesh] OR "Rehabilitation Centers"[Mesh] OR "Physical and Rehabilitation Medicine"[Mesh] OR "Hospitals, Rehabilitation"[Mesh] OR "Psychotherapy"[Mesh] OR "Mental Health Recovery"[Mesh] OR "Recovery of Function"[Mesh] OR "Convalescence"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Occupational Therapy"[Mesh] OR "Drug Therapy"[Mesh] OR "Activities of Daily Living"[Mesh] OR "Quality of Life"[Mesh]) NOT ("Anesthesia"[Mesh] OR "Enhanced Recovery After Surgery"[Mesh] OR "Recovery Room"[Mesh] OR "Anesthesia Recovery Period"[Mesh])) NOT ("Editorial"[Publication Type] OR "Letter"[Publication Type] OR "Case Reports"[Publication Type]) Filters: Systematic Reviews

Appendix 1.2. Search terms for primary studies on predictors

(("ICU"[Title/Abstract] OR "i c u"[Title/Abstract] OR "IC"[Title/Abstract] OR "CCU"[Title/Abstract] OR "intensive care"[Title/Abstract] OR "intensive therapy"[Title/Abstract] OR "critical illness"[Title/Abstract] OR "critical ill"[Title/Abstract] OR "critically ill"[Title/Abstract] OR "Critical Care"[Title/Abstract] OR "Intensive Care Units"[MeSH Terms] OR "Critical Care"[MeSH Terms] OR "Critical Care Nursing"[MeSH Terms]) NOT ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn"[All Fields] OR "newborn infant"[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonates"[All Fields] OR "neonatality"[All Fields] OR "neonatals"[All Fields] OR "neonate s"[All Fields] OR "intensive care units, neonatal"[MeSH Terms] OR "neonatal intensive care units"[All Fields] OR "nicu"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn infant"[All Fields]) OR "newborns"[All Fields] OR ("intensive"[All Fields] AND "care"[All Fields] AND "units"[All Fields] AND "neonatal"[All Fields])) AND ((("Mental Disorders"[MeSH Terms] OR "Cognitive Dysfunction"[MeSH Terms] OR “Cognitive decline”[Title/Abstract] OR "stress disorders, post-traumatic"[MeSH Terms] OR “psychological symptoms”[Title/Abstract] OR "Anxiety"[MeSH Terms] OR "Depression"[MeSH Terms] OR "Depressive Disorder"[MeSH Terms] OR "post-sepsis syndrome"[Title/Abstract) OR "post-sepsis syndrome"[Title/Abstract] OR "cipsm"[Title/Abstract] OR "cipn"[Title/Abstract] OR "critical illness neuromyopathy"[Title/Abstract] OR "critical illness myopathy"[Title/Abstract] OR "critical illness polyneuropathy"[Title/Abstract] OR "ICU-AW"[Title/Abstract] OR "icuaw"[Title/Abstract] OR "ICU-acquired paresis"[Title/Abstract]) OR (("Critical Care"[MeSH Terms] OR ("critical"[Title/Abstract] AND "care"[Title/Abstract]) OR "Critical Care"[Title/Abstract] OR ("intensive"[Title/Abstract] AND "care"[Title/Abstract]) OR "intensive care"[Title/Abstract]) AND ("acquirable"[Title/Abstract] OR "acquire"[Title/Abstract] OR "acquired"[Title/Abstract] OR "acquirement"[Title/Abstract] OR "acquirements"[Title/Abstract] OR "acquires"[Title/Abstract] OR "acquiring"[Title/Abstract]) AND ("paresis"[MeSH Terms] OR "paresis"[Title/Abstract] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "muscle weakness"[Title/Abstract] OR "muscle weakness"[MeSH Terms] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "intensive care acquired weakness"[Title/Abstract] OR "Intensive Care Unit-Acquired Weakness"[Title/Abstract] OR "ICU-acquired weakness"[Title/Abstract] OR "muscle wasting"[Title/Abstract]) OR ("post-intensive care syndrome"[Title/Abstract] OR "post-ICU syndrome"[Title/Abstract] OR "critical care illness"[Title/Abstract] OR "post critical illness"[Title/Abstract] OR "postintensive care syndrome"[Title/Abstract] OR "post-intensive care syndrome"[Title/Abstract] OR "p s s"[Title/Abstract] OR "pics"[Title/Abstract]))) AND (“predict*”) NOT ("Editorial"[Publication Type] OR "Letter"[Publication Type] OR "Case Reports"[Publication Type])

Appendix 1.3. Search terms for detection of PICS-related disorders

(("ICU"[Title/Abstract] OR "i c u"[Title/Abstract] OR "IC"[Title/Abstract] OR "CCU"[Title/Abstract] OR "intensive care"[Title/Abstract] OR "intensive therapy"[Title/Abstract] OR "critical illness"[Title/Abstract] OR "critical ill"[Title/Abstract] OR "critically ill"[Title/Abstract] OR "ARDS"[Title/Abstract] OR "adult respiratory distress syndrome"[Title/Abstract] OR "a r d s"[Title/Abstract] OR "respiratory distress syndrome, adult"[MeSH Terms] OR "acute respiratory distress syndrome"[Title/Abstract] OR "Critical Care"[Title/Abstract] OR "high dependency"[Title/Abstract] OR "Intensive Care Units"[MeSH Terms] OR "Critical Care"[MeSH Terms] OR "Critical Care Nursing"[MeSH Terms]) **NOT** ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn"[All Fields] OR "newborn infant"[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR 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"inattentive"[Title/Abstract] OR "inattentiveness"[Title/Abstract] OR "confusability"[Title/Abstract] OR "confusable"[Title/Abstract] OR "confuse"[Title/Abstract] OR "confuses"[Title/Abstract] OR "confusing"[Title/Abstract] OR "confusion"[MeSH Terms] OR "confusion"[Title/Abstract] OR "confused"[Title/Abstract] OR "confusions"[Title/Abstract] OR "agitate"[Title/Abstract] OR "agitated"[Title/Abstract] OR "agitates"[Title/Abstract] OR "agitating"[Title/Abstract] OR "agitation"[Title/Abstract] OR "agitations"[Title/Abstract] OR "agitator"[Title/Abstract] OR "agitators"[Title/Abstract] OR "intensive care delirium"[Title/Abstract] OR "Mental Disorders"[MeSH Terms] OR "Cognitive Dysfunction"[MeSH Terms] OR “Cognitive decline”[Title/Abstract] OR "stress disorders, post-traumatic"[MeSH Terms] OR “psychological symptoms”[Title/Abstract] OR "Anxiety"[MeSH Terms] OR "Depression"[MeSH Terms] OR "Depressive Disorder"[MeSH Terms] OR "post-sepsis syndrome"[Title/Abstract) OR "post-sepsis syndrome"[Title/Abstract] OR "cipsm"[Title/Abstract] OR "cipn"[Title/Abstract] OR "critical illness neuromyopathy"[Title/Abstract] OR "critical illness myopathy"[Title/Abstract] OR "critical illness polyneuropathy"[Title/Abstract] OR "ICU-AW"[Title/Abstract] OR "icuaw"[Title/Abstract] OR "ICU-acquired paresis"[Title/Abstract]) OR (("Critical Care"[MeSH Terms] OR ("critical"[Title/Abstract] AND "care"[Title/Abstract]) OR "Critical Care"[Title/Abstract] OR ("intensive"[Title/Abstract] AND "care"[Title/Abstract]) OR "intensive care"[Title/Abstract]) AND ("acquirable"[Title/Abstract] OR "acquire"[Title/Abstract] OR "acquired"[Title/Abstract] OR "acquirement"[Title/Abstract] OR "acquirements"[Title/Abstract] OR "acquires"[Title/Abstract] OR "acquiring"[Title/Abstract]) AND ("paresis"[MeSH Terms] OR "paresis"[Title/Abstract] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "muscle weakness"[Title/Abstract] OR "muscle weakness"[MeSH Terms] OR ("muscle"[Title/Abstract] AND 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“diagnostic”[Title/Abstract] OR “clinical”[Title/Abstract] OR “detection”[Title/Abstract] OR “screening”[Title/Abstract]) AND (“tool”[Title/Abstract] OR “instrument”[Title/Abstract]))) **NOT** ("systematic review"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Title/Abstract] OR "systematic reviews as topic"[MeSH Terms] OR "meta-analysis"[Publication Type] OR "meta-analysis"[Title/Abstract] OR "Editorial"[Publication Type] OR "Letter"[Publication Type] OR "Case Reports"[Publication Type])

⇨ Results for the period 2010 up till 27/04/2020: 2568 studies

Appendix 1.4. Search terms for the effectiveness of interventions and patient experience

For primary studies, run on 24 April 2020:

(("ICU"[Title/Abstract] OR "i c u"[Title/Abstract] OR "IC"[Title/Abstract] OR "CCU"[Title/Abstract] OR "intensive care"[Title/Abstract] OR "intensive therapy"[Title/Abstract] OR "critical illness"[Title/Abstract] OR "critical ill"[Title/Abstract] OR "critically ill"[Title/Abstract] OR "ARDS"[Title/Abstract] OR "adult respiratory distress syndrome"[Title/Abstract] OR "a r d s"[Title/Abstract] OR "respiratory distress syndrome, adult"[MeSH Terms] OR "acute respiratory distress syndrome"[Title/Abstract] OR "Critical Care"[Title/Abstract] OR "high dependency"[Title/Abstract] OR "Intensive Care Units"[MeSH Terms] OR "Critical Care"[MeSH Terms] OR "Critical Care Nursing"[MeSH Terms]) **NOT** ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn"[All Fields] OR "newborn infant"[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonates"[All Fields] OR "neonatality"[All Fields] OR "neonatals"[All Fields] OR "neonate s"[All Fields] OR "intensive care units, neonatal"[MeSH Terms] OR "neonatal intensive care units"[All Fields] OR "nicu"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn infant"[All Fields]) OR "newborns"[All Fields] OR ("intensive"[All Fields] AND "care"[All Fields] AND "units"[All Fields] AND "neonatal"[All Fields])) **AND** ((("Mental Disorders"[MeSH Terms] OR "Cognitive Dysfunction"[MeSH Terms] OR “Cognitive decline”[Title/Abstract] OR "stress disorders, post-traumatic"[MeSH Terms] OR “psychological symptoms”[Title/Abstract] OR "Anxiety"[MeSH Terms] OR "Depression"[MeSH Terms] OR "Depressive Disorder"[MeSH Terms] OR "post-sepsis syndrome"[Title/Abstract) OR "post-sepsis syndrome"[Title/Abstract] OR "cipsm"[Title/Abstract] OR "cipn"[Title/Abstract] OR "critical illness neuromyopathy"[Title/Abstract] OR "critical illness myopathy"[Title/Abstract] OR "critical illness polyneuropathy"[Title/Abstract] OR "ICU-AW"[Title/Abstract] OR "icuaw"[Title/Abstract] OR "ICU-acquired paresis"[Title/Abstract]) OR (("Critical Care"[MeSH Terms] OR ("critical"[Title/Abstract] AND "care"[Title/Abstract]) OR "Critical Care"[Title/Abstract] OR ("intensive"[Title/Abstract] AND "care"[Title/Abstract]) OR "intensive care"[Title/Abstract]) AND ("acquirable"[Title/Abstract] OR "acquire"[Title/Abstract] OR "acquired"[Title/Abstract] OR "acquirement"[Title/Abstract] OR "acquirements"[Title/Abstract] OR "acquires"[Title/Abstract] OR "acquiring"[Title/Abstract]) AND ("paresis"[MeSH Terms] OR "paresis"[Title/Abstract] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "muscle weakness"[Title/Abstract] OR "muscle weakness"[MeSH Terms] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "intensive care acquired weakness"[Title/Abstract] OR "Intensive Care Unit-Acquired Weakness"[Title/Abstract] OR "ICU-acquired weakness"[Title/Abstract] OR "muscle wasting"[Title/Abstract]) OR ("post-intensive care syndrome"[Title/Abstract] OR "post-ICU syndrome"[Title/Abstract] OR "critical care illness"[Title/Abstract] OR "post critical illness"[Title/Abstract] OR "postintensive care syndrome"[Title/Abstract] OR "post-intensive care syndrome"[Title/Abstract] OR "p s s"[Title/Abstract] OR "pics"[Title/Abstract]))) **AND** ((“Treatment”[Title/Abstract] OR “Approach”[Title/Abstract] OR “Therapy”[Title/Abstract] OR “Mobilisation”[Title/Abstract] OR “reorientation”[Title/Abstract] OR “recovery”[Title/Abstract] OR “Convalescence”[Title/Abstract] OR "Therapeutics"[Mesh] OR "therapy"[Subheading] OR "Rehabilitation"[Mesh] OR "Rehabilitation Centers"[Mesh] OR "Physical and Rehabilitation Medicine"[Mesh] OR "Hospitals, Rehabilitation"[Mesh] OR "Psychotherapy"[Mesh] OR "Mental Health Recovery"[Mesh] OR "Recovery of Function"[Mesh] OR "Convalescence"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Occupational Therapy"[Mesh] OR "Drug Therapy"[Mesh] OR "Activities of Daily Living"[Mesh] OR "Quality of Life"[Mesh]) NOT ("Anesthesia"[Mesh] OR "Enhanced Recovery After Surgery"[Mesh] OR "Recovery Room"[Mesh] OR "Anesthesia Recovery Period"[Mesh])) **NOT** ("systematic review"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Title/Abstract] OR "systematic reviews as topic"[MeSH Terms] OR "meta-analysis"[Publication Type] OR "meta-analysis"[Title/Abstract] OR "Editorial"[Publication Type] OR "Letter"[Publication Type] OR "Case Reports"[Publication Type])

For systematic reviews, run on 28 May 2020:

(("ICU"[Title/Abstract] OR "i c u"[Title/Abstract] OR "IC"[Title/Abstract] OR "CCU"[Title/Abstract] OR "intensive care"[Title/Abstract] OR "intensive therapy"[Title/Abstract] OR "critical illness"[Title/Abstract] OR "critical ill"[Title/Abstract] OR "critically ill"[Title/Abstract] OR "ARDS"[Title/Abstract] OR "adult respiratory distress syndrome"[Title/Abstract] OR "a r d s"[Title/Abstract]

OR "respiratory distress syndrome, adult"[MeSH Terms] OR "acute respiratory distress syndrome"[Title/Abstract] OR "Critical Care"[Title/Abstract] OR "high dependency"[Title/Abstract] OR "Intensive Care Units"[MeSH Terms] OR "Critical Care"[MeSH Terms] OR "Critical Care Nursing"[MeSH Terms]) **NOT** ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn"[All Fields] OR "newborn infant"[All Fields] OR "neonatal"[All Fields] OR "neonate"[All Fields] OR "neonates"[All Fields] OR "neonatality"[All Fields] OR "neonatals"[All Fields] OR "neonate s"[All Fields] OR "intensive care units, neonatal"[MeSH Terms] OR "neonatal intensive care units"[All Fields] OR "nicu"[All Fields] OR "infant, newborn"[MeSH Terms] OR "infant"[All Fields] OR "newborn infant"[All Fields]) OR "newborns"[All Fields] OR ("intensive"[All Fields] AND "care"[All Fields] AND "units"[All Fields] AND "neonatal"[All Fields])) **AND** ((("Mental Disorders"[MeSH Terms] OR "Cognitive Dysfunction"[MeSH Terms] OR “Cognitive decline”[Title/Abstract] OR "stress disorders, post-traumatic"[MeSH Terms] OR “psychological symptoms”[Title/Abstract] OR "Anxiety"[MeSH Terms] OR "Depression"[MeSH Terms] OR "Depressive Disorder"[MeSH Terms] OR "post-sepsis syndrome"[Title/Abstract) OR "post-sepsis syndrome"[Title/Abstract] OR "cipsm"[Title/Abstract] OR "cipn"[Title/Abstract] OR "critical illness neuromyopathy"[Title/Abstract] OR "critical illness myopathy"[Title/Abstract] OR "critical illness polyneuropathy"[Title/Abstract] OR "ICU-AW"[Title/Abstract] OR "icuaw"[Title/Abstract] OR "ICU-acquired paresis"[Title/Abstract]) OR (("Critical Care"[MeSH Terms] OR ("critical"[Title/Abstract] AND "care"[Title/Abstract]) OR "Critical Care"[Title/Abstract] OR ("intensive"[Title/Abstract] AND "care"[Title/Abstract]) OR "intensive care"[Title/Abstract]) AND ("acquirable"[Title/Abstract] OR "acquire"[Title/Abstract] OR "acquired"[Title/Abstract] OR "acquirement"[Title/Abstract] OR "acquirements"[Title/Abstract] OR "acquires"[Title/Abstract] OR "acquiring"[Title/Abstract]) AND ("paresis"[MeSH Terms] OR "paresis"[Title/Abstract] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "muscle weakness"[Title/Abstract] OR "muscle weakness"[MeSH Terms] OR ("muscle"[Title/Abstract] AND "weakness"[Title/Abstract]) OR "intensive care acquired weakness"[Title/Abstract] OR "Intensive Care Unit-Acquired Weakness"[Title/Abstract] OR "ICU-acquired weakness"[Title/Abstract] OR "muscle wasting"[Title/Abstract]) OR ("post-intensive care syndrome"[Title/Abstract] OR "post-ICU syndrome"[Title/Abstract] OR "critical care illness"[Title/Abstract] OR "post critical illness"[Title/Abstract] OR "postintensive care syndrome"[Title/Abstract] OR "post-intensive care syndrome"[Title/Abstract] OR "p s s"[Title/Abstract] OR "pics"[Title/Abstract]))) **AND** ((“Treatment”[Title/Abstract] OR “Approach”[Title/Abstract] OR “Therapy”[Title/Abstract] OR “Mobilisation”[Title/Abstract] OR “reorientation”[Title/Abstract] OR “recovery”[Title/Abstract] OR “Convalescence”[Title/Abstract] OR "Therapeutics"[Mesh] OR "therapy"[Subheading] OR "Rehabilitation"[Mesh] OR "Rehabilitation Centers"[Mesh] OR "Physical and Rehabilitation Medicine"[Mesh] OR "Hospitals, Rehabilitation"[Mesh] OR "Psychotherapy"[Mesh] OR "Mental Health Recovery"[Mesh] OR "Recovery of Function"[Mesh] OR "Convalescence"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Occupational Therapy"[Mesh] OR "Drug Therapy"[Mesh] OR "Activities of Daily Living"[Mesh] OR "Quality of Life"[Mesh]) NOT ("Anesthesia"[Mesh] OR "Enhanced Recovery After Surgery"[Mesh] OR "Recovery Room"[Mesh] OR "Anesthesia Recovery Period"[Mesh])) **NOT** ("Editorial"[Publication Type] OR "Letter"[Publication Type] OR "Case Reports"[Publication Type]) Filters: Systematic Reviews

APPENDIX 2. DESCRIPTION OF SYSTEMATIC REVIEWS ON PREVALENCE AND RISK FACTORS, PER DIMENSION

Author, year	Outcome and time post-ICU discharge	N and type studies (period)	Patients	Risk factors	Prevalence
Physical disorders					
Lee 2020[1]*	Physical outcomes	32 studies (2008-18)	Adults	Y	N
Yang 2018[2]	ICU-AW at 2 weeks	14 prospective cohort studies including 3 Belgian ones (till 2017)	Adults, criteria differ per study	Y	Y
Appleton 2015[3]	ICU-AW at any time point	33 studies (1977-2011), cohorts and RCT	Adults	N	Y
Mental health problems					
Lee 2020[1]*	Mental health problems	33 studies (2008-18)	Adults	Y	N
Nikayin 2016[4]	Anxiety at different timing (2-14 months)	27 RCT, cohort, cross sectional, mostly EU (1970-2015)	Adult, studies with >50% ICU patients	Y	Y
Rabiee 2016[5]	Depression, at different timing	38 RCT, cohort and cross sectional (1970-2015)	Adults, not specialized ICU	Y	Y
Righy 2019	PTSD, at different time points	48 observational (1996-2018)	Adults, any	N	Y
Parker 2015[6]	PTSD at ≥1 month post-ICU	40 RCT, cohort and cross sectional (up to 2014)	Adults, not specialized ICU	Y	Y
Wade 2013[7]	PTSD at 1-12 months after	18 RCT, cohort, cross sectional, ≥30 patients. 13 studies (2008-12)	Adults, general ICU, >24h LoS	Y	Y
Cognitive disorders					
Kohler 2019[8]	Cognitive impairment	14 observational studies (up to 2019)	Adults, nonsurgical patients	Y	Y
Sakusic 2018[9]	Cognitive deficits (modifiable risk factors only)	28, 27 observational studies and 1 RCT	Adults, 2 months post discharge	Y	N
Wolters 2013[10]	Cognitive at 2 months to 13 years	19 (1980-2012)	Adults, not cardiac surgery	N	Y
Lee 2020[1]*	Cognitive impairment	15 studies (2008-18)	Adults	Y	N
Other consequences					
Oeyen 2010[11]	Quality of life at ≥12 months	53 studies, all designs (1999-2009), ≥50 cases	Adults	Y*	Y
Kamdar[12]	Return to work any time	52 studies, cohort studies (1970-2018)	Adults, not specialty ICU	Y	Y
Consequences in family members (PICS-F)					
Van Beusekom	Burden in informal caregivers, any time point	28 studies, including 24 observational (up to 2014)	Informal caregivers of ICU adult patients	N	Y
Haines 2015[13]	Psychosocial outcomes any time	14 mostly observational studies (up to 2014)	Caregivers, family members of ICU patients	Y	Y

ICU-AW: ICU-acquired weakness; PTSD: post-traumatic stress disorder. RCT: randomized clinical trial.: not prevalence but measures of QoL*

APPENDIX 3. SELECTION OF PICS DETECTION TOOLS

Appendix 3.1. Selection process

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. Nevertheless, only validation studies were included for further analysis, 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). 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 MRC criteria to handgrip dynamometry. Per health domain, an overview of all retrieved detection tools and the validation data are presented in following sections.

Physical function

A variety of tools, either assessing specific muscle strength or more comprehensive assessments of performance in daily life activities, was found in the exploratory literature search, however, only 1 validation study was found, which compared the hand dynamometry with MRC criteria.[14] The choice of tools was on the one hand based on the paper of Spies et al (2020)[15] and on the other hand the need for functional tests who are applicable in GP's practice or even at home of the patient. Therefore, tools were chosen which are context-independent, for example for the execution of the 6min walk test, reasonable space is needed and the walking ability could be hampered by restricted space, underground, etc. The TUG is less context dependent and could even be performed in small spaces.

Regarding handgrip strength, the study of Braganca et al, 2019[14] showed that handgrip dynamometry may provide a simple and accurate alternative to the MRC examination for the diagnosis of ICU acquired muscle weakness (ICUAW). In this study a cut-off of <11kg force for men and <7kg force in women were used to identify ICUAW. Based on the paper of Spies et al (2020)[15] and the easy clinical applicability of the assessment, the choice was made to include the hand dynamometry in the screening tool for Belgian GPs.

Mental health: anxiety, depression and PTSD

The most commonly used instruments were HADS-A and STAI for anxiety and depression[4] and PTSS-10, IES-R, CAPS, UK PTSS-14 for PTSD.[16] From the list of tools in the mental health domain (see below), only 2 tools met all selection criteria, with the lack of recent validation studies as the main raison to exclude all other tools. The two remaining tools were the Hospital Anxiety and Depression Scale (HADS) and the Patient Health Questionnaire (PHQ).

Although some psychometric performance was demonstrated for both tools (see below in evidence tables), the final selection was based on its current use in clinical practice:

- **Hospital Anxiety and Depression Scale (HADS)**: The systematic review of Rabiee et al (2016)[5] refers to the HADS-D (depression subscale) as one of the most common measurement instruments, followed by the Center for Epidemiological Studies Depression scale (CES-d) and the Beck Depression Inventory-II. The authors conclude that the HADS would be a particularly relevant instrument for validation in a population of ICU survivors and some preliminary validation has been done in subgroups of critical illness survivors. In the cohort study of Jutte et al (2015)[17] in acute lung injury survivors, a good internal consistency was shown and both HADS subscales were substantially correlated with the EQ-5D-3L anxiety/depression item and the SF-36 mental health-related domain scores. Nevertheless these correlations, the authors conclude that the SF-36 mental health domain may be a particularly good measure of psychological distress, but not for general anxiety or depressive symptoms in particular. Also the authors warn that although the HADS has been cross-validated with other measures to assess anxiety and deprssive symptoms in ICU survivors, it has not yet been validated against "gold standard"

clinical diagnoses in this population. Another cohort study[18] examined the predicitive value of HADS assessed 1 week after ICU stay and compared with 3-month psychological outcome and came to the conclusion that the HADS may be a useful aid to identify ICU survivors at high risk for clinically significant symptoms of post-traumatic stress, anxiety and depression 3 months post ICU stay. In a cohort study of Kerckhoffs et al (2019)[19] a self-reported outcome of ICU treatment in ICU survivors 1 y after ICU discharge was compared to measures on the different determinants of a potential unacceptable outcome (QoL by EQ-5D-3L, physical function by Barthel Index, cognition by Cognitive Failures Questionnaire, depression by HADS and PTSS by IES): only the HADS was significantly associated with a self-reported unacceptable outcome. A comparison between paper-based and web-based questionnaires (including HADS) found no significant difference between both types of versions in outcomes of questionnaires, except significant higher prevalence of PTSD (measured by TSQ)[20]. Some additonal findings throughout the study showed that ICU survivors in the web-based module were significantly younger and had a longer ICU stay. In both groups a larger prevalence of possible mental, physical and nutritional problems were found. Also not all survivors with problems seemed to had contact with the appropriate health professional.

Although the HADS screens for both anxiety and depression, no Belgian guideline could be found which refers to the HADS as screening tool for depression and anxiety. In the research of Spies et al (2020)[15] a preference was given to the PHQ due to copyright issues with the German version of the HADS, with high fees to have acces to this instrument.

- **Patient Health Questionnaire (PHQ)**: The original 59-items of the PHQ aims to detect different types of mental health disorders, such as depression, anxeity, alcohol, eating and somatoform disorders. The most commonly known shorter version (PHQ-9) screens for the presence of a depression and its potential severity. A disadvantage of this instrument is the solely focus on depression, and not the combination of anxiety and depression. In the study of Downey et al (2016)[21] a comparison was made between the 9-item, 8-item and 2-item versions of the PHQ in families of ICU survivors: the item on suicidal ideation in the 9-item version showed significant misfit (majority of family members scored 0 or 1) (P<.001). The 8-item version (without suicidal ideation) showed already a modest improvement in fit at baseline (P<.005), however the 2-item version (anhedonia and depressed mood) showed to be the most reflective model for depression severity.

In the Belgian guideline for primary care on the diagnosis of depression in adults[22], the **Whooley questions** are recommended as screening tool in GP practice. These Whooley questions are very similar to the PHQ-2, except for the response type which is binary in the Whooley questions (yes/no) versus a 4 point-Likert scale (0= not at all;1= several days; 2=more than half of the days; 3=nearly everyday) in the PHQ-2.

The Whooley questions are the following:

- During the past month, have you often been bothered by feeling down, depressed or hopeless?
- During the past month, have you often been bothered by little interest or pleasure in doing things?

The comparison between the Whooley Questions and the PHQ-2 showed some differences between both questionnaires[23]: the PHQ-2 has a different time frame (last 2 weeks vs. past month), response format (multiple choice vs. yes/no), and range of scores (0 to 6 vs. 0 to 2) than the Whooley questions. For these reasons, the (yes/no) Whooley Questions are more sensitive, easier to administer and simpler to score than the (multiple choice) PHQ-2. The most important similarity between both is the poor specificity (i.e. many false positives), indicating that a positive screen on either questionnaire must be followed by a clinical interview to establish the diagnosis of major depressive disorder.

The choice to include the Whooley Questions rather than the PHQ-2 (in contrast to Spies et al, 2020)[15] was mainly based on the better performance of the Whooley Questions on the sensitivity[24]: a pooled sensitivity of 0.95 (95% CI 0.88-0.97) compared to a gold standard diagnostic interview for depression, whereas a pooled sensitivity of 0.76 (95% CI 0.68-0.82) was found for PHQ-2 (with cut-off point ≥3) and a pooled sensitivity of 0.91 (95% CI 0.85-0.94) with cut-off point ≥2. In one study the Whooley Questions and the PHQ-2 were both compared with a gold standard diagnostic interview in the same patients and the authors reported a sensitivity of 0.90 in the Whooley Questions versus a sensitivity of 0.82 (with a cut point of ≥2) with the PHQ-2. These studies confirm our choice to include the Whooley questions in a rapid screening tool for GPs in Belgium.

To assess also **anxiety**, which is considered as an important impairment in mental health, an additional tool is required next to the PHQ. The systematic review of Nikayin et al (2016)[4] refers to the HADS-A (anxiety subscale of the HADS) and the State-Trait Anxiety Inventory (STAI) as the most commonly used instruments to assess anxiety in critical illness survivors. Similar to Rabiee et al (2016)[5] (a systematic review on depression in ICU survivors), the authors recommend further validation of the HADS in ICU survivors, mainly based on the common use of this instrument among the studies and the positive evaluation of the psychometric performance in other populations (referring to a good internal consistency and sensitivity to change).

In the set of outcome measurement instruments (OMIs) to detect PICS[15] the choice was made to use the PHQ-4[a], which is a combination of the PHQ-2 (2 items on anhedonia and depressed mood) and the GAD-2 (2 items on anxiety) covering both anxiety and depression. The same research group made a psychometric analysis of the PHQ-4 in pre-operative surgical patients and found a sensitivity of 80.5% and specificity of 80.2% (with a lowered cut-off point of ≥4) for detecting clinically significant psycholgical distress.[25] They concluded that the PHQ-4 had sufficient psychometric quality to detect self-reported clinically significant psychological distress including depression and/or anxiety in surgical patients. However, the PHQ-2 and GAD-2 are not recommened as exclusive measures of depression and anxiety (i.e. to classify patients into groups of only depression, only anxiety or both depression and anxiety) in these patients.

A similar approach was found in the NICE pathway[26] on the identification of common mental health problems (2011 and evidence review in 2018): a rapid screening for depression with 2 questions (Whooley questions with yes/no response) and the use of the GAD-2 scale to ask about the feeling of anxiety and the ability to stop or control worry (with a 4-point scale from 0-3). If a person answers 'yes' to either question on depression, a depression should be considered. If the person scores three or more on the GAD-2 scale, an anxiety disorder should be considered. In case of a lower score, but with some concern about the potential presence of an anxiety disorder, an additional question could be asked ('Do you find yourself avoiding places or activities and does this cause you problems?). If person answers 'yes' to this question, an anxiety disorder should be considered. This additional question is not included in the set of instruments by Spies et al (2020).[15]

The Current Belgian guidelines for primary care are less clear, either a clinical test to detect anxiety is not mentioned[b] or another instrument is mentioned (Vier Dimensionale Klachtenlijst (4dkl))[c], which has not been cited in the literature on ICU survivors. From a rapid screening perspective, this instrument can be considered as less applicable in clinical practice, because it consists of 50 questions and should rather be considered in a more comprehensive assessment.

A systematic review on the PHQ and the GAD showed that the GAD-7 and its abbreviated two-item (GAD-2) versions have good sensitivity and specificity for detecting generalized anxiety, panic, social anxiety and PTSD.[27] Therefore the choice was made for the GAD-2 (shorter version of the original GAD-7). The authors of the systematic review also recommended to use a cut-off point of ≥3 on the PHQ-2 and the GAD-2.

From a research point of view, both reviews on the detection of depression[5] or anxiety[4] considered also some potential limitations of existing tools across the primary studies. For example, the past psychiatric history before hospital admission is sometimes considered as exclusion criterion in studies. However it is considered as a risk factor for development of PICS. Also none of the primary studies assessed the prevalence of anxiety at baseline prior to onset of critical illness.[4]

PTSD

In our exploratory literature search some validation studies were found on the psychometric performance of different tools to assess PTSD, such as the IES, PTSS-10, PCL, CAPS and TSQ (see below). The systematic review of Parker et al (2015) on PTSD in critical illness survivors refers to the IES, the IES-revised, and the PTSS-10 as the most commonly used instruments. Across the primary studies a variety of instruments was used, making comparisons across studies difficult. The

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[a] https://www.midss.org/content/patient-health-questionnaire-4-phq-4

[b] https://www.ebpnet.be/nl/pages/display.aspx?ebmid=ebm00729

[c] https://dkp.nl/apps/4dkl/

https://farmaka.bcfi.be/nl/formularium/166#main

authors recommend from a more research perspective, to validate common survey instruments against “gold standard” diagnostic instruments, with standardized follow-up time points, scoring methods and thresholds and reporting of both continuous and binary PTSD symptom data. The decision not to include a separate instrument for the detection of PTSD is further explained in the scientific report.

PICS-F

Only one study was found which assessed depression in family members of ICU survivors and came to the conclusion that the PHQ-2 version was the most suitable version compared to the 9-item and 8-item versions of the PHQ. This finding is in line with our decision to include the Whooley Questions (which are very similar to the PHQ-2) for the screening for depression in ICU survivors and that the same tool can be used in the family members.

Cognition

A systematic review on the cognitive impairment after ICU admission (Wolters et al, 2013[28]) did not recommend one test over another but mentioned more in general that although the range of cognitive impairment was comparable, the studies with extensive neuropsychological testing reported a higher incidence of cognitive impairment than those with screening test data, suggesting that screening tests could lead to underreporting of cognitive impairment. Within the screening tests used in the primary studies of the review, the Mini-Cog could not be retrieved (MMSE did). The choice to include the Mini-Cog was made based on the research of Spies et al (2020)[15] and the already common use of this tool in Belgian clinical practice. The single retrieved validation on the Mini Mental State Examination (MMSE)[29] concluded that the MMSE should not be used as a screening tool for cognitive impairment in acute respiratory failure survivors, due to its poor sensitivity and the weak to moderate correlations with corresponding neuropsychological tests. Another single validation study was found on the Cognitive Failure Questionnaire (CFQ) and found a similar performance between the CFQ-25 and the abbreviated version CFQ-14 for the screening for self-reported cognitive failure in ICU survivors.[30]

Across the primary studies in the review of Wolters et al, 2013[28], memory was the most tested domain. The domains of memory, attention, verbal fluency and executive functioning were most frequently impaired.

From a research point of view, a major limitation of the current studies on the cognition in ICU survivors is the lack of baseline assessment of the cognitive status before ICU admission. Ideally, cognition should be measured before and after ICU admission, to observe the change in cognitive functioning.[28]

Quality of Life

For feasibility reasons (not to overload the screening tool with a large variety of different tools, with an increased administration time as major consequence), it was decided not to include detection tool to assess the health-related quality of life (QoL). Also this is in line with the primary aim of this rapid screening tool, namely facilitating the decision-making if further assessment and/or management is needed. It was estimated that the assessment of the QoL of the ICU survivor, despite its importance for the patient himself, not be an added value in the decision-making to which care services the GP could refer his patient to.

Appendix 3.2. Detection tools for physical function

Table 1 – Overview of all retrieved clinical tools for the detection of physical function

Instrument	Validation studies	Reviews	Expert consensus papers
Medical research Council (MRC) criteria	Braganca, 2019[14]	Turnbull, 2016[31]	/
Handgrip Dynamometry	Braganca, 2019[14]	Turnbull, 2016[31]	Needham, 2017[32]
Timed Up-and-Go Test (TUG)	/	Major, 2016[33]	Spies, 2020[15]
2/6-min Walk test	/	Major, 2016[33] Robinson, 2017[16]	Needham, 2017[32] Spies, 2020[15]
Short Physical Performance Battery (SPPB)	/	Major, 2016[33]	Spies, 2020[15]
Barthel Index	/	Turnbull, 2016[31] Major, 2016[33]	/
Return to work	/	Turnbull, 2016[31]	/
Katz Activities of Daily Living	/	Turnbull, 2016[31] Major, 2016[33]	
Glasgow Outcome Scale (extended) (GOS)	/	Turnbull, 2016[31]	/
Lawton Instrumental Activities of Daily Living (IADL)	/	Turnbull, 2016[31] Major, 2016[33]	/
Karnofsky Performance Status Scale	/	Turnbull, 2016[31]	/
Functional Independence Measure (FIM)	/	Turnbull, 2016[31] Major, 2016[33]	/
New York Heart Association (NYHA) Functional Classification	/	Turnbull, 2016[31]	/
Cerebral Performance Category (CPC) Scale	/	Turnbull, 2016[31]	/
Modified Rankin Scale (MRS)	/	Turnbull, 2016[31]	/
De Morton Mobility Index (DEMMI)	/	Turnbull, 2016[31]	/

Table 2 – Validation studies of detection tools for physical function in ICU survivors

Clinical tool	Psychometric assessment
Medical research Council (MRC) criteria	*Primary validation studies in ICU survivors:* • ICU-acquired muscle weakness in Brazilian ICU (baseline, 6mo, 12mo) (n=45) (Braganca, 2019)[14] o High agreement between handgrip strength and MRC criteria for ICUAW diagnosis (100% accuracy, Kappa Coef=1; p<0.001) o ICUAW was associated with more days of mechanical ventilation, longer length of ICU stay and hospital stay in 6 mo. No differences were found in mortality. *Validation data found in reviews on ICU survivors:* • No validation data were found *Prevalence data were found in:* Turnbull, 2016[31]
Handgrip dynamometry	*Primary validation studies in ICU survivors:* • ICU-acquired muscle weakness in Brazilian ICU (baseline, 6mo, 12mo) (n=45) (Braganca, 2019)[14] o High agreement between handgrip strength and MRC criteria for ICUAW diagnosis (100% accuracy, Kappa Coef=1; p<0.001) o ICUAW was associated with more days of mechanical ventilation, longer length of ICU stay and hospital stay in 6 mo. No differences were found in mortality. *Validation data found in reviews on ICU survivors:* • No validation data were found *Prevalence data were found in:* Turnbull, 2016[31], Needham, 2017[32]

Appendix 3.3. Detection tools for anxiety and depression

Table 3 – Overview of all retrieved clinical tools for the detection of anxiety and/or depression

Instrument	Validation studies	Reviews	Expert consensus papers
HADS (-A) (-D)	Jutte, 2015[17] Kerckhoffs, 2019[19]	Robinson, 2017[16] Turnbull, 2016[31] Nikayin, 2016[4]	Needham, 2017[32]
BDI (depression)	/	Turnbull, 2016[31]	/
PHQ 9/8/4/2	Downey, 2016[21]	Turnbull, 2016[31]	Spies, 2020[15]
CES-d	/	Turnbull, 2016[31]	/
BAI (anxiety)	/	Turnbull, 2016[31]	/

STAI	/	Turnbull, 2016[31]	/
GAD-7	/	/	Spies, 2020[15]

Table 4 – Validation studies of detection tools for anxiety and depression in ICU survivors

Clinical tool	Tool assessment
Hospital Anxiety and Depression Scale (HADS) depression subscale (HADS-D) and anxiety subscale (HADS-A)	*Primary validation studies in ICU survivors:* • in acute lung injury survivors (after 3 months post ALI)(prospective cohort study, n=151) (Jutte, 2015)[17] o **good internal consistency**: Cronbach's alpha 0.79 for HADS-A; 0.70 for HADS-D; 0.58 between both o **moderately to strongly correlated**: EQ-5D-3L anxiety/depression item positively correlated with HADS-A (Spearman ρ=0.54, P<.01) and HADS-D (ρ=0.41, P<.01); SF-36 (4 domains) negatively correlated with HADS-A (ρ=-0.48 to -0.70, P<.01) and HADS-D (ρ=-0.48 to -0.52, P<.01) with particularly high correlation between HADS-A and SF-36 mental health domain (ρ=0.70, P<.01) o **limited discriminative power** (AUROC values) of EQ-5D-3L anxiety/depression item and SF-36 mental health domain to discriminate HADS-A and HADS-D score thresholds. Fairly good discriminator was SF-36 mental health domain to HADS-A score threshold (AUROC=0.84, P<.01) • In ICU survivors (1y after ICU discharge) (n=1453) (Kerckhoffs, 2019)[19] o **Association** between "unacceptable outcome after ICU treatment" and EQ-5D (unadjusted OR 2.09, 99% CI 1.62-2.69), HADS (unadjusted OR 2.20, 99% CI 1.60-3.02), IES (unadjusted OR 1.74, 99% CI 1.26-2.40) o After adjustment for demographic and for both demographic and ICU factors: lower EQ-5D index value, higher HADS score, higher IES score significantly associated with self-reported unacceptable outcome (p<.001) o After adjustment for other components of PICS (+ demographic and ICU factors): only HADS score significantly associated with self-reported unacceptable outcome (OR 2.06, 99% CI 1.18-3.61) *Validation data found in reviews on ICU survivors:* • Internal consistency: Cronbach's alpha 0.82 to 0.86 (Robinson, 2017)[16] • Criterion validity: strong correlation between HADS and DASS for anxiety (r=0.88, p<0.0001) and depression (r=0.96, p<0.0001) (Robinson, 2017)[16] *Prevalence data were found in:* Turnbull, 2016[31]; Nikayin, 2016[4]; Needham, 2017[32]
Patient Health Questionnaire (PHQ) 4/8	*Primary validation studies in ICU survivors:* • Families of ICU survivors (baseline, 3mo, 6mo) (n= 193) (Downey, 2016)[21] o Comparison between 9-item, 8-item and 2-item versions: ▪ 9-item version: item on suicidal ideation showed significant misfit (majority of family members scored 0 or 1) (P<.001) ▪ 8-item version (without suicidal ideation): modest improvement in fit at baseline (P<.005) ▪ 2-item version (anhedonia and depressed mood): most reflective model of depression severity o Association of patient/family characteristics on depression severity:

- At baseline: patient age (family members of older patients reporting less severe symptoms); gender (female respondents more depressive symptoms, nearly statistically significant)
- At 3 months: baseline depression severity was significant predictor of 3 mo severity; effect of patient-family relationship (higher severity when family member was patient's spouse/partner); patient's mortality status at hospital discharge (higher severity when patient died)
- At 6 months: depression severity at 3mo is significantly carried over to 6mo; no other significant predictors (even not effect of baseline severity)

Validation data found in reviews on ICU survivors:

- No validation data were found

Prevalence data were found in: Turnbull, 2016[31], Spies, 2020[15]

Appendix 3.4. Detection tools for PTSD

Table 5 – Overview of all retrieved clinical tools for the detection of PTSD

Instrument	Validation studies	Reviews	Expert consensus papers
Impact of Event Scale (IES) **IES-Revised** **IES-6**	Kerckhoffs, 2019[19] Hosey, 2019[34]	Robinson, 2017[16] Turnbull, 2016[31] Parker, 2015[6]	Needham, 2017[32]
PTSS-10/PTSS-14	Rosendahl, 2019[35]	Turnbull, 2016[31] Parker, 2015[6] Robinson, 2017[16]	/
PTSD Diagnostic Scale (PDS)	/	Turnbull, 2016[31] Robinson, 2017[16]	/
PCL **PCL-C** **PCL-S**	Parsons, 2017[36] Rosendahl, 2019[35]	Turnbull, 2016[31]	/
Clinician administered PTSD Scale (CAPS)	Hosey, 2019[34]	Turnbull, 2016[31] Robinson, 2017[16]	/
Symptom Checklist-90-R (SCL-90-R)	/	Turnbull, 2016[31]	/

Table 6 – Validation studies of detection tools for PTSD in ICU survivors

Clinical tool	Psychometric assessment
Impact of Event Scale (IES) **IES-revised (IES-R)** **IES-6**	*Primary validation studies in ICU survivors:* • In ICU survivors (1y after ICU discharge) (n=1453) (Kerckhoffs, 2019)[19] o **Association** between "unacceptable outcome after ICU treatment" and EQ-5D (unadjusted OR 2.09, 99% CI 1.62-2.69), HADS (unadjusted OR 2.20, 99% CI 1.60-3.02), IES (unadjusted OR 1.74, 99% CI 1.26-2.40) o After adjustment for demographic and for both demographic and ICU factors: lower EQ-5D index value, higher HADS score, higher IES score significantly associated with self-reported unacceptable outcome (p<.001) o After adjustment for other components of PICS (+ demographic and ICU factors): only HADS score significantly associated with self-reported unacceptable outcome (OR 2.06, 99% CI 1.18-3.61) • In acute respiratory distress syndrome (ARDS) survivors (up to 5y after ARDS) (n=1001) (Hosey, 2019)[34] o Correlation IES-6 with IES-R: 0.96 (0.94 to 0.97, 95%CI) o Internal consistency of IES-6: good to excellent over time (Cronbach's alpha of 0.86 to 0.91) o External construct validity of IES-6: ▪ Moderately correlated with measures of mental health: SF-36 mental health domain (0.42; 95% CI 0.39-0.46) and mental component summary (0.46; 95% CI 0.42-0.49); HADS-A (0.52; 95% CI 0.49-0.55); HADS-D (0.40; 95% CI 0.37-0.44); EQ-5D-3L anxiety/depression item (0.32; 95% CI 0.28-0.35) ▪ Similar patterns of associations between IES-R and other measures ▪ Weaker correlations with unrelated measures: healthcare utilization variables (MRI: 0.02; 95% CI 0.02-0.07; X-rays: 0.05; 95% CI 0.01-0.10); EQ-5D-3L mobility (0.15; 95% CI 0.11-0.19) and self-care items (0.12; 95% CI 0.09-0.16); SF-36 physical (0.27; 95% CI 0.24-0.32) and physical function domains (0.21; 95% CI 0.18-0.24); and FPI body care (0.22; 95% CI 0.18-0.27), maintain household (0.26; 95% CI 0.21-0.30) and physical exercise domains (0.24; 95% CI 0.20-0.29) ▪ Same patterns of correlations between IES-R and other measures o Criterion validity of IES-6: AUROC of 0.93 (95% CI 0.86-1.00) compared with clinician-based current CAP diagnosis of PTSD. Optimal cut-off point of 1.75, resulting in sensitivity of 0.88, specificity of 0.85 and PPV of 0.47 and NPV of 0.98 *Validation data found in reviews on ICU survivors:* • No validation data were found *Prevalence data were found in:* Parker, 2015[6]; Turnbull, 2016[31]; Needham, 2017[32]; Robinson, 2017[16]
PTSS-10 **PTSS-14**	*Primary validation studies in ICU survivors:* • In ICU survivors after sepsis (4 months after ICU stay) (n=83) (Rosendahl, 2019)[35]

	o PTSS-10, PTSS-14 and PCL-5 revealed good reliability and concurrent validity o Although PTSS-10, PTSS-14 and PCL-5 are clinically useful screening tools for PTSD, PTSS-14 showed the best accuracy in screening patients at risk for PTSD (80% sensitivity and 92% specificity, with cut-off score of 40) *Validation data found in reviews on ICU survivors:* • *No validation data were found* *Prevalence data were found in:* Parker, 2015[6]; Turnbull, 2016[31]; Robinson, 2017[16]
PTSD Checklist (PCL) **civilian version (PCL-C)** **specific (PCL-S)**	*Primary validation studies in ICU survivors:* • PCL-C compared to Insomnia severity Index (Parsons, 2017)[36]: reasonable screen to identify insomnia • In ICU survivors after sepsis (4 months after ICU stay) (n=83) (Rosendahl, 2019)[35] o PTSS-10, PTSS-14 and PCL-5 revealed good reliability and concurrent validity o Although PTSS-10, PTSS-14 and PCL-5 are clinically useful screening tools for PTSD, PTSS-14 showed the best accuracy in screening patients at risk for PTSD (80% sensitivity and 92% specificity, with cut-off score of 40) *Validation data found in reviews on ICU survivors:* • *No validation data were found* *Prevalence data were found in:* Turnbull, 2016[31]
Clinician administered PTSD Scale (CAPS)	*Primary validation studies in ICU survivors:* • In acute respiratory distress syndrome (ARDS) survivors (up to 5y after ARDS) (n=1001) (Hosey, 2019)[34] o Criterion validity of IES-6: AUROC of 0.93 (95% CI 0.86-1.00) compared with clinician-based current CAP diagnosis of PTSD. Optimal cut-off point of 1.75, resulting in sensitivity of 0.88, specificity of 0.85 and PPV of 0.47 and NPV of 0.98 *Validation data found in reviews on ICU survivors:* • *No validation data were found* *Prevalence data were found in:* Turnbull, 2016[31]; Robinson, 2017[16]

Appendix 3.5. Detection tools for cognition

Table 7 – Overview of all retrieved clinical tools for the detection of cognition impairments

Instrument	Validation studies	Reviews	Expert consensus papers
MiniCog	Ketterer, 2016[37]	/	Spies, 2020[15]
Mini Mental State Examination (MMSE)	Pfoh, 2015[29]	Turnbull, 2016[31]	Spies, 2020[15]
Cognitive Failure Questionnaire (CFQ)	Wassenaar, 2018[30]	/	/
Trail Making Test Part A & B	/	Turnbull, 2016[31]	Spies, 2020[15]
Animal Naming	/	/	Spies, 2020[15]
ICU Memory Tool (ICUM)	/	Turnbull, 2016[31]	/
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	/	/	Spies, 2020[15]

Table 8 – Validation studies of detection tools for cognition in ICU survivors

Clinical tool	Psychometric assessment
Mini-Cog	*Primary validation studies in ICU survivors:* • In patients at ICU (n=107) (Ketterer, 2016)[37] o A positive central nervous system scan was associated with a diminished performance on the Mini-Cog o A same association was found for a positive observation on one or more of the behavioural variables o The Mini-Cog was considered as a valid measure of CNS dysfunction and also enhances sensitivity of evaluation at the bedside. *Validation data found in reviews on ICU survivors:* • No validation data were found *Prevalence data were found in:* Spies, 2020[15]
Mini Mental State Examination (MMSE)	*Primary validation studies in ICU survivors:* • In acute respiratory failure survivors (n= 242) (Pfoh, 2015)[29] o MMSE vs neuropsychological tests: fair agreement, excellent specificity, but poor sensitivity, weak to moderate correlations o Not as screening tool for cognitive impairment in ARDS survivors *Validation data found in reviews on ICU survivors:*

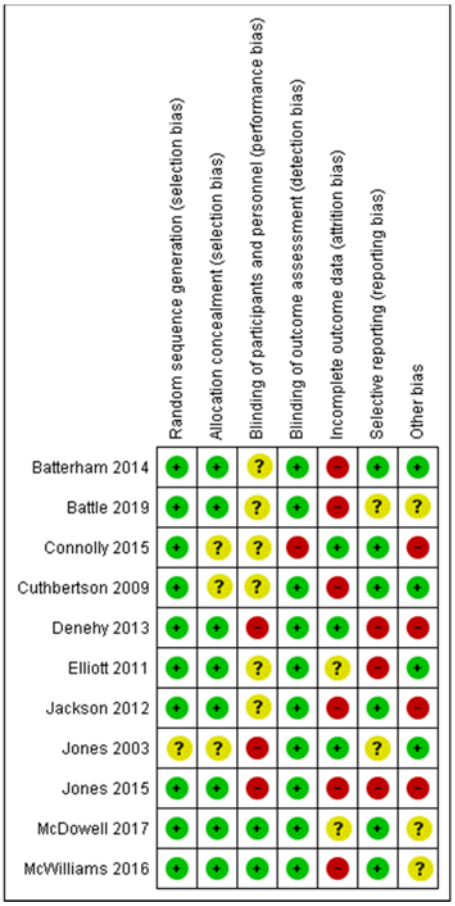
	• No validation data were found *Prevalence data were found in:* Spies, 2020[15], Turnbull, 2016[31]
Cognitive Failure Questionnaire (CFQ)	*Primary validation studies in ICU survivors:* • In ICU survivors (n= 1737) (Wassenaar, 2018)[30] o A similar performance was found between the CFQ-25 and the CFQ-14, therefore the abbreviated CFQ-14 can be used as screening tool for self-reported cognitive failure in ICU survivors *Validation data found in reviews on ICU survivors:* • No validation data were found

APPENDIX 4. SUPPLEMENT OF CHAPTER 4

Appendix 4.1. Quality assessment

Appendix 4.1.1. Physical rehabilitation

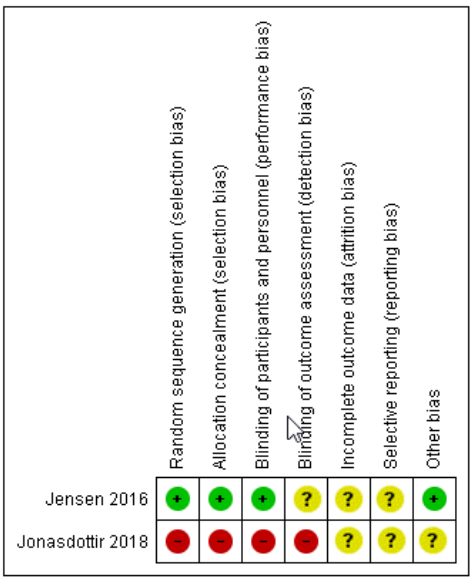
Among the 11 included RCT, the quality appraisal of 8 RCT[38-45] was performed by Geense et al.[46] Two others[47, 48] were appraised by Trethewey et al.[49] and the last one[50] by Connolly et al.[51].



Appendix 4.1.2. Follow-up consultations

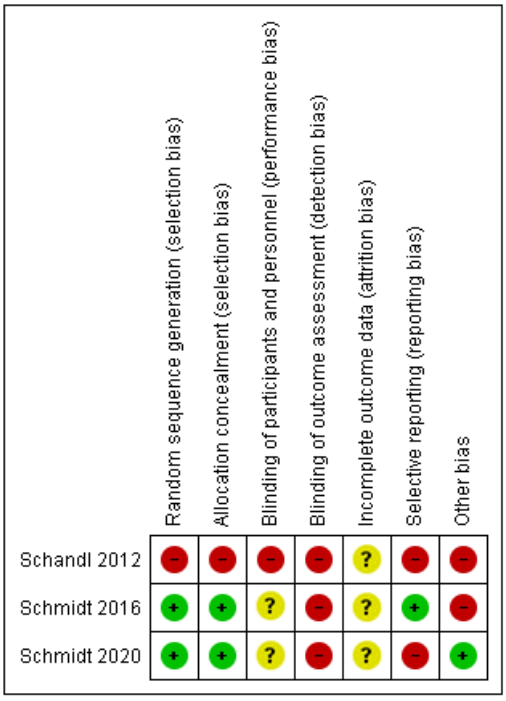
Nurse-led follow-up consultations

The quality appraisal of 2 RCT[52, 53] was performed by Geense et al.[46]



Multidisciplinary consultations

Two studies[54, 55] were assessed by Gensen et al.[46] and one[56] was assessed by NBE.



Follow-up consultation combined with rehabilitation programme

See above

Follow-up consultations combined with diaries

The two studies[57, 58] were quality appraised by Barreto et al.[59]

Table 9 – Results of quality appraisal by ROBIN-1 performed by Barreto at al 59

Study ID	Risk of bias
Akerman 2018	Moderate
Svenningsen 2014	Moderate

Appendix 4.1.3. Diaries

All quality appraisals were performed by Barreto et al.[59]

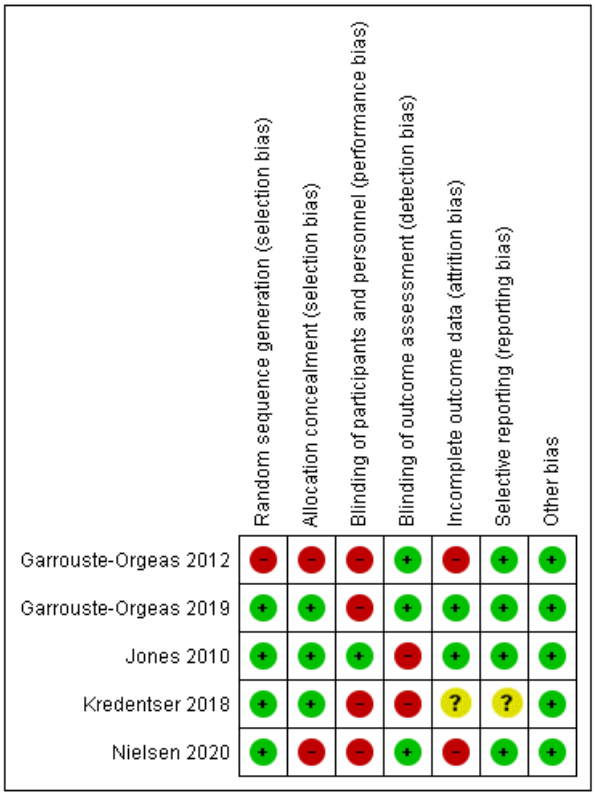
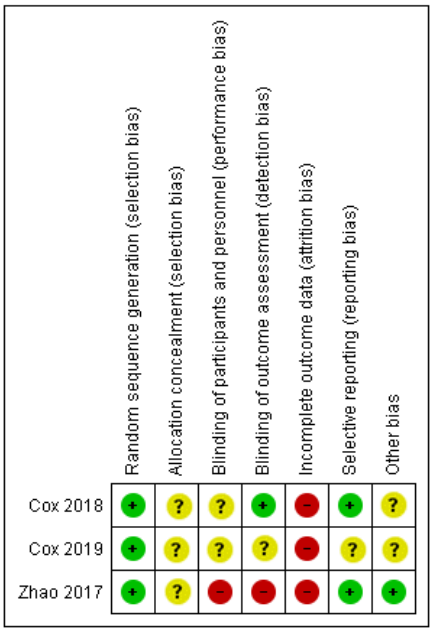


Table 10 – Results of quality appraisal by ROBIN-1 performed by Barreto at al 59

Study ID	Risk of bias
Akerman 2018	Moderate
Backerman 2010	Moderate
Svenningsen 2014	Moderate

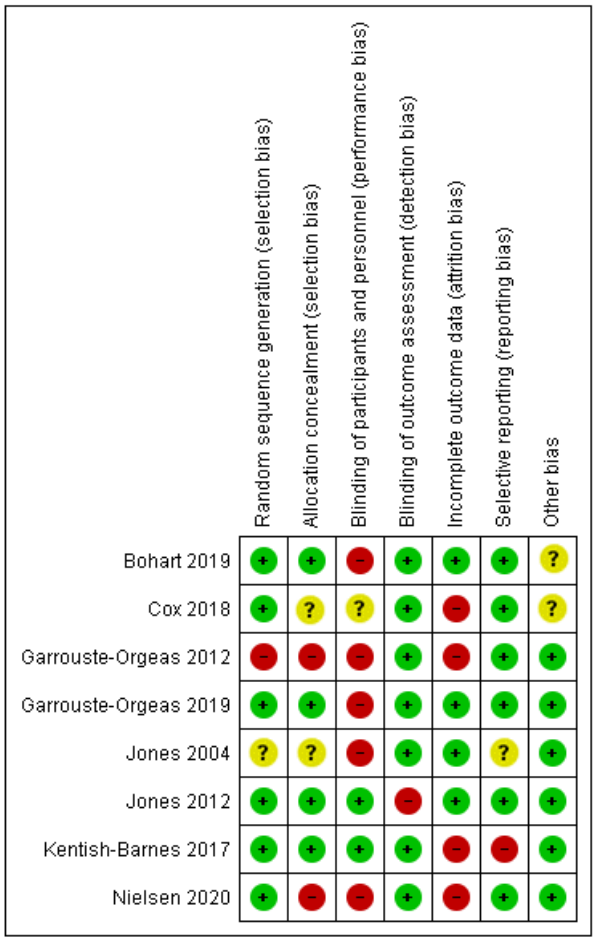
Appendix 4.1.4. Other mental health interventions and cognitive intervention

Among the four included studies, two[60, 61] were appraised by Geense et al[46] and the two others[62, 63] by NBE



Appendix 4.1.5. PICS-F

Four studies[64-67] were assessed by Barreto et al., 2 others[60, 68] were assessed by Geense et al. and the 2 last studies[62, 69] by NBE.



Appendix 4.2. Evidence tables

Appendix 4.2.1. Physical rehabilitation

Batterham 2014[38]	
Methods	
• **Design**	Parallel-group minimized controlled trial
• **Source of funding and competing interest**	Funding: National Institute for Health Research under its Research for Patient Benefit Programme. Competing interest: The authors declare no conflict of interest.
• **Setting**	Two large teaching hospitals un UK
• **Sample size**	59 patients (30 in intervention group and 29 in control group). In intervention group, 5 patients withdrawn before start of intervention and one was lost to follow-up (n=24). In control group, 8 patients withdrew before start of intervention and 3 was lost to follow-up (n=18).
• **Duration and follow-up**	Duration: between June 2008 and May 2011. Follow-up: at 8-weeks after intervention (week 9 post-hospital discharge) and at 18 weeks after the end of the intervention period (week 26 post-hospital discharge).
• **Statistical analysis**	Mean difference (95% CI)
Patient characteristics	
• **Eligibility criteria**	Patients aged [18–65] years with minimum of 3 days of ventilator support (for the emergency management of trauma or sepsis), and discharged home within 6 months of hospital admission.
• **Exclusion criteria**	Inability to climb a flight of stairs, enrolment in another rehabilitation programme, and medical contraindication to cardiopulmonary exercise testing.
• **Patient & disease characteristics**	Age in years [mean (range)]: Control group 40.5 (19–60) vs Intervention group 42.7 (18–65) Sex (number female/male): Control group 11/19 vs Intervention group 10/19 Diagnosis (number with trauma/sepsis): Control group 13/17 vs Intervention group 15/14 APACHE-II [mean (SD)]: Control group 16.4 (7.8) vs Intervention group 15.9 (7.9) ICNARC physiology score [mean (SD)]: Control group 23.2 (9.5) vs Intervention group 18.4 (8.2) ICU LOS (days) [median (IQR)]: Control group 15 (7–23) vs Intervention group 15 (10–23) Total hospital LOS (days) [median (IQR)]: Control group 35 (26–50) vs Intervention group 45 (31–93)

	Timing of baseline measures post-hospital discharge (weeks) [mean (SD)]: : Control group 11.1 (2.6) vs Intervention group 10.3 (1.9) Number of ventilator days [median (IQR)]: Control group 10 (5–19) vs Intervention group 12 (8–18) AT (ml O2 kg21 min21) [mean (SD)]: Control group 10.4 (2.8) vs Intervention group 10.4 (3.5) SF-36 PF [mean (SD)]: Control group 37.4 (13.1) vs Intervention group 36.7 (13.2) SF-36 MH[mean (SD)]: Control group 48.8 (11.6) vs Intervention group 43.0 (13.1) SF-36 PF pre-morbid estimate [mean (SD)]: Control group 50.0 (10.9) vs Intervention group 50.0 (12.2) SF-36 MH pre-morbid estimate [mean (SD)]: Control group 50.0 (12.1) vs Intervention group 48.7 (11.6) Peak oxygen uptake (ml O2 kg21 min21) [mean (SD)]: Control group 17.7 (6.9) vs Intervention group 17.8 (7.7) EQ-5D index [median (IQR)]: Control group 0.725 (0.516–0.814) vs Intervention group 0.689 (0.258–0.822) EQ-5D VAS [mean (SD)]: Control group 64 (23) vs Intervention group 61 (26) HADS-Anxiety [median (IQR)]: Control group 7.0 (2.5–11.0) vs Intervention group 7.0 (4.0–12.0) HADS-Depression [median (IQR)]: Control group 3.0 (1.0–7.5) vs Intervention group 5.0 (2.0–8.5)
Exposures	
• **Intervention group**	**Duration:** 8-weeks exercise intervention, delivered after hospital discharge (patients enrolled 8–16 weeks after discharge). **Starting date:** starting 8-16 weeks after discharge **Setting:** Supervised sessions at hospital **Frequency:** 2 physiotherapist-led supervised sessions per week + 1 unsupervised session each week of the same duration and intensity **Content:** Supervised sessions included 40 min on a cycle ergometer (including 5 min each of warm-up and cool-down). Unsupervised sessions included 30 min walk
• **Control group**	Current usual care of follow-up by appropriate medical and surgical specialties but no formal rehabilitation programme
Results	
• **Anaerobic threshold**	Mean difference (95% CI) between control and intervention group • At week 9 1.8 (0.4 to 3.2) ml O_2 kg^{-1} min^{-1} • At week 26 0.6 (-1.6 to 2.8) ml O_2 kg^{-1} min^{-1}
• **HRQoL**	Mean difference (95% CI) between control and intervention group • SF-36 physical function sub-scale

	o At week 9 3.4 (-1.4 to 8.2) points o At week 26 0.1 (-6.0 to 6.2) points • SF-36 mental health sub-scale o At week 9 1.9 (-3.9 to 7.7) points o At Week 26 4.4 (-2.4 to 11.2) points • EQ-5D index score o At week 9 0.016 (-0.104 to 0.137) o At week 26 - 0.043 (-0.174 to 0.088) • EQ-5D VAS o At week 9 -0.2 (-8.7 to 8.3) mm o At week 26 -4.1 (-14.9 to 6.7) mm
• **Peak oxygen uptake**	Mean difference (95% CI) between control and intervention group • At week 9 0.6 (-1.8 to 3.0)ml O_2 kg^{-1} min^{-1} • At week 26 1.6 (-1.0 to 4.2) ml O_2 kg^{-1} min^{-1}
• **Mood disorder**	Mean difference (95% CI) between control and intervention group • HADS - Anxiety o At week 9 0.1 (-1.6 to 1.8) points o At week 26 -0.7 (-2.9 to 1.5)points • HADS - Depression o At week 9 -0.8 (-2.1 to 0.5) points o At Week 26 -0.8 (-2.6 to 1.0) points
Limitations and other comments	
• **Limitations and notes**	• Small sample size, no calculation of minimum sample size • Substantial missing data

	• Target population limited to ICU admitted patients for sepsis or trauma • Relatively young patients in comparison with the general ICU patients • Imbalance in baseline characteristic between control and intervention groups • No outcome to assess ICU-AW
• **Authors' conclusions**	An 8-weeks supervised hospital-based aerobic exercise rehabilitation programme led to a small benefit in physical fitness that accelerated the natural recovery process but the fitness benefit was only short term.

Battle 2019[39]	
Methods	
• **Design**	Single-centre, assessor-blinded, parallel group, randomised controlled trial.
• **Source of funding and competing interest**	Funding: The authors received no financial support for the research, authorship, and/or publication. Competing interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication.
• **Setting**	Outpatient department of a university teaching hospital in the UK (Wales).
• **Sample size**	62 patients were included (30 in both intervention and control group – 1 patient withdrawn in each group). Lost to follow-up: 15 in intervention group and 11 in the control group.
• **Duration and follow-up**	Duration: November 2011 to October 2013 Follow-up: 12 months
• **Statistical analysis**	Descriptive statistics. MANCOVA (two-way repeated measures analysis of covariance), linear mixed model.
Patient characteristics	
• **Eligibility criteria**	All participants on the medical and surgical ICU for a length of stay of 48 h or more.
• **Exclusion criteria**	Age < 18 years, burns, cardiac conditions, living outside of a commutable area, any medical contraindications to exercise and participation in any other concurrent rehabilitation programme
• **Patient & disease characteristics**	Male: 31/60 [Intervention 15/30, Control 16/30 p=0.797] Age (median IQR): 62 (49–72) [Intervention 61 (49–70), Control 62.5 (46–70), p= 0.503] APACHE II (median IQR): 14 (11–19) [Intervention 15 (12–19), Control 13 (9–19), p=0.174]

	Functional Comorbidity Index (median IQR): 1 (0–2) [Intervention 1 (0–2), Control 1 (0–2), p=0.741] ICU LOS (median IQR): 9 (4–17) [Intervention 12 (5–21), Control 7 (4–15), p=0.082] Mechanical ventilation days 4 (median IQR): (1–12) [Intervention 5 (2–14), Control 2 (1–11), p=0.019] Total hospital LOS (median IQR): 20 (10–30) [Intervention 23 (15–45), Control 15 (9–25), p=0.046] Primary diagnosis: Surgical 32/60 [Intervention 15/30, Control 17/30, p=0.796]; Respiratory 15/60 [Intervention 9/30, Control 6/30, p=0.552]; Medical 9 (15%) [Intervention 5/30, Control 4/30, p>0.999]; Trauma 4/60 [Intervention 1/30, Control 3/30, p >0.999]; Neurology 2/60 [Intervention 1 (3%), Control 1/30] 12-Month mortality 5 (8%) [Intervention 4 (13%), Control 1 (3%) 0.353] Readmissions 25 (42%) [Intervention 13 (43%), Control 12 (40%) >0.999]
Exposures	
• **Intervention group**	**Duration:** Six weeks **Starting date:** at 12 weeks post-hospital discharge. **Setting:** Outpatient department of a university teaching hospital in the UK **Frequency:** Twice weekly **Content:** A six weeks, individualised, supervised exercise programme with associated advice to home exercise modification and including cardiopulmonary exercises and balances exercises.
• **Control group**	No intervention
Results	
• **Six-Minute Walk test**	Mean difference (95%CI), p-value (negative values are in favour of intervention group) • 7 weeks : -70.54 (-179.08–38.00), p=0.112 • 6 months : -26.34 (-158.42–105.73), p=0.596 • 12 months : -49.94 (-223.7–123.63), p=0.373 Repeated measure p value (results of multivariate analysis of covariance (MANCOVA) analysis showing results over time between groups): p=0.491. Within group changes over time: control group: p=0.452; treatment group: p=0.546
• **Anxiety (HADS-A)**	Mean difference (95%CI), p-value • 7 weeks : -3.0 (1.02–2.36), p=0.043 • 6 months : -1.9 (0.84–2.11), p=0.250 • 12 months : -4.1 (1.23–5.24), p=0.006 p-value repeated measure: p=0.491
• **Depression (HADS-D)**	Mean difference (95%CI), p-value • 7 weeks : -2.5 (0.99–2.34), p=0.084

	• 6 months : -1.5 (0.86–2.05), p=0.239 • 12 months : -2.7 (0.90–3.41), p=0.110 p-value repeated measure: p=0.761
• **BERG Balance Score**	Mean difference (95%CI), p-value • 7 weeks : 2.7 (0.87–1.04), p=0.264 • 6 months : 2.2 (0.86–1.06), p=0.442 • 12 months : 7.0 (0.76–0.99), p=0.040 p-value repeated measure: p=0.990
• **GRIP Left (Jamar Dynamometer)**	Mean difference (95%CI), p-value • 7 weeks : 1 (0.66–1.36), p=0.795 • 6 months : -1.7 (0.68–1.78), p=0.731 • 12 months : -5.8 (0.80–2.33), p=0.286 p-value repeated measure: p=0.283
• **GRIP Right (Jamar Dynamometer)**	Mean difference (95%CI), p-value • 7 weeks : -1.1 (0.76–1.58), p=0.767 • 6 months : -0.6 (0.63–1.51), p=0.912 • 12 months : -2.8 (0.69–1.92), p=0.651 p-value repeated measure: p=0.807
Limitations and other comments	
• **Limitations and notes**	• Single centre study • Target sample size not being achieved at later time points because of the loss to follow-up (15 in intervention group and 11 in control group) • No blinding of participants or clinicians but blinding of the outcome assessor • Possible recruitment bias (all patients stemmed of an ICU follow-up clinic and are possible those with less good function) • Variation in timing at which patients commenced participation in the study (at least 12 weeks post-hospital discharge but may be longer) • Training intensity in each session by each participant, adherence to home exercises, proportion of patient with ICU-AW are unknown • No stratification based on the pre-existing disease • Patients in control group received significantly longer mechanical ventilation, experienced longer length of stay • Patients rated the intervention very positively. Qualitative assessment of the intervention would be an added value
• **Authors' conclusions**	The six-week supervised programme did not significantly improved physical function, anxiety, depression and balance at 12 months

Connolly 2015[40]	
Methods	
• **Design**	Pilot feasibility RCT
• **Source of funding and competing interest**	Funding: National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London Competing interest: The authors declare no conflict of interest.
• **Setting**	ICUs of 2 London teaching hospitals within an Academic Health Sciences Centre
• **Sample size**	20 patients were included (10 in both intervention and control group). All patients in the intervention group and 6 patients in the standard care group completed follow-up at 3 months.
• **Duration and follow-up**	Duration: February 2010 to August 2012 Follow-up: at 3 months after programme completion
• **Statistical analysis**	All data are expressed as median (IQR). Comparative tests were applied to determine within-group and between-group differences.
Patient characteristics	
• **Eligibility criteria**	Adult survivors of critical illness (≥ 18 y) with ICU-AW diagnosis, mechanical ventilation for 48 hours or more, Glasgow Coma Scale 15/15, and sufficient mobility to participate in an exercise-based rehabilitation programme after hospital discharge.
• **Exclusion criteria**	Palliative patients, patients with unstable cardiac disease, limb amputation, neurological diagnoses, peripheral vascular disease awaiting revascularization, any musculoskeletal condition or extensive medical comorbidity precluding ability to exercise, psychiatric illness, requirement for ongoing renal dialysis, an extra-contractual referral, patients that could not return to the hospital site, or benefiting an existing rehabilitation pathway in place.
• **Patient & disease characteristics**	*n=20, no statistical difference between control group and intervention group* Age (median (IQR)): Control group 68.5y (64.3-78.0) vs Intervention group 63.0y (46.8-71.8) Sex (male/female): Control group 3:7 vs Intervention group 3:7 ICU diagnosis: Control group medical 6/10 & surgical 4/10 vs Intervention group medical 7/10 & surgical 3/10 APACHE II: Control group medical 23.5 (21.0-30.3) vs Intervention group 24.5 (18.8-29.5) Sequential Organ Failure Assessment (ICU admission): Control group 12.0 (7.5-14.3) vs Intervention group 9.5 (8.0-12.5) Duration of multiorgan failure (days): Control group 10.5 (5.8-13.3) vs Intervention group 9.5 (6.8-15.3) Mechanical Ventilation (days): Control group 11.2 (6.0-15.2) vs Intervention group 9.3 (6.0-13.9)

	CPAP (days): Control group 2.0 (0.3-4.6) vs Intervention group 1.3 (0.04-6.9) Tracheostomy :Control group 3/10 vs Intervention group 5/10 ICU length of stay (days): Control group 13.0 (9.8-20.5) vs Intervention group 14.5 (7.0-17.8) Critical Care length of stay (days): Control group 18.0 (13.8-36.5) vs Intervention group 17.5 (9.0-27.3) Ward length of stay (days): Control group 27.5 (10.0-46.3) vs Intervention group 20.0 (10.0-43.0) Hospital length of stay (days): Control group 47.5 (26.5-68.5) vs Intervention group 39.0 (22.3-66.5)
Exposures	
• **Intervention group**	**Duration:** over a 3-month period **Starting date:** Patients commenced participation in the programme within two weeks of hospital discharge. **Setting:** outpatient physiotherapy gymnasium **Frequency:** 2X/week **Content**: Exercise-based rehabilitation programme in 16 supervised sessions of 40 minutes' duration, including warm-up and cool-down periods and a combination of cardiovascular, upper and lower limb strength, balance, and functional exercises individually tailored for patients + education sessions covering breathlessness management, benefits of exercise, and nutrition.
• **Control group**	Weekly telephone call from the research team to monitor general progress of recovery without specific advice on exercise rehabilitation provided during these telephone call
Results	
• **Exercise capacity**	*Change between baseline and completion (median (IQR))* • Incremental Shuttle Walk Test (m): Control group: 170.0 (40.0 to 315.0) vs Intervention group: 115.0 (− 2.5 to 237.5), p= ns. • Six Minute Walking Test (m): Control group: 185.0 (40.0 to 285.0) vs Intervention group: 140.0 (35.8 to 210.3), p= ns.
• **HRQoL**	*Change between baseline and completion (median (IQR))* • SF-36 v2 Physical Component Score (/100) Control group: 11.0 (4.3 to 28.3) vs Intervention group: 1.8 (− 6.8 to 15.9), p= ns. • SF-36 v2 Mental Component Score (/100) Control group: − 11.4 (− 19.0 to 19.1) vs Intervention group: 14.3 (− 3.2 to 26.7), p= ns.
• **Anxiety and depression**	*Change between baseline and completion (median (IQR))* • HADS total (/42)

	Control group: − 4.5 (− 13.3 to − 2.5) vs Intervention group: − 6 (− 9.3 to − 2.8), p= ns • HADS anxiety (/21) Control group: 0.0 (− 7.0 to 0.0) vs Intervention group: − 3.5 (− 5.0 to − 1.3), p= ns • HADS depression (/21) Control group: − 4.5 (− 6.3 to − 1.8) vs Intervention group: − 1.5 (− 3.3 to 2.0), p= ns
• **Adverse events**	No adverse events during any of sessions of the exercise-based rehabilitation programme.
Limitations and other comments	
• **Limitations and notes**	• Feasibility design • Very low sample size despite a long recruitment period leading to underpowered for detecting differences between groups across outcomes • 8 out 10 patients completed the programme
• **Authors' conclusions**	In this pilot trial, an EBRP after hospital discharge for survivors of critical illness with ICU-AW was feasible in delivery and patient acceptance, albeit the study was underpowered to demonstrate intervention effectiveness.

Cuthbertson 2009[41]	
Methods	
• **Design**	Pragmatic, non-blinded, multicentre, randomised controlled trial
• **Source of funding and competing interest**	Funding: Chief Scientist Office of the Scottish Government Health Directorates, University of Aberdeen Competing interest: The authors declare that they have no competing interests
• **Setting**	3 UK hospitals (two teaching hospitals and one district general hospital)
• **Sample size**	286 patients were randomised (143 in each group). After 12 months, 14 patients died, 27 were lost to follow-up and 2 gave formal withdrawal
• **Duration and follow-up**	Duration: September 2006 and October 2007 Follow-up: 3, 9 and 12 months
• **Statistical analysis**	Comparison between the groups using analysis of covariance, adjusting for minimisation factors and the baseline measurement of the outcome variable. For dichotomous outcomes, logistic regression. Sensitivity analyses using the treatment received (at least one of the two clinics) and per protocol methods. Sensitivity analysis for loss to follow-up used multiple imputation methods.
Patient characteristics	
• **Eligibility criteria**	All patients receiving level 3 dependency (intensive care unit) care whatever the length of stay and who survived until hospital discharge.

• **Exclusion criteria**	Patients less than 18 years old, not expected to survive to leave hospital, unable to complete questionnaires or attend clinics, and who did not consent to participate.
• **Patient & disease characteristics**	Intervention (n=143) Standard care (n=143) Male: Intervention 60%, Control 60% Age [Median (IQR)]: Intervention 59y (46–49), Control 60y (46–71) APACHE II score [Median (IQR)]: Intervention 19 (15–24), Control 19 (15–24) APACHE II predictive mortality [Median (IQR)]: Intervention 28.1 (12.3–45.2), Control 28.5 (12.8–44.9) APACHE II system failure: Respiratory Intervention 33.6%, Control 29.4% – Cardiovascular Intervention 30.1%, Control 29.4% – Neurological Intervention 3.5%, Control 7.7% – Gastrointestinal Intervention 18.9%, Control 18.9% – Renal Intervention 3.5%, Control 2.1% – Metabolic or endocrine Intervention 1.4%, Control 1.4% – Haematological Intervention 0%, Control 0.7% – Trauma Introduction 9.1%, Control 10.5% APACHE II chronic health evaluation: Intervention 13%, Control 8% Ventilated during intensive care: Intervention 99%, Control 97% Renal replacement therapy during intensive care: Intervention 13%, Control 9% Inotropes during intensive care: Intervention 59%, Control 54% Length of stay in intensive care [Median (IQR)]: Intervention 2.9 days (1.7–9.5), Control 3.1 days (1.2–7.5) Time from discharge to randomisation[Median (IQR)]: Intervention 9.5 days (6.7–16.1), Control 8.6 days (4.8–13.3) SF-36 score [Mean (SD)]: physical component Intervention 33.4 (10.0), Control 32.6 (9.9) – mental component Intervention 40.9 (15.2), Control 41.4 (14.2) EQ-5D score [Median (IQR)]: Intervention 0.52 (0.26–0.73), Control 0.49 (0.19–0.69) HADS [Median (IQR)]: anxiety component Intervention 7 (3–10), Control 7 (4–10) – depression component Intervention 6 (3–9), Control 5 (3–9) ICE score [Median (IQR)]: awareness Intervention 34 (27–38), Control 34 (28–40) –frightening Intervention 17 (12–20), Control 16 (12–21) – recall Intervention 14 (12–17), Control 15 (12–18) –satisfaction Intervention 16 (14–17), Control 15 (14–17) Sedative use during intensive care: Propofol Intervention 80%, Control 78% – Morphine Intervention 6%, Control 15% – Short acting opiate (fentanyl or remifentanil) Intervention 80%, Control 76% – Benzodiazepines Intervention 12%, Control 15%
Exposures	
• **Intervention group**	**Duration**: Physical rehabilitation: 3 months. Follow-up clinic: 6 months post discharge. **Starting date:** Physical rehabilitation started at ICU until 3 months after discharge. Follow-up clinic started at 3 months after discharge until 9 months post discharge.

	Setting: nurse led clinics **Frequency**: Two consultations (at 3 months and 9 months) **Content**: The intervention contented a self-directed physical rehabilitation programme to follow at home until 3 months after discharge. Progress was reviewed at nurse led clinics at 3 months and 9 months after discharge. During the clinic appointments the ICU follow-up nurse discussed experiences of intensive care with the patients, formal assessed the patient's requirement for specialist medical referral, and screened the patient for psychological morbidity relating to admission to the ICU. Patients in whom there was clinical concern were referred for review by a mental health professional, review of current drug treatment, visit to the intensive care unit if appropriate, and physiotherapy if appropriate, and a review letter on the patient's progress was sent to each patient's GP.
• **Control group**	No intensive care follow-up after hospital discharge
Results	
Results are reported in ITT. For SF-36, results are available in PP and treatment received but are not reported here. They led to the same conclusions	
• **HRQoL**	Mean difference (95% CI), p-value • SF-36 Mental Component Score o at 6 months after ICU −0.6 (−3.9 to2.8), p=0.74 o at 12 months after ICU 0.4 (−3.0 to 3.7), p=0.83 • SF-36 Physical Component Score o at 6 months after ICU −0.8 (−3.6 to2.0), p=0.59 o at 12 months after ICU 1.1 (−1.9 to 4.2), p=0.46 • ED-5D Quality of Life score: o at 6 months after ICU 0.0 (−0.1 to 0.1), p=0.83 o at 12 months after ICU −0.0 (−0.1 to 0.1), p=0.57
• **PTSD**	Mean difference (95% CI), p-value Davidson trauma score • Incidence o at 6 months −3.6 (−7.6 to 0.4), p=0.07 o at 12 months −3.7 (−7.4 to 0.0), p=0.05 • Severity

	o at 6 months −3.1 (−6.7 to 0.6), p=0.10 o at 12 months −1.6 (−5.0 to 1.9), p=0.37
• **Anxiety**	HADS – A • at 6 months −0.9 (−2.0 to 0.1), p=0.09 • at 12 months −0.8 (−1.9 to 0.4), p=0.18
• **Depression**	HADS – D • at 6 months −0.0 (−1.0 to 1.0), p=0.99 • at 12 months −0.1 (−1.2 to 1.0), p=0.86
• **Returned to work**	• at 6 months Intervention group 16/40 vs Controls 15/41, OR (95% CI): 1.16 (0.43 to 3.12) • at 12 months Intervention group 18/32 vs Controls 17/31, OR (95% CI): 1.06 (0.35 to 3.21)
• **GP consultation**	Percentages of patients who had seen their GP • at 6 months Intervention group 92/102 vs Controls 98/110, OR (95% CI): 1.13 (0.42 to 3.06) • at 12 months Intervention group 75/92 vs Controls 85/97, OR (95% CI): 0.62 (0.25 to 1.49)
• **Satisfaction rates**	No significant difference in satisfaction rates between groups (data not shown in the publication).
Limitations and other comments	
• **Limitations and notes**	• Target sample achieved but small sample size to detect changes in less common outcomes • Non-restrictive selection of patients • No blinding of participants and nurses
• **Authors' conclusions**	No evidence that a nurse led follow-up programme was effective or cost effective in improving patients' health related quality of life in the first year after their discharge from intensive care.

Denehy 2013[47]	
Methods	
• **Design**	Single-centre, assessor-blinded, randomized controlled trial.
• **Source of funding and competing interest**	Funding: NHMRC (grant 454717), Physiotherapy Research Foundation, Austin Hospital Medical Research Foundation and the Australian and New Zealand Intensive Care Society. Competing interest: The authors declare that they have no competing interests.
• **Setting**	20-bed tertiary ICU in Melbourne (Australia)
• **Sample size**	150 patients were randomised (74 in Intervention group and 76 in Control group). Intervention group included 49, 48 and 43 patients, respectively at 3, 6 and 12 months. Control group encompassed 56, 49, 39 patients, respectively for the same time points. After 12 months, 13 patients deceased, 7 withdrew and 11 was lost to follow-up in the Intervention group. At the same time, 18 patients deceased, 8 withdrew and 10 was lost to follow-up in the Control group.
• **Duration and follow-up**	Duration: May 2007 to September 2010 Follow-up: 3, 6 and 12 months
• **Statistical analysis**	Descriptive statistics, linear mixed models, t-test
Patient characteristics	
• **Eligibility criteria**	Adult patients with an ICU LOS ≥ 5 days residing within a 50-km radius of the hospital and without neurological, spinal or musculoskeletal dysfunction preventing participation in physical rehabilitation
• **Exclusion criteria**	None reported
• **Patient & disease characteristics**	*Control group (n = 76) and Intervention (n = 74)* Mean age (SD) : Control group 60.1y (15.8), Intervention group 61.4y (15.9) Gender (% male): Control group 68.4%, Intervention group 58.1% Mean BMI (SD): Control group 27.7 (6.1), Intervention group 27.5 (5.4) Mean APACHE II score (SD): Control group 20.7 (7.7), Intervention group 19 (6) ICU diagnosis (Control group/ Intervention group): Pneumonia 17% / 17% –Cardiac 12% / 11% – Cardiac surgery 22% / 23% – Other surgery 16% / 15% – Liver disease or transplant 7% / 14% – Cardiac arrest 8% / 3% – Sepsis 7% / 10% – Renal 4% / 3% – Other 7% / 4% Chronic disease: Control group 74%, Intervention group 76% 28-day mortality: Control group 7.9%, Intervention group 8.1% 12-month mortality: Control group 25.0%, Intervention group 17.6% ICU LOS [median (IQR)] : Control group 7.0 days (6.0 – 11.0) Intervention group 8.0 days (6.0 – 12.0) ICU LOS ≥10 days: Control group 32.0%, Intervention group 40.5%

	Acute LOS [median (IQR)]: Control group 20.0 days (13.0-30.8) , Intervention group 23.5 days (16.0 - 41.5) ICUAW (% yes): Control group 17.1%, Intervention group 21.6% Mechanical Ventilation [median (IQR)]: Control group 98.0 hours (47.5-160.5), Intervention group 105.0 hours (52.0-216.5) Mechanical Ventilation at day 5: Control group 42/76, Intervention group 41/74 Readmissions: Control group 31/76, Intervention group 41.9 (31/74) Discharge location: Control group – Home 40/76, Rehabilitation 19/76, Acute hospital 4/76, Other 13/76, Intervention group – Home 44/74, Rehabilitation 15/74, Acute hospital 4/74, Other 11/74
Exposures	
• **Intervention group**	**Duration**: From ICU admission to at least 8 weeks post-hospital discharge (Outpatient group classes were commenced an average (SD) of 11 (13) days after hospital discharge) **Starting date:** ICU admission **Setting**: starting in ICU ending at outpatient through ward **Frequency**: • ICU: when mechanically ventilated15 min/day, when weaned 2 × 15 min/day • Ward: 2 × 30 min/day progressed to 1 × 60 min/day • Outpatient: 60 min twice weekly for 8 weeks **Content**: • ICU: Marching in place, moving from sitting to standing, arm and leg active and active resistance movements • Ward: Cardiovascular, progressive resistance strength training and functional exercise • Outpatient: Cardiovascular, progressive resistance strength training and functional exercise
• **Control group**	Respiratory and mobility management based upon individual patient assessment according to unit protocols No outpatient exercise classes
Results	
Only out-patient outcomes are reported	
• **Exercise capacity**	6MWT six minute walk test distance (metres) • Difference in mean distance between Intervention group and Control group (95% IC), p-value o 3 months post–ICU discharge: 15.4 (−40.1 to 71), p=0.583 o 6 months post–ICU discharge: −4.9 (−68.0 to 58.3), p=0.879 o 12 months post–ICU discharge: 4.7 (−59.7 to 69.2), p=0.884 • Difference in mean change from first assessment between Intervention group and Control group (95% IC) o At 3 months : 63.67 (14.17 to 113.18), $p < 0.05$ o At 12 months: 72.55 (9.29 to 135.81) $p < 0.05$

• **Physical functioning**	Difference in mean change from first assessment between Intervention group and Control group (95% IC) • Timed Up and Go (TUG) Test (details on test see Jackson 2012) o At 3 months : −8.31 (−24.90 to 8.28) o At 12 months: −9.57 (−27.42 to 8.28)
• **HRQoL**	Difference in mean change from first assessment between Intervention group and Control group (95% IC) • AQoL utility (Assessment of Quality of Life Measure) o At 3 months : 0.12 (-0.03 to 0.26) o At 12 months: 0.14 (-0.03 to 0.31) • SF-36 v2 Physical Function o At 3 months : 6.8 (1.2 to 12.5) o At 12 months: 3.5 (−3.5 to 10.5) • SF-36 Physical Component Score o At 3 months : 5.6 (0.09 to 11.1) o At 12 months: 3.1 (-3.2 to 9.5) • SF-36 Mental Component Score o At 3 months : 2.4 (-3.6 to 8.5) o At 12 months: 4.9 (-2.7 to 12.5)
Limitations and other comments	
• **Limitations and notes**	• Single centre study • Sample size calculation was 200 patients but it was not reached • Variation in starting the outpatient intervention • No adverse event observed
• **Authors' conclusions**	During the therapist-led exercise rehabilitation in three phases from ICU though to outpatient classes, physical function recovery as measured by the 6MWT at 12 months and HRQoL at any time point after randomization were not different between usual-care and intervention groups.

Elliott 2011[42]	
Methods	
• **Design**	Multi-centre randomised controlled trial
• **Source of funding and competing interest**	Funding: Australian National Health and Medical Research Council Competing interest: The authors declare that they have no competing interests
• **Setting**	ICUs from 6 teaching hospitals, 5 district hospitals and 1 private from Sidney, Brisbane and Perth (Australia).

• **Sample size**	195 patients were randomized (97 in Intervention group and 98 in Control group). At week 8, it remained 173 patients (85 in Intervention group [withdrawal (6), lost to follow-up (3), death (3)], 88 in Control group [withdrawal (6), lost to follow-up (1), death (3)]. At week 26, it remained 161 patients (76 in Intervention group [withdrawal (2), lost to follow-up (2), death (5)], 85 in Control group [withdrawal (2), lost to follow-up (1), death (0)].
• **Duration and follow-up**	Duration: June 2005 to February 2009 Follow-up: at 8 and 26 weeks after discharge
• **Statistical analysis**	Descriptive statistics, Norm-based scores were calculated for SF-36, Mixed linear regression models estimated by residual maximum likelihood, the difference between groups in mean change was calculated from baseline divided by the pooled standard deviation for change.
Patient characteristics	
• **Eligibility criteria**	1) age ≥ 18 years; 2) ICU LOS ≥48 hours; 3) mechanical ventilation ≥24 hours; 4) discharge home to self-care or carer (non-institutional care); 5) residence in an approximately 50 km radius; 6) no neurological, spinal or skeletal dysfunction preventing participation in physical rehabilitation; 7) no palliative care; 8) no other rehabilitation related to ongoing chronic disease management and 9) cognitively able to complete the self-report measures and comply with physical testing instructions.
• **Exclusion criteria**	None reported
• **Patient & disease characteristics**	*Control group (n = 91) and Intervention (n = 92) at Week 1* Age [mean (sd)]: Control group 57.5 (15.1), Intervention group 57.2 (17.0) Gender [% Male]: Control group 61%, Intervention group 62% APACHE II [mean (sd)]: Control group 19.5 (7.2) Intervention group 19.4 (12.6) Mechanical Ventilation hours [mean (sd)]: Control group 135 (117), Intervention group 142 (159) ICU LOS days [mean (sd)]: Control group 8.6 (7.5), Intervention group 9.4 (8.7) Hospital LOS days [mean (sd)]: Control group 23.2 (16.9), Intervention group 24.8 (20.4) SF-36 Physical Functioning [mean (sd)]: Control group 28.8 (10.2), Intervention group 27.1 (12.3) 6MWT distance metres [mean (sd)]: Control group 324 (143), Intervention group 291 (129) SF-36 physical components summary (PCS) [mean (sd)]: Control group 32.7 (8.6), Intervention group 31.7 (10.0) SF-36 mental components summary (MCS) mean (sd) Control group 39.8 (13.5), Intervention group 36.7 (15.1)
Exposures	
• **Intervention group**	**Duration**: 8 weeks

	Starting date: within 1 week post-discharge **Setting**: Patient's home **Frequency**: Weeks 1, 3 and 6: home visits (60 to 90 minutes) by physiotherapist, exercise physiologist or registered nurse to provide individualised verbal and written instructions on their planned exercise program. Weeks 2, 4, 5 and 7: telephone call to monitor participants' progress **Content**: The exercise program consisted of five components- endurance exercise (walking), lower and upper limb strengthening, core stabilisation, flexibility, and stretches.
• **Control group**	Usual community- based care after hospital discharge and the three study assessment visits, but no other placebo or sham interventions.
Results	
• **Physical Functioning**	SF-36 Physical Functioning sub-scale • At week 8 Difference between group (95% CI): 0.7 (-2.5, 3.8) • At week 26 Difference between group (95% CI): 0.9 (-2.7, 4.6)
• **Exercise capacity**	6MWT six minute walk test distance (metres) • At week 8 Difference between group (95% CI): 8.4 (-29.6, 46.4) • At week 26 Difference between group (95% CI): 9.6 (-31.4, 50.5)
• **HRQoL**	SF-36 Physical Component Summary (PCS) sub-scale • At week 8 Difference between group (95% CI): -1.3 (-4.3, 1.7) • At week 26 Difference between group (95% CI): 0.3 (-3.2, 3.7) SF-36 Mental Component Summary (MCS) sub-scale • At week 8 Difference between group (95% CI): 1.8 (-2.6, 6.2) • At week 26 Difference between group (95% CI): 1.5 (-3.1, 6.2)
Limitations and other comments	
• **Limitations and notes**	• Sample size calculation 240 patients but it was not reached • Large number of patients were excluded due to the design of the intervention based on city resident • Potential placebo effect in the Control group • Self-reported compliance to unsupervised exercises
• **Authors' conclusions**	An 8-week home-based rehabilitation intervention had no significant effect on physical recovery, functional status and HRQoL.

Jackson 2012[43]	
Methods	
• **Design**	Single-site, feasibility, pilot randomized trial
• **Source of funding and competing interest**	Funding: National Institutes of Health. Competing interest: Dr. Hoenig received an AFAR Beeson Award. The remaining authors have not disclosed any potential conflicts of interest.
• **Setting**	Vanderbilt University Medical Center (USA)
• **Sample size**	20 patients were randomized (8 in control group and 12 in intervention group). In intervention group, one pilot patient was added, 1 patient died and 3 withdrawn leading to 9 patients that completed the intervention.
• **Duration and follow-up**	Duration: August 2008 and February 2009 Follow-up: 3 months
• **Statistical analysis**	Descriptive analyses, Mann-Whitney U-tests, chi-square tests for categorical, linear regression, ANCOVA models and logistic regression (Katz ADL outcome).
Patient characteristics	
• **Eligibility criteria**	Adult (>18 years of age), English-speaking, medical or surgical intensive care unit patients enrolled in a sponsored observational cohort
• **Exclusion criteria**	• Cumulative ICU time >5 days in the past 30 days, not including the current ICU stay • Severe cognitive or neurodegenerative diseases that prevented a patient from living independently at baseline • ICU admission post cardiopulmonary resuscitation with suspected anoxic injury • Active substance abuse or psychotic disorder, or a recent (within the past 6 months) serious suicidal gesture necessitating hospitalization • Blind, deaf, or unable to speak English • Overly moribund and not expected to survive for an additional 24 hours and / or withdrawing life support to focus on comfort measures only • Prisoners • Patients who lived outside a 125 mile radius from Nashville • Patients who were homeless and had no secondary contact person available • The onset of the episode of respiratory failure, cardiogenic shock, or septic shock was > 72 hours prior to admission • Patients who had cardiac bypass surgery within the past 3 months (including index hospitalization).

	• Presence of both normal cognition and normal physical function at time of screening (i.e. at hospital discharge) • Lack of telephone service with an analogue telephone line (required for telephonic and tele video interventions)
• **Patient & disease characteristics**	*Characteristics of control patients (n=8) and complete intervention patients (n=7)* Age (median [IQR]): Control group 50y [46- 69], Intervention group 44y [41- 63] Sex (Female/ Male): Control group 5/3, Intervention group 5/2 Education (median [IQR]): Control group 12.0y [11.8- 12.0], Intervention group 12.0 [12.0- 16.0] Admission Diagnosis (Control group vs Intervention group): Sepsis/ Acute Respiratory Distress Syndrome 2/8 vs 2/7, Acute Myocardial Infarction 0/8 vs 1/7, Airway Protection 0/8 vs 1/7, Cardiogenic Shock/ Congestive Heart Failure 1/8 vs 1/7, Cirrhosis 1/8 vs 1/7, ENT Surgery 1/8 vs 0/7, Transplants (excl Liver) 1/8 vs 0/7, Hepatobiliary Surgery 1/8 vs 1/7, Pulmonary Control group 1/8 vs 0/7 ICU Type (Control group vs Intervention group): Medical 4/8 vs 4/7, Surgical 4/8 vs 3/7 APACHE II (median [IQR]): Control group 25.5 [19.5- 33.0], Intervention group 21.0 [18.5- 27.5] Sequential Organ Failure Assessment (median [IQR]): Control group 10.5 [6.8- 12.0]], Intervention group 11.0 [9.5- 13.0] Hospital LOS (days): Control group 11.5 [9.2-14.4], Intervention group 6.2 [3.7-10.1] ICU LOS (days): Control group 5.8 [4.3- 7.0], Intervention group 2.1 [2.0- 3.5] Vent Duration (days): Control group 4.8, Intervention group 1.4 [0.4-2.6] Discharge Disposition (Control group vs Intervention group): Home 7/8 vs 7/7, Rehabilitation Facility: Control group 1/8, 0/7 Charlson Co-Morbidity (median [IQR]): Control group 2.00 [0.75- 6.00], Intervention group 2.00 [0.50- 3.00] Duke Comorbidity Index (median [IQR]): Control group 3.5 [2.8- 6.8], Intervention group 2.0 [2.0- 3.0]
Exposures	
• **Intervention group**	**Duration**: over a 12-week period post-discharge **Starting date:** post-hospital discharge **Setting**: Patient's home using traditional "face-to-face" interventions and telephonic and video-based interventions **Frequency**: Orientation/Exercise – week 1; Exercise training/ Functional training – weeks 2, 4, 6, 8, 10, 12 (tele-visits - length 60-75 minutes); Cognitive therapy – weeks 3, 5, 7, 9, 11 (in person visits); Therapy consultation – 5 consultations by phone occurring between weeks 3/4, 5/6, 7/8, 9/10, 11 **Content**: Cognitive rehabilitation was based on the Goal Management aiming to improve a patient's executive function (among the most frequent and most profoundly affected neuropsychological domains following critical illness) including (a) learn to be reflective (to "stop and

	think" about consequences of decisions) prior to making decisions and executing specific tasks, and (b) achieve success in engaging complex tasks by dividing them into manageable units, so as to increase the likelihood that these tasks will be completed. Cognitive training was delivered in the home by a master's level psychology technician supervised by a licensed neuropsychologist. Physical Rehabilitation aimed to promote home-based endurance and strength exercises. The exercise intervention was delivered by a remote a bachelor's level exercise trainer supervised by a doctoral level exercise physiologist via tele-technology communication in "real time" with the patient with the assistance of a trained social worker in the home. Exercise prescriptions were individually tailored to correspond to patient's functional status levels and primarily targeted lower extremity function and endurance using exercises that could be easily performed in the home (e.g., chair stands, toe rises, stair climbing, walking, etc.). Six motivational telephone calls between sessions were provided. In between visits and calls, the patients carried out exercises independently. Functional Rehabilitation consisted of 4 tele-visits with an occupational therapist who was communicating in "real time" with the patient via tele-technology and assistance of a trained social worker in the home supplementary telephone calls, and participant homework between sessions. The functional training used education [helping the participant understand the relationship between "person, "environment", and "activity"] and "Action Plan" Development [using tailored homework to foster problem-solving using the "Person-Environment-Activity" approach and application of the principles taught in the cognitive training and the physical rehabilitation].
• **Control group**	Usual care: physical therapy, occupational therapy, and nursing care, delivered to in-patient, out-patient, or home-health settings but no cognitive therapy nor speech therapy.
Results	
• **Executive cognitive function**	• TOWER (median [IQR] at 3 months) *Tower refers to the Tower Test Achievement Score, the primary outcome on the Tower Test, which assesses overall executive functioning ability on a test of planning and strategy. Scores range from 1 to 9, with higher scores reflecting better performance. Normal score range from 7 to 13.* Control group: 7.5 [4.0- 8.5] vs Intervention group: 13.0 [11.5- 14.0], p<0.01 • DEX (median [IQR] at 3 months) *DEX refers to the Dysexecutive Questionnaire (DEX), a brief self-report measure that rates behavioural markers of executive functioning. Scores range from 0 to 80 and higher scores reflect poorer functioning.* Control group: 16.0 [7.8-19.2] vs Intervention group: 8.0 [6.0- 13.5], p=0.74 • MMSE (median [IQR] at 3 months) *MMSE refers to the Mini Mental State Examination (MMSE), a brief objective measure of overall cognitive ability. Scores range from 0 to 30 and higher scores reflect better functioning.* Control group: 26.5 [24.8-28.5] vs Intervention group: 30.0 [29.0-30.0], p=0.25

• **Physical functioning and mobility**	• TUG test (median [IQR] at 3 months) *TUG refers to the Timed Up and Go (TUG) Test, a test that assesses ambulation ability (stand up from a chair, walk 10 feet, return to the chair, and sit down). Scores refer to time in seconds and higher scores reflect worse performance. Scores > 13.5 seconds are believed to reflect significant problems.* Control group: 10.2 [9.2 -11.7] vs Intervention group: 9.0 [8.5-11.8], p=0.51 • ABC score (median [IQR] at 3 months) *Scale refers to Activities Balance and Confidence (ABC) Scale, a brief measure that rates an individual's confidence in their balance. Higher scores reflect greater confidence in balance and reflect a percentage (0% to 100%).* Control group: 83 [38- 91] vs Intervention group: 82 [78- 89], p=0.35
• **Functional ability**	• Katz *Katz ADL refers to the Katz Activities of Daily Living (ADL) scale, a self-reported measure of basic activities required for independent functioning. Overall scores on the Katz ADL range from 0 to 18. Stratification in 2 categories of outcomes was - little to no dependency (0 to 1, indicative of no more than partial dependency in 1 of 6 ADL categories) vs. moderate to severe dependency (>1, indicative of at least partial dependency in at least 2 of 6 ADL categories).* o Little to no dependency vs Moderate to severe dependency Control group: 6/8 vs 2/8 – Intervention group: 7/7vs 0/7 p=0.78 • FAQ (median [IQR] at 3 months) *FAQ refers to the Functional Activities Questionnaire (FAQ), a 10 item self-report measure of complex instrumental activities of daily living (IADLs). Scores range from 0 to 30 and higher scores reflect poorer performance.* Control group: 8.0 [6.0- 11.8] vs Intervention group: 1.0 [0.0 - 2.5], p=0.04
Limitations and other comments	
• **Limitations and notes**	• Single centre study • Small sample size leading to underpowered outcomes • Change in eligibility criteria during the trial (inclusion of participants discharged to a nursing home or rehabilitation centre) • High proportion of drop-out in the intervention group • Imbalance in baseline characteristic between control group and group of patients that completed in intervention • Results for Katz is partial reported
• **Authors' conclusions**	A multi-component home rehabilitation programme for ICU survivors combining cognitive, physical, and functional training and using social workers/technicians and telemedicine resulted in superior executive functioning and self-perceived complex daily functioning in 3 months. Future investigations with a larger sample size should be conducted to confirm these results as well as to elucidate the elements of rehabilitation contributing most to improved outcomes.

Jones 2003[50] & Jones 2004[68]	
Methods	
• **Design**	Randomized controlled trial
• **Source of funding and competing interest**	Funding: Stanley Thomas Johnson Foundation, Berne, Switzerland, and REMEDI, UK Competing interest: not mentioned
• **Setting**	Whiston Hospital (Merseyside), Manchester Royal Infirmary, and Royal Berkshire Hospital (Reading) – UK
• **Sample size**	126 patients were randomized (69 in Intervention group, 57 in Control group). At 6 months, 10 patients died and 14 patients were missing. 104 relatives (58 in Intervention group, 46 in Control group). At 6 months, 84 relatives dead and 14 patients completed the full 6-month follow-up.
• **Duration and follow-up**	Duration: not mentioned Follow-up: 6 months
• **Statistical analysis**	Descriptive statistics, Levene statistic (equality of group variances), Kruskal-Wallis one-way ANOVA test, repeated-measures ANOVA
Patient characteristics	
• **Eligibility criteria**	ICU and ventilated patients
• **Exclusion criteria**	a) ICU stay < 48 h; b) burn injury; c) unable to follow the manual or language difficulties; d) neurosurgical patients; e) pre-existing psychotic illness; or f) discharged for terminal care and unlikely to survive the 6-month follow-up period.
• **Patient & disease characteristics**	**Patients' characteristics** • At admission to ICU Age [Mean (range, SD)]: Intervention group 57y (17–77, 17), Control group 59y (17–84, 16), p=0.8 Male/female ratio: Intervention group 37:32, Control group 33:24, p=0.7 SF-36 general health score [Mean (range, SD)]: Intervention group 55 (20–100, 17), Control group 55 (30–100, 16), p=0.67 ICU stay [Mean (range, SD)]: Intervention group 14 days (2–114, 20), Control group 13 days (2–110, 18), p=0.13 Admission APACHE II score [Mean (range, SD)]: Intervention group 17 (4–28, 5), Control group 16 (4–34, 5), p=0.12 APACHE II risk of death prediction [Mean (range, SD)]: Intervention group 0.17 (0–0.49, 0.13), Control group 0.20 (0.07–0.80, 0.17), p=0.83 Admission TISS [Mean (range, SD)]: Intervention group 36 (29–49, 5), Control group 37 (20–48, 6), p=0.5 • At recruitment to study (+/-1 week post-ICU discharge) HAD anxiety score[Mean (range, SD)]: Intervention group 8 (0–20, 5), Control group 8 (0–17, 4), p=0.38

	HAD depression score [Mean (range, SD)]: Intervention group 6 (0–17, 4), Control group 6 (0–18, 6), p=0.94 Trait anxiety scores [Mean (range, SD)]: Intervention group 42 (22–75, 12), Control group 42 (23–61, 9), p=0.26 Cumulative TISS score [Mean (range)]: Intervention group 391 (73–1820), Control group 367 (83–1000), p=0.15 **Relatives' characteristics at recruitement** Family member type: Spouse/partner Intervention group 29/58, Control group 25/46 - Adult child Intervention group 12/58 Control group 8/46 – Parent Intervention group 10/58, Control group 9/46, Sibling 4/58, Control group 3/46, Grandchild/Niece 3/58, Control group 1/46 Age [Mean (range, SD)]: Intervention group 62 (17–82,17), Control group 60 (18–80, 15.4) HAD anxiety score [Median (range)]: Intervention group 11 (0–20), Control group 12 (0–20), p=0.6 HAD depression score [Median (range)]: Intervention group 7 (0–17), Control group 7 (0–17), p=0.25 Trait anxiety scores [Median (range)]: Intervention group 47 (0–64), Control group47.5 (0–64), p=0.5
Exposures	
• **Intervention group**	**Duration**: 6 weeks **Starting date:** 8 weeks after discharge to home **Setting**: Home and ICU follow-up clinic **Frequency**: Every 2 weeks **Content**: Routine ICU Follow-Up 3 telephone calls when patient back home and ICU follow-up clinic visits at 8 weeks and 6 months – 6-wk rehabilitation package consisting of 93 pages of text, diagrams, and supporting illustrations including advice on a wide range of psychological, psychosocial, and physical problems and a self-directed exercise programme + 3 weekly telephone calls reinforced the use of the rehabilitation manual. Patients kept a diary to measure their use of the rehabilitation package.
• **Control group**	Routine ICU Follow-Up
Results	
Patient outcomes	
• **Physical function**	Intervention patients showed closer to normal SF-36 physical function scores at 8 weeks and 6 months than control patients. Data not shown
• **Depression**	• HAD scale for depression at 8 weeks ≥ 11 Intervention group 8/63 vs. Control group 13/51, p=0.066 • HAD scale for depression at 6 months ≥ 11 Intervention group 10% vs. Control group 12%, p not reported
• **Social support**	Norbeck Social Support Questionnaire No difference between group – data not shown

• **Anxiety**	• HAD scale for anxiety at 8 weeks ≥ 11 No difference between groups, data not shown • HAD scale for anxiety at 6 months ≥ 11 Intervention group 32.7% vs. Control group 34%, p not reported
• **PTSD**	• IES scores at 8 weeks Lower in the intervention group (p=0.026). • IES ≥ 19 at 6 months post- ICU Intervention group 31/ 58 vs. Control groups 21/44, p=0.57
Family outcomes	
• **Anxiety**	HADS anxiety score [median (rage)] • at 8 weeks Intervention group 7 (0–20), Control group 8 (0–17), p=0.94 • at 6 months Intervention group 7 (0–20), Control group 8 (0–17), p=0.72
• **Depression**	HADS depression score [median (rage)] • at 8 weeks Intervention group 3 (0–12), Control group 3 (0–14), p=0.91 • at 6 months Intervention group 3 (0–12), Control group 4 (0–16), p=0.29
• **PTSD**	IES scores [median (rage)] • at 8 weeks Intervention group 18 (0–71), Control group 25 (0–62), p=0.90 • at 6 months Intervention group 16 (0–61), Control group 25 (0–69), p=0.20
• **Correlation between patient characteristics and IES scores in relatives at 6 months**	Patient characteristics • In ICU (Spearman's rho, p-value) o Illness severity (APACHE II) 0.07, p=0.48 o Age at admission -0.08, p=0.48 o Length of ICU stay -0.04, p=0.66 • In hospital (Spearman's rho, p-value) o HAD anxiety scores at recruitment 0.21, p=0.03 o HAD depression scores at recruitment 0.10, p=0.28 o Length of hospital stay -0.03, p=0.72 • At 6-month follow-up (Spearman's rho, p-value) o IES scores at 6 months 0.40, p=0.0001 o HAD anxiety scores at 6 months 0.32, p=0.001 o HAD depression scores at 6 months 0.23, p=0.015
Limitations and other comments	

• **Limitations and notes**	• Small sample size • Sample size calculation was 150, not reached leading to underpowered sample. Size calculation for relatives was 42 experimental subjects and 42 controls. It was almost achieved at 6 months (47 in intervention group and 37 in control group) • Poor data reporting: some results are reported in graph or some figures are lacking • Lack of true baseline data for physical function leading to recall bias • No information on the relatives' previous psychological health • No information on the relatives perceived level of social support. • Not all the patients in the study having family available
• **Authors' conclusions**	A rehabilitation package is effective in aiding physical recovery and reducing depression. Written information concerning recovery from ICU provided to the patient and their close family did not reduce relatives' psychological distress. High levels of psychological distress in patients were found to be correlated with high levels in relatives.

Jones 2015[48]	
Methods	
• **Design**	2 × 2 factorial design randomized controlled study, with the nutrient double blind and the physiotherapy single blind to assessment
• **Source of funding and competing interest**	Funding: National Institute for Health Research under its Research for Patient Benefit Programme Competing interest: The authors declare that they have no competing interests
• **Setting**	2 hospitals in the UK: Whiston Hospital and Manchester Royal Infirmary.
• **Sample size**	93 patients were randomized to the study, and 72 patients completed the 3-month follow-up (4 dead, 17 withdrawn). The patients are allocated in four groups: control supplement and no PEPSE (n=17), control supplement and PEPSE (n=20), EAA supplement and no PEPSE (n=18), EAA supplement and PEPSE (n=17). *PEPSE: 6-week program of enhanced physiotherapy and structured exercise* *EAA: essential amino acid supplement drink*
• **Duration and follow-up**	Duration: between 2010 and 2014 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, Levene statistic test (equality of group variances), t tests, ANOVA, Scheffé post hoc test, Kruskal-Wallis 1-way ANOVA, repeated-measures ANOVA.
Patient characteristics	

• **Eligibility criteria**	Patients ≥ 45 years, had a combined ICU and pre-ICU stay of 5 days or more, and able to undertake the physiotherapy programme
• **Exclusion criteria**	Patients (a) < 45 years; (b) had a combined ICU and pre-ICU stay of less than 5 days; (c) unable to undertake physiotherapy (assessed by an experienced physiotherapist); (d) unable to take the nutritional supplement drink; (e) too confused to give informed consent (including traumatic brain injury); (f) discharged for palliative care; (g) had malignant disease if not surgically removed and not discharged for palliative care or chemotherapy; or (h) had persistent non recovering severe liver failure or renal failure (requiring regular dialysis).
• **Patient & disease characteristics**	*Results presented by study group as follow: Control supplement, no PEPSE / Control supplement, PEPSE / EAA supplement, no PEPSE / EAA supplement, PEPSE* Age [median (SD)]: 60y (±12) / 64y (±13) / 64y (±18) / 62y (±14) Hours in ICU [median (SD)]: At recruitment 309 (±707) / 306 (±369) / 306 (±341) / 262 (±347) – At 3 months 240 (±450) / 200 (±238) / 300 (±194) / 300 (±377) Hours ventilated [median (SD)]: 207 (±549) / 180 (±370) / 121 (±493) / 210 (±285) APACHE II [median (SD)]: 14 (±4) / 17 (±10) / 18 (±6) / 14 (±10) Sex (female/male): 10:10 / 8:14 / 10:18 / 12:11 Admission type: Elective 3/20, 4/22, 6/28, 4/23 – Emergency 17/20, 18/22, 22/28, 19/23 Diagnosis group: Planned post operation 1/20, 3/22, 4/28, 2/23 – Cardiovascular 0/20, 0/22, 1/28, 0/23 – Gastrointestinal 2/20, 2/22, 3/28, 3/23 – Multiple-organ failure 2/20, 0/22, 1/28, 0/23 – Neurological 1/20, 0/22, 1/28, 2/23 – Respiratory 8/20, 11/22, 10/28, 5/23 – Sepsis 5/20, 6/22, 6/28, 10/23 – Trauma 1/20, 0/22, 1/28, 0/23 – Other 0/20, 0/22, 1/28, 1/23
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** at ICU discharge **Setting**: Hospital **Frequency**: Nutritional intervention twice daily for 3 months, Physiotherapy intervention 3 times weekly at hospital and weekly after hospital discharge in structured rehabilitation class organised in gymnasium **Content**: Nutritional intervention Supplement drink within 1 hour of physical activity giving a daily supplement of 20-g EAA and 20-g glutamine – Physiotherapy intervention (PEPSE) Early active physical therapy and mobilization throughout their hospital stay + 6-week ICU Recovery Manual including an educational self-help programme to address psychological issues and a self-guided exercise program + 6-week program of supervised physiotherapy sessions
• **Control group**	Nutritional intervention Placebo supplement drink within 1 hour of physical activity with the same flavour the nutritional intervention Physiotherapy intervention (PEPSE) Early active physical therapy and mobilization throughout their hospital stay + 6-week ICU Recovery

	Manual including an educational self-help programme to address psychological issues and a self-guided exercise program
Results	
• **6MWT**	The study groups control supplement/ PEPSE and GEAA supplement/PEPSE had the steepest slopes of recovery (p<0.0001). Study group GEAA supplement/PEPSEmade the most progress in the distance covered in 6MWT increasing by 124% from 170 to 380 m
• **Anxiety**	HADS Anxiety ≥ 11 (proportion at recruitment vs proportion at 3 months) Control supplement, no PEPSE 15% vs 14% – Control supplement, PEPSE 19% vs 5%*– EAA supplement, no PEPSE 36% vs 32% – EAA supplement, PEPSE 31% vs 12%** * p = 0.047 ** p = 0.036
• **Depression**	HADS Depression ≥ 11 at 3 months (proportion at recruitment vs proportion at 3 months) Control supplement, no PEPSE 15% vs 7% – Control supplement, PEPSE 9.5% vs 0%– EAA supplement, no PEPSE 28% vs 21% – EAA supplement, PEPSE 30% vs 12%* * p = 0.009
Limitations and other comments	
• **Limitations and notes**	• Small sample size • Total recruitment target of 180 patients, not reached leading to underpowered sample • Some results are reported in graph • Patients population (older patients mean age > 60y)
• **Authors' conclusions**	In older patients recovering from a prolonged period of illness, the provision of an outpatient rehabilitation programme such as PEPSE and the addition of GEAA supplements between meals aid physical and psychological recovery after critical illness.

McDowell 2017[44]	
Methods	
• **Design**	Multicentre prospective phase II, allocation-concealed, assessor-blinded, randomised controlled clinical trial.
• **Source of funding and competing interest**	Funding: REVIVE, a charity of the Regional Intensive Care Unit, Northern Ireland. Additional funding provided by the Health and Social Care Research and Development Office, Northern Ireland. This trial was also supported by the Northern Ireland Clinical Research Network (NICRN) (Critical Care and Respiratory Health interest groups) and the Northern Ireland Clinical Trials Unit (NICTU), a UK Clinical Research Collaboration (UKCRC) registered clinical trials unit. Competing interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication.
• **Setting**	Six hospitals in Northern Ireland, UK

• **Sample size**	60 patients were included (30 in both intervention and control group). Lost to follow-up: 8 in intervention group and 3 in the control group.
• **Duration and follow-up**	Duration: December 2011 until December 2014. Follow-up: 6 weeks and 6 months
• **Statistical analysis**	Differences between groups were tested using independent samples t-tests or non-parametric equivalents. Adjustments were made by analysis of covariance (ANCOVA) to explore trends across time and differences between the groups. χ2 tests (or Fisher's exact tests) were used for categorical variables.
Patient characteristics	
• **Eligibility criteria**	≥18 years, mechanical ventilation for >96 hours, planned to be discharged home, medically fit to participate.
• **Exclusion criteria**	Participating in cardiac rehabilitation or pulmonary rehabilitation.
• **Patient & disease characteristics**	Age, years (mean (SD)): Intervention group 51 (13), Control group 51 (14) Gender (Female): Intervention group 17/30, Control group 9/30 ICU primary diagnosis: *Respiratory* Intervention group 17/30, Control group 13/30 – *Cardiovascular* Intervention group 4/30, Control group 4/30 – *Gastrointestinal* Intervention group 3/30, Control group 6/30 – *Neurological* Intervention group 2/30, Control group 3/30 –*Trauma* Intervention group 2/30, Control group 3/30 – *Genitourinary* Intervention group 1/30, Control group 0/30 – *Other* Intervention group 1/30, Control group 1/30 APACHE 2 (mean (SD)): Intervention group 17.3 (7.7) , Control group 15.2 (5.6) Length of stay in ICU, days (Median (IQR)): Intervention group 16.0 (8.0–21.5), Control group 13.0 (9.8–23.8) Duration of mechanical ventilation, hours (mean (SD)): Intervention group 293.6 (269.8), Control group 311.9 (235.8) Length of stay in hospital, days (Median (IQR)): Intervention group 27.5 (18.8–46.3), Control group 32.5 (20.8–53.8) Time between hospital discharge and visit1 (baseline), days (mean (SD)): Intervention group 48.9 (29.4), Control group 44.3 (28.6) Time between visit 1 (baseline) and visit 2 (6 weeks), days (mean (SD)): Intervention group 78.19 (26.6), Control group 73.3 (21.0) Time between visit 1 (baseline) and visit 3 (6 months), days (mean (SD)): Intervention group 191.8 (26.6), Control group 183.1 (20.6)
Exposures	
• **Intervention group**	**Duration:** 6 weeks (up to 11 weeks if not complete adherence) **Starting date:** The physiotherapist also determined the suitability of the participant to start **Setting:** Outpatient supervised sessions took take place in the hospital gymnasium or if this was not possible, in the participant's home (5 patients), and unsupervised sessions took place at home.

	Frequency: Once a week **Content:** Standard care + a personalised exercise programme that consisted of two supervised and one unsupervised exercise sessions per week. The exercise sessions (total duration 1h) consisted of (i) a warmup period; (ii) a circuit of 10 arm, leg and whole-body conditioning and strengthening exercises; (iii) an additional period of aerobic exercise (eg, walking, cycle ergometry or treadmill walking for at least 10 min and progressing as able up to a maximum of 30 min) to maintain moderate breathlessness; and finally, (iv) a cool-down period and relaxation. Intensity of exercises is adapted to the patient status. Patients were called weekly phone calls by the research team to discuss individual patient treatment plans and regular training updates.
• **Control group**	Standard care
Results	
Only results at 6 months were reported. These results reported in graph.	
• **Physical functioning (SF-36 PF)**	SF-36 scores: a higher score represents better self-reported HRQoL No statistically significant between groups at 6 months between groups. No significant change in mean from baseline to 6 months between the two groups (p=0.79).
• **Functional limitations profile**	Scale ranging 0–100 : a lower score indicated a better self-reported HRQoL No statistically significant decrease in score across time in both groups (improvement); however, this decrease was between. No statistically significant difference from baseline to 6 months in the intervention compared with the control group (p=0.81).
• **Incremental Shuttle Walk Test**	Incremental shuttle walk test (ISWT) range 0–1020 m: a higher distance indicating better exercise capacity. No statistically significant increase in ISWT across time in both groups (p=0.33). No statistically significant difference in mean ISWT from baseline to 6 months (p=0.16).
• **Self-efficacy to exercise**	Chronic disease self-efficacy scale range 1 to 10: higher score indicating better self-reported self-efficacy to exercise. No statistically significant increase in self-efficacy in the intervention group from baseline to 6 months. No statistically significant difference in the intervention compared with the control group from baseline to 6 months (p=0.08).
• **Readiness to exercise**	Readiness to change questionnaire (self-reported outcome). Significantly larger increase in readiness to exercise from baseline to 6 months in the intervention compared with the control group (p=0.012).
Limitations and other comments	
• **Limitations and notes**	• Proportion of patient with ICU-AW are unknown • No stratification based on patient characteristics (age, ICU length of stay and functional dependency 7 days after ICU discharge) • Small sample size

	• Large proportion of patients excluded because they were included in pulmonary or cardiac rehabilitation programmes • Many patients declined to participate • No blinding of participants or clinicians but blinding of the outcome assessor • Low rate of lost to follow-up
• **Authors' conclusions**	A 6-week personalised exercise programme, initiated after discharge from hospital following critical illness, found at 6 month post intervention no statistically significant self-reported physical function and no statistically significant improvements in HRQoL and performance-based outcomes.

McWilliams 2016[45]	
Methods	
• **Design**	Single centre, randomized controlled trial.
• **Source of funding and competing interest**	Funding: Award of a Manchester Wellcome Trust Clinical Research Facility grant and a Central Manchester NHS Foundation Trust Research for Patient Benefit grant Competing interest: The authors report no declarations of interest.
• **Setting**	A tertiary centre UK general intensive care unit.
• **Sample size**	73 patients were included (37 in intervention group and 36 in control group). Withdrawn before study start: 3 and 2 respectively in intervention and control group. Lost to follow-up: 4 in intervention group and 1 in the control group
• **Duration and follow-up**	Duration: between October 2007 and December 2011. Follow-up: between 8 to 10 weeks after baseline assessment occurring within 6-week post-hospital discharge.
• **Statistical analysis**	Descriptive summary statistics and covariance adjustment.
Patient characteristics	
• **Eligibility criteria**	Adult patients > 18y admitted in ICU and invasively ventilated for ≥5 days.
• **Exclusion criteria**	physical condition resulting in an inability to perform a cardiopulmonary exercise test or to participate in the rehabilitation classes; psychiatric condition or impairment not allowing informed consent or compliance with the rehabilitation program; participation in an alternative rehabilitation program; terminal illness; and poorly controlled cardiorespiratory disease.
• **Patient & disease characteristics**	Type of patients: surgical (44%), medical (50%), trauma (6%). Commonest reasons for ICU admission: medical respiratory failure (35%); emergency vascular surgery (10%); severe acute pancreatitis

	(8%); respiratory failure following cardioesophagectomy (7%); and bowel perforation (7%). Age (mean (SD)): Control group 60.8 (12.3), Intervention group 55.0 (12.9) Gender (% male): Control group 64%, Intervention group 68% APACHE II (mean (SD)): Control group 15.9 (5.3), Intervention group 16.6 (5.7) Days ventilated (geometric mean (range)): Control group 12.7 (5–47), Intervention group 19.8 (6–78) Critical care LOS (geometric mean (range)): Control group 22.2 (9–59), Intervention group 29.1 (8–105) Hospital LOS (geometric mean (range)): Control group 39.3 (17–123), Intervention group 51.0 (15–170)
Exposures	
• **Intervention group**	**Duration:** 7weeks **Starting date:** programme started 6 weeks post discharge **Setting:** Supervised exercises are performed at hospital and self-directed at home **Frequency:** 3x/weeks **Content**: The program included exercise and education sessions supervised by a physiotherapy team. Exercise sessions consisting in cardiovascular exercises were organised during 20 minutes (1 session was supervised and 2 self-directed). Six education sessions of 1 hour were foreseen during the programme. These sessions are dedicated to education on the benefits of exercise, relaxation techniques, managing breathlessness, smoking cessation, anxiety management as well as a group discussion forum.
• **Control group**	No intervention.
Results	
• **Peak VO_2**	• Mean percentage of change in peak VO2 (95% CI) adjusted for age and period of ventilation: Control group: 14.0 (7.6–23.0) vs Intervention group: 18.8 (9.8 to 25.5), p= 0.68. *Stratified analysis based ventilation and adjusted for age:* o 5-14 days ventilated Control group: 12.0 (−0.3, 24.3) vs Intervention group: 13.1 (−3.8, 30.0), p = 0.92 o > 14 days ventilated Control group: 16.1 (5.9, 26.4) vs Intervention group: 21.0 (12.3, 29.7), p = 0.47
• **Anaerobic threshold**	• Mean percentage anaerobic threshold improvement (95% CI) adjusted for age and period of ventilation: Control group: 11.7 (6.1–26.4) vs Intervention group: 14.6 (4.6 to 23.2), p= 0.74. *Stratified analysis based ventilation and adjusted for age:*

	o 5-14 days ventilated Control group: 13.3 (−3.2, 29.8) vs Intervention group: 5.6 (−15.1, 26.2), p = 0.54 o > 14 days ventilated Control group: 16.0 (4.2, 27.7) vs Intervention group: 18.6 (9.5, 27.7), p = 0.72 *No AT assessment in 7/33 patients in the control group and 2/31 patients in the treatment group.*
• **HRQoL (SF-36)**	• Physical Function score: mean improvement (points (95% CI)) Control group: 14.8 (8.5–23.0) vs Intervention group: 28.0 (19.4–34.7), p= 0.004. • Physical component summary score: mean improvement (points (95% CI)) Control group: 3.5 (1.6–6.7) vs Intervention group: 8.6 (5.4–10.6), p= 0.048. Stratified analysis based ventilation and adjusted for age: o 5-14 days ventilated Control group: 3.9 (1.0, 6.8) vs Intervention group: 5.0 (0.9, 9.1), p = 0.64 o > 14 days ventilated Control group: 3.6 (−0.3, 7.4) vs Intervention group: 9.5 (6.2, 12.8), p = 0.024 • Mental component summary score : mean improvement (points (95% CI)) Control group: 4.3 (0.5–7.6) vs Intervention group: 10.2 (6.9–14.4), p= 0.017. Stratified analysis based ventilation and adjusted for age: o 5-14 days ventilated Control group: 3.7 (0.9, 9.9) vs Intervention group: 10.5 (1.5, 19.4), p = 0.21 o > 14 days ventilated Control group: 3.9 (−0.6, 8.4) vs Intervention group: 11.0 (7.0, 14.9), p = 0.024
Limitations and other comments	
• **Limitations and notes**	• Single centre study. • Study underpowered (73/100 over 4-year recruitment period) leading to fail to detect change in SF-36. • Variation in intervention: adherence issues for both unsupervised sessions at home and for supervised session in patients living too far away from the hospital. Outpatient intervention in the community might be considered. • Physical activity in the control subjects is unknown. • No significant adverse events reported during the rehabilitation classes or the self-directed exercise component of the program.

	• Alternative primary outcome measurement of an endurance test of functional capacity might be considered such as on a cycle ergometer or an endurance shuttle walk test. • No premorbid baseline data for physical function or QoL was collected for participants leading to unclear impact of those parameters on outcomes. • Longer follow-up (e.g. 6 months or 1 year) would be valuable.
• **Authors' conclusions**	A 7-week, outpatient-based exercise and education programme for survivors of prolonged critical illness resulted in improved HRQoL scores but not improved exercise capacity at 8 to weeks post intervention. Significant improvement in HRQoLwas seen for both physical and mental health component scores, especially in patients with long ventilation period (>14 days).

Appendix 4.2.2. Follow-up services

Jónasdóttir 2018[53]	
Methods	
• **Design**	Prospective, quasi-experimental, non-blinded study
• **Source of funding and competing interest**	Funding: Landspitali University Hospital Research Fund; The Icelandic Nurses Association and Ingibjörg R. Magnúsdóttir Fund Competing interest: No conflicts of interest are declared by the authors.
• **Setting**	Single centre, university hospital, mixed intensive care patient population (Iceland)
• **Sample size**	168 patients were allocated in Intervention group (83) and in control group (85). At 3 months, 25 patients were lost to follow-up. At 6 months, 10 additional patients were lost to follow-up and 2 patients died. At 12 months, 12 adddtional patients were lost to follow-up.
• **Duration and follow-up**	Duration: from November 2012 to May 2016 Follow-up: at 3, 6 and 12 months
• **Statistical analysis**	Independent samples t-test, Mann-Whitney U test, Chi-square test and linear mixed effect model (time effect), multiple linear regression with forward selection for predictive factor of PTSD (not reported here)
Patient characteristics	
• **Eligibility criteria**	≥18 years, ICU stay ≥72 hour, native speakers, likely to survive the general ward stay, likely to be alert or mentally able to communicate after the ICU discharge, both acute and elective ICU admissions
• **Exclusion criteria**	Dementia, active drug and/or alcohol abusers
• **Patient & disease characteristics**	<u>Sociodemographic variables</u> Age [median (IQR)]: Intervention group 59y (46–66) Control group 70y (64–77), p=0.000 Sex [n male]: Intervention group 40/68, Control group 48/75 , p=ns

	Education level: Level I education (basic) Intervention group 32/68, Control group 42/75 , p=ns – Level II education (secondary) Intervention group 24/68, Control group 24/75 , p=ns – Level III education (university) Intervention group 12/68, Control group 9/75 , p=ns Cohabiting: Intervention group 42/68, Control group 45/75 , p=ns Employment status: Employed Intervention group 41/68, Control group 15/75, p=ns – Unemployed Intervention group 4/68, Control group 3/75 , p=ns, Retired Intervention group 15/68, Control group 48/75, p=ns On disability benefits: Intervention group 8/68, Control group 9/75, p=ns Comorbidity: No comorbidity Intervention group 8/68, Control group 8/75 – Cardiovascular diseases Intervention group 42/68, Control group 75/75, p=ns – Diabetes mellitus (I, II) Intervention group 14/68, Control group 16/75, p=ns – COPD Intervention group 13/68, Control group 12/75, p=ns – Depression and/or anxiety Intervention group 17/68, Control group 6/75, p=ns – Anti-depressant and/or – anxiety drug use Intervention group 12/68, Control group 8/75, p=ns Clinical variables Admission diagnosis: Medical Intervention group 42/68, Control group 29/75, p=ns – Surgical Intervention group 26/68, Control group 46/75, p=ns ICU admissions acute | elective Intervention group 65 | 3/68, Control group 61 | 14/75, p=ns APACHE II [median (IQR)]: Intervention group 16 (12–21), Control group 18 (15–26), p=0.010 ICU LOS [median (IQR)]: Intervention group 7 days (5–11), Control group 8 days (5–14), p=0.188 Mechanical ventilation: Intervention group 53/68, Control group 65/75, p=ns Mechanical ventilation [median (IQR)]: Intervention group 5 days (3–8), Control group 5 days (2–11), p=0.814 LOS ward [median (IQR)]: Intervention group 12 days (7–20), Control group 21 (10–38), p=0.000 LOS hospital [median (IQR)]: Intervention group 17 (8–57), Control group 21 (12–54), p=0.234
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** within 24h of ICU discharge to the ward **Setting**: Hospital **Frequency**: 2 ward visits during hospital stay, 1 phone call and one appointment at 3 months **Content**: All interventions are performed by clinical nurse-specialist. Ward visits before hospital discharge: minimum 2 visits within 24h of ICU discharge to the ward, patients' clinical condition (dream/nightmares, delirium/confusion, hallucination, depression state, and anxiety), and information regarding recovery after critical illness. Phone call at first week after hospital discharge: Information about recovery after critical illness + interview of patients' concerns regarding recovery, mobilisation, nutrition and sleep. Three months appointment: maximum 1 hour (with closest relative), conversation about ICU experience, patient referral if

	IES-R score ≥23, HADS-A≥8 or HADS-D≥8, visit the ICU and invitation to contact the clinical nurse-specialist.
• **Control group**	Unstructured ward visit
Results	
• **PTSD**	• IES-R total score [Mean (SD)] o at 3 months Intervention group (n=66):11 (16) vs Control group (n=64): 12 (14), p=0.157 o at 6 months Intervention group (n=55): 18 (18) vs Control group (n=55): 13 (16), p=0.097 o at 12 months Intervention group (n=53): 20 (17) vs Control group (n=49): 14 (15), p=0.066 • IES-R ≥ 23–88 (patients with partial or full PTSD) o at 3 months Intervention group (n=19):36 (13) vs Control group (n=15): 33 (11), p=0.422 o at 6 months Intervention group (n=18): 39 (14) vs Control group (n=7): 50 (9), p=0.039 o at 12 months Intervention group (n=20): 37 (14) vs Control group (n=10): 39 (11), p=0.613 • Mixed effect model (time effect) Estimate 4.06 (SD 1.62, 95% CI 0.870-7.25), p=0.013 Intervention patients experienced more symptoms of PTSD than those in the control group over time
• **Anxiety**	• HADS-A total score [Mean (SD)] o Ward discharge Intervention group (n=63): 4.0 (4.1) vs Control group (n=74): 2.7 (3.8), p=0.064 o at 3 months Intervention group (n=66):4.4 (4.2) vs Control group (n=70): 2.8 (3.1), p=0.011 o at 6 months Intervention group (n=58): 3.7 (3.6) vs Control group (n=61): 2.4 (2.8), p=0.030 o at 12 months Intervention group (n=54): 4.0 (3.2) vs Control group (n=56): 2.5 (2.8), p=0.005 • Mixed effect model (time effect)

	Estimate 1.07 (SD 0.32, 95% CI 0.442-1.70), p=0.001 Intervention patients experienced more anxiety than those in the control group over time
• **Depression**	• HADS-D total score [Mean (SD)] o Ward discharge Intervention group (n=62): 4.3 (3.4) vs Control group (n=73): 4.0 (3.4), p=0.539 o at 3 months Intervention group (n=67):3.7 (3.4) vs Control group (n=69): 3.5 (3.0), p=0.745 o at 6 months Intervention group (n=58): 4.7 (3.9) vs Control group (n=59) 3.4 (3.2), p=0.053 o at 12 months Intervention group (n=55): 3.8 (2.9) vs Control group (n=57): 3.7 (3.6), p=0.895 • Mixed effect model (time effect) Estimate 0.362 (SD 0.327, 95% CI -0.280 to 1.00), p=0.280 Intervention patients did not experience more depression than those in the control group over time
Limitations and other comments	
• **Limitations and notes**	• No calculation of the minimum sample size. Possible underpowered outcomes because of the small sample size • No randomization leading to baseline differences between groups • Potential Hawthorn effect because of no blinding of professionals • Full intervention was performed in half of participants (phone call was missing in 50% of the participants)
• **Authors' conclusions**	The structured nurse-led follow-up did not improve patients' measured outcomes of psychological recovery after intensive care. Persistent distress indicated by severe symptoms of PTSD by a high percentage of patients in this study is of concern. Dealing with disturbing memories of the ICU stay and psychological reactions needs to be prioritized when constructing the ICU nurse-led follow-up to a greater extent than has previously been acknowledged.

Jensen 2016[52]	
Methods	
• **Design**	Multicentre, non-blinded, two-armed, parallel-group, pragmatic RCT
• **Source of funding and competing interest**	Funding: Danish Nursing Organization, The Novo Nordisk Foundation and Nordsjællands Hospital, University of Copenhagen, Denmark Competing interest: No conflicts of interest have been declared by the authors.

• **Setting**	10 (level II-III) ICUs in Denmark; 1 cardiac and 9 general ICUs, in four out of the five regions in Denmark.
• **Sample size**	386 patients were randomized (190 in intervention group and 196 in control group). At 3 months, 38 patients died, 38 invalid questionnaires, 79 lost to follow-up. At 12 months, 49 patients died, 23 invalid questionnaires, 49 lost to follow-up.
• **Duration and follow-up**	Duration: between December 2012 and December 2015 Follow-up: 3 and 12 months
• **Statistical analysis**	Independent sample t test, linear models (adjustment for trial centres), logistic models (dichotomous data)
Patient characteristics	
• **Eligibility criteria**	Danish-speaking adults (≥18 years), mechanically ventilated ≥48 h
• **Exclusion criteria**	Dementia, not oriented according to Glasgow Coma Score
• **Patient & disease characteristics**	<u>Sociodemographic data</u> Age [Median (IQR)]: Intervention group 66y (57.75–73.5), Control group 67.5y (58–75) Sex (male) : Intervention group 58.9%, Control group 59.7% Educational level [Median (IQR)]: Intervention group 10.0y (7.9–13), Control group 10.0y (7–13) Marital status: Cohabiting Intervention group 53.7%, Control group 59.2% – Living alone Intervention group 46.3%, Control group 41.8% Occupational status pre-ICU (employment): Intervention group 24.2%, Control group 23.0% Pre-existing diseases, (>1 disease): Intervention group 62.1%, Control group 57.5% Pre-existing diseases [median (IQR)] : Intervention group 2.0 (1–3), Control group 2.0 (1–3) <u>Diagnostic at ICU admission</u>: Neurological: Intervention group 6.3%, Control group 3.1% – Respiratory: Intervention group 36.8%, Control group 33.7% – Cardiovascular: Intervention group 13.8%, Control group 16.8% – Gastrointestinal: Intervention group 11.1%, Control group 9.2% – Renal: Intervention group 0.5%, Control group 2.0% – Haematological Intervention group 0.5%, Control group 0% – Endocrinology or metabolic Intervention group 0%, Control group 1.5% – Sepsis: Intervention group 29.4%, Control group 28.6% – Trauma: Intervention group 0.5%, Control group 0% <u>Clinical variables during ICU stay</u> Medical ICU: Intervention group 68.9 %, Control group 62.2 % APACHE II score [median (IQR)]: Intervention group 25.0 (19.0–30.3) , Control group 24.5 (20.0–30.0) SAPS II score [median (IQR)]: Intervention group 44.5 (35.0–54.3) , Control group 48.5 (39.3–60) Mechanically ventilation [median (IQR)]: Intervention group 159.1h (83.5–384.7) , Control group 172.0h (90.0–346.0) Sedative used: Intervention group 82.1 %, Control group 83.2 % <u>Co-morbidities during ICU stay</u>

	No. co-morbidities [median (IQR)]: Intervention group 2.0 (1–3), Control group 2.0 (1–3) Delirium [median (IQR)]: Intervention group 0 days (1–2), Control group 0 days (0–1) Days measured delirium [median (IQR)] Intervention group 6 (3–11), Control group 6 (2–11) Not assessed delirium during ICU-stay: Intervention group 9.5 %, Control group 9.7 % Delirium unable to assess: Intervention group 1 (0–3), Control group 1 (0–3) Renal replacement therapy: Intervention group 8.9 %, Control group 13.3 % <u>Specific healthcare services planned or initiated during ICU</u> Physiotherapist (ICU) Intervention group 66.3 %, Control group 70.4 % Physiotherapist (continuing at the general ward): Intervention group 74.2 %, Control group 77.0 % Occupational therapist: Intervention group 38.9 %, Control group 36.7 % Dietitian: Intervention group 39.5 %, Control group 40.3 % <u>At ICU discharge</u> Length of ICU stay [median (IQR)]: Intervention group 10 days (5–20), Control group 9 days (6–18) MMSE at enrolment [median (IQR)]: Intervention group 27.0 (24.0–29.0) , Control group 26.5 (23.0–29.0) HTQ-VI at enrolment [median (IQR)]: Intervention group 28.5 (24.0–33.0) , Control group 28.5 (24.0–36.0)
Exposures	
• **Intervention group**	**Duration**: 10 months post-ICU **Starting date:** at one month post-ICU **Setting**: at hospital and by phone **Frequency**: Three consultations conducted by specially trained study nurses **Content**: The first consultation was conducted with the patient and relatives at one to three months post-ICU and consisted in a dialogue on supporting the patient in constructing an illness narrative aided by photographs of the patient during the ICU-stay and revisiting ICU. The second and third consultations were conducted by telephone with patients at 5 and 10 months post-ICU and consisted in a dialogue focused on issues of importance to the patients.
• **Control group**	ICU discharge without follow-up.
Results	
Results are presented in ITT only, results in PP led to the same conclusions	
• **HRQoL**	Absolute difference in scores between standard care and the intervention group (95 % CI), p value • SF-36 Physical component score o At 3 months

	1.87 (-0.93;4.67), p= 0.19 o At 12 months 1.41 (-1.53;4.35), p=0.35 o Change between 3-12 months 0.24 (-2.15;2.62), p=0.85 • SF-36 Mental component score o At 3 months -0.41 (-3.20; 2.39), p=0.78 o At 12 months 1.92 (-1.06;4.90), p=0.21 o Change between 3-12 months 1.63 (-1.38;4.63), p=0.29
• **Sense of coherence (SOC)**	Details on the scale (see above Bohart 2019) Absolute difference in scores between standard care and the intervention group (95 % CI), p value • At 3 months 2.02 (-1.35;5.38), p=0.24 • At 12 months -0.93 (-4.72;2.85), p=0.63 • Change between 3-12 months -2.44 (-6.07;1.19), p=0.19
• **Anxiety**	Absolute difference in scores in HADS-A between standard care and the intervention group (95 % CI), p value • All patients o At 3 months -0.16 (-1.15;0.82), p=0.75 o At 12 months -0.21 (-1.22;0.80), p=0.68 o Change between 3-12 months -0.05 (-0.99;0.89), p=0.92 • Patients with score ≥ 11 (OR (95% CI) o At 3 months 0.50 (0.24;1.06), p=0.07 o At 12 months 0.91 (0.40;2.07), p=0.82
• **Depression**	Absolute difference in HADS-D scores between standard care and the intervention group (95 % CI), p value • All patients o At 3 months 0.10 (-0.84;1.03), p=0.84

	o At 12 months -0.20 (-1.12;0.72), p=0.67 o Change between 3-12 months -0.31 (-1.19;0.57), p=0.48 • Patients with score ≥ 11 (OR (95% CI) o At 3 months 0.66 (0.29;1.48),p=0.31 o At 12 months 1.10 (0.47;2.59), p=0.83
• **PTSD**	Absolute difference in scores HTQ-IV between standard care and the intervention group (95 % CI), p value • All patients o At 3 months 0.24 (-2.07;2.55), p=0.84 o At 12 months -1.42 (-3.94;1.11),p=0.27 o Change between 3-12 months -0.89 (-3.13;1.35), p=0.43 • Patients with score ≥ 40 [OR (95% CI)] o At 3 months 1.23 (0.74; 2.06), p=0.43 o At 12 months 1.00 (0.58;1.73), p=1.00 • New onset of PTSD (ns) o At 3 months Intervention group 16, Control group 17 o At 3 months and 12 months Intervention group 24, Control group 23
Limitations and other comments	
• **Limitations and notes**	• Strength of the study o Target sample size achieved o Multicentre design o Intervention replicability is ensured by use of trained nurses • All first consultation were not provided within the 3 months • Baseline HRQoL is unknown
• **Authors' conclusions**	No effectiveness of a nurse-led post-ICU recovery programme in improving HRQOL, SOC, or reducing symptoms of anxiety, depression, and PTSD in the first 12 months after ICU discharge. Patients had a high MCS, maintained a strong sense of coherence, and low levels of anxiety and depression. PTSD was still high at 12 months post-ICU.

Schandl 2012[56]	
Methods	
• **Design**	Quasi-experimental study
• **Source of funding and competing interest**	Funding: Lena and Per Sjöberg Research Foundation and the Karolinska University Hospital and Karolinska Institutet Committé of Strategic Research. Funding was also provided by the Department of Anesthesiology, Surgical Services and Intensive Care Medicine and from the Olle Engkvist Foundation Competing interest: The authors declare that they have no competing interests.
• **Setting**	A 12-bed general ICU at Karolinska University Hospital in Sweden
• **Sample size**	Patients (n= 151 patients) treated from January to December 2006 represented the control group. At 14 months, 46 patient died, 2 patients did not speak Swedish, 1 lived abroad and 29 did not respond. Patients (n= 259 patients) treated from January 2007 to September 2008 represented the intervention group. At 14 months, 79 patient died, 10 patients did not speak Swedish, 5 lived abroad, 5 attended other follow-up, 4 did not have known address and 58 did not respond.
• **Duration and follow-up**	Duration: from January 2006 to September 2008 Follow-up: at 14 months after ICU
• **Statistical analysis**	Student's t-test, Mann Whitney U-test and Chi²-test, logistic quantile regression analysis
Patient characteristics	
• **Eligibility criteria**	≥16y, LOS> 96 hours in the general ICU
• **Exclusion criteria**	not speaking Swedish and no having an address
• **Patient & disease characteristics**	Control Follow-up Men (n = 64) Women (n = 38) Men (n = 102) Women (n = 54) Age [Mean (SD)]: Control group Men 52y (17) Women 54 (20.5); Intervention group Men 53 (17) Women 52 (18) APACHE II [Mean (SD)]: Control group Men 21 (8) Women 19 (10); Intervention group Men 23 (9) Women 21 (8) Charlson Comorbidity Index [Mean (SD)]: Control group Men 1.4 (2.1) Women 1.4 (1.5); Intervention group Men 1.2 (1.6) Women 1.1 (1.6) Previous psychological problems: Control group Men 12% Women 29% ; Intervention group Men 14% Women 17% ICU-length of stay [Mean (SD)]: Control group Men 9 days (7) Women 9 days (8); Intervention group Men 11days (7) Women 10 days (7) Diagnosis: Trauma Control group Men 32% Women 21%; Intervention group Men 36% Women 20% – Surgical Control group Men 11% Women 11%; Intervention group Men 15% Women 19% – Medical Control group Men 22% Women 26%; Intervention group Men 19% Women 13% – Infection Control group Men 35% Women 42%; Intervention group Men 30% Women 48%

	Ventilator: Control group Men 72% Women 79%; Intervention group Men 83% Women 81% Sedation [Median (IQR)]: Control group Men 2 days (0 to 4) Women 2 days (0 to 4); Intervention group Men 3 days (1 to 6) Women 3 days (1 to 5)
Exposures	
• **Intervention group**	**Duration**: 12 months **Starting date:** Within one week from ICU discharge **Setting**: Hospital **Frequency**: follow-up consultations at 3, 6 and 12 months after ICU **Content**: Within one week from ICU discharge, patients received a visit at hospital ward from a nurse from the follow-up team to discuss briefly their treatments in ICU and memories. At 3, 6 and 12 months after ICU, multidisciplinary follow-up consultations with a nurse, a physician and a physiotherapist from the general ICU were offered. The consultation involved recapitulating ICU-care and treatment. Memories, delusions and/or nightmares were discussed. At the six-month consultation patients were offered a visit of the ICU. At each time point, patients with IES > 25 points or HADS > 10 points were offered a referral to an appointed at hospital psychiatric unit. Additional interventions may be offered such as consultations with pain clinic, patient counsellor, local physiotherapist or physical training instructions or with other specialists.
• **Control group**	No multidisciplinary ICU follow-up programme
Results	
• **PTSD**	IES at 14 months (points) • Difference between genders in control group (median) Women 31 vs Men 10, p< 0.01 • Women (median) Control group 31 vs Intervention group 20, p=0.01 • Men (median) Control group 10 vs Intervention group 16, p=0.27 • Differences between control group and follow-up group after adjustment for age, length of intensive care unit stay and previous psychological problems (quantile regression) o 25th percentile Women -6.6 (ns) Men 1.9 (ns) o 50th percentile Women -10.8 (p< 0.05) Men 1.8 (ns) o 75th percentile Women -17.6 (p< 0.05) Men 4.4 (ns)
• **Anxiety**	HADS-A at 14 months (points) • Women (median) Control group 6 vs Intervention group 3, p=0.14

	• Men (median) Control group 3 vs Intervention group 4, p=0.78 • Differences between control group and follow-up group after adjustement for for age, length of intensive care unit stay and previous psychological problems (quantile regression) o 25th percentile Women -1.8 (p< 0.05) Men 0.5 (ns) o 50th percentile Women -1.2 (ns) Men 0.4 (ns) o 75th percentile Women -3.2 (ns) Men -0.8 (ns)
• **Depression**	HADS-D at 14 months (points) • Women (median) Control group 7 vs Intervention group 3, p=0.09 • Men (median) Control group 4 vs Intervention group 4, p=0.47 • Differences between control group and follow-up group after adjustment for age, length of intensive care unit stay and previous psychological problems (quantile regression) o 25th percentile Women -1.7 (ns) Men -0.2 (ns) o 50th percentile Women -1.7 (ns) Men -0.9 (ns) o 75th percentile Women -5.4 (p< 0.05) Men 1.0 (ns)
• **Memories**	ICU Memory Tool at 14 months (points) • Factual memories [memories of family, alarms or ward rounds] o Women (median) Control group 3 vs Intervention group 3.5, p=0.75 o Men (median) Control group 2 vs Intervention group 2, p=0.57 • Emotional memories [negative emotions, such as fear, pain or feelings of confusion] o Women (median) Control group 1 vs Intervention group 2, p=0.78 o Men (median) Control group 1 vs Intervention group 1, p=0.50 • Delusions [hallucinations, nightmares or dreams] o Women (median) Control group 1 vs Intervention group 1, p=0.51

	o Men (median) Control group 0 vs Intervention group 1, p=0.12
Limitations and other comments	
• **Limitations and notes**	• Small sample size under the power calculation (a questionnaire must be sent to 150 patients in intervention group only 98 were sent) • Design not allowing randomization but no difference between baseline characteristics • Poor data reporting: not IQR around the median for crude data, no confident interval around mean difference
• **Authors' conclusions**	Women surviving critical illness and intensive care appear to have more psychological problems than men and multidisciplinary ICU follow-up may reduce the incidence of long-term symptoms of posttraumatic stress and post-ICU depression for these women.

Schmidt 2016[54] & Schmidt 2020[55]	
Methods	
• **Design**	Multicentre, non-blinded, two-arm randomized clinical trial
• **Source of funding and competing interest**	Funding: Center of Sepsis Control & Care, German Federal Ministry of Education and Research, German Sepsis Society (GSS); Thuringian Ministry of Education, Science, Thuringian Foundation for Technology, Innovation and Research; National Institutes of Health, Primary Health Care Foundation, Jena/Frankfurt. Competing interest: All authors declare that they have no competing interest and therefore have nothing to declare
• **Setting**	Nine ICU study centres across Germany
• **Sample size**	291 patients were randomised (148 in intervention group and 143 in control group). At 12 months, 202 patients remained (107 in intervention group and 95 in Control group): 54 deaths, 22 refusals to participate, 9 not reachable, 4 missing data. At 24 months, 186 patients remained (98 completed the 24 months follow-up in intervention group and 88 in control group): 10 deaths, 7 refusals to participate and 3 not reachable).
• **Duration and follow-up**	Duration: between February 2011 and December 2014 Follow-up: 12 months (Schmidt 2016), 24 months (Schmidt 2020)
• **Statistical analysis**	Descriptive statistics, t-test, Fisher's exact test and the Wilcoxon-Mann-Whitney test, Welch's t-test, Kaplan-Meier method (overall survival) using the log-rank test
Patient characteristics	
• **Eligibility criteria**	≥18y, survivors of severe sepsis (ICD-10) or septic shock, and fluent in the German language.
• **Exclusion criteria**	Cognitive impairment, as determined by the Telephone Interview of Cognitive Status (TICS-M, score≤27).

- **Patient & disease characteristics**

Sociodemographic

Age [mean (SD)]: Intervention group 62.1y (14.1) vs Control group 61.2y (14.9)

Sex (Male): Intervention group 70.9% vs Control group 61.3%

Family status “Married”: Intervention group 57.9% vs Control group 46.0%

Educational status “< High school”: Intervention group 36.7% vs Control group 31.1%

Care measures

Recent surgical history: Emergency Intervention group 33.6% vs Control group 40.1% – Elective surgery Intervention group 23.3% vs Control group 19.7% – No history Intervention group 26.7% vs Control group 23.9%

Source of infection: Community acquired Intervention group 37.2% vs Control group 34.8% – Nosocomial (ICU or IMC) Intervention group 48.3% vs Control group 50.0% – Nosocomial (general ward or nursing home) Intervention group 14.5% vs Control group 15.2%

ICU length of stay days [mean (SD)]: Intervention group 31.5 days (27.7) vs Control group 35.2 days (26.7)

Mechanical ventilation: Intervention group 82.3% vs Control group 86.6% - Duration [mean (SD)]: Intervention group 17.0 (17.5) vs Control group 19.9 (20.7)

Renal replacement therapy: Intervention group 29.3% vs Control group 27.7% – Duration [mean (SD)]: Intervention group 11.9 (13.7) vs Control group 12.8 (12.8)

Clinical Measures

Comorbidity: Charlson Index [mean (SD)]: Intervention group 4.0 (3.0) vs Control group 4.0 (2.9)

ICD-diagnoses [mean (SD)]: Intervention group 9.6 (4.4) vs Control group 10.6 (5.1)

BMI [mean (SD)]: Intervention group 27.3 (6.0) vs Control group 27.3 (5.9)

Depression: MDI [mean (SD)] Intervention group 18.4 (9.8) vs Control group 17.8 (10.1) – Depressive symptoms Intervention group 24.8% vs Control group 32 (23.5)

PTSD: PTSS-10 [mean (SD)]: Intervention group 24.0 (11.0) vs Control group 23.2 (9.7) – Score >35: Intervention group 15.2% vs Control group 14.0%

Cognition TICS-M [mean (SD)]: Intervention group 33.7 (3.4) vs Control group 33.1 (3.9)

Neuropathic symptoms NSS mean (SD): Intervention group 3.6 (3.3) vs Control group 3.7 (3.1) – Score 3-10: Intervention group 57.6% vs Control group 60.9%

Pain

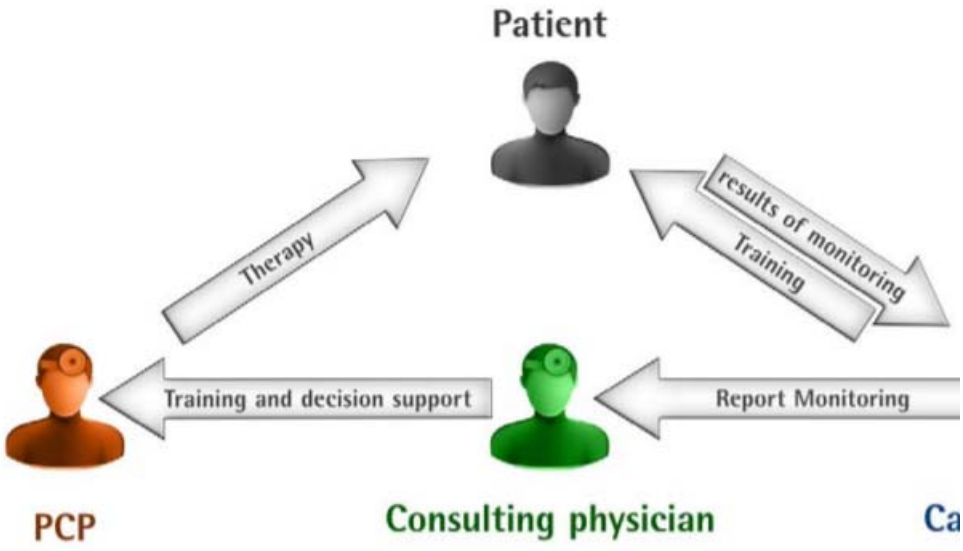
Intensity GCPS PI [mean (SD)]: Intervention group 43.7 (25.6) vs Control group 43.9 (23.1)

Disability: GCPS DS [mean (SD)]: Intervention group 36.0 (34.5) vs Control group 36.4 (34.8) – Severe pain: GCPS cat. >1: Intervention group 18.2% vs Control group 21.0%

HRQoL

SF-36 Mental Component Summary score [mean (SD)]: Intervention group 48.8 (12.5) vs Control group 49.2 (12.6)

SF-36 Physical Component Summary score [mean (SD)]: Intervention group 25.9 (9.4) vs Control group 24.7 (8.0)

Exposures	
• **Intervention group**	**Duration**: 12 months **Starting date:** median of 8 days after ICU discharge **Setting**: GP practice (Primary Care Physician - PCP) **Frequency**: Monthly **Content**: The intervention was based on the Chronic Care Model. Its core components included case management (nurses with specific training) focusing on pro-active patient symptom monitoring, clinical decision support for the PCP and training for both patients and their PCPs in evidence-based care. Patient training: a 60-minute face-to-face training on sepsis sequelae at a median of eight days after ICU discharge delivered by the case manager. Monthly telephone contact for six months, every 3 months for the final six months: case managers monitored patients' symptoms using validated screening tools (on critical illness polyneuropathy/myopathy, wasting, neurocognitive deficits, PTSD, depressive and pain symptoms, physical activity and individual self-management goals) + results were reported to consulting physicians (medical doctors with background in primary and critical care), who provided clinical decision support to the PCPs Patients' PCPs training: An evidence-based sepsis aftercare training for the patients' PCPs was provided individual, in-person by the consulting physicians. (see figure below from Schmidt 2016) 
• **Control group**	Usual care from their PCPs without additional information or monitoring. Usual sepsis aftercare included periodic contacts, referrals to specialists and prescription of medication and therapeutic aids, at quantities comparable to those for other populations with multiple chronic conditions.
Results	
• **Training rate**	87.8% of patients received patient training from case managers 84.5% of their PCPs received training from a consulting physician (mean gap between ICU discharge and PCP training: 62.38 days [Q1=36, Q3=99])
• **HRQoL**	SF-36 scales and sub-scales Intervention/Control [mean difference between follow-up (6 or 12 months baseline) and baseline (SD)]. Treatment effect: difference variation from baseline in both group (intervention – Control) (95% CI), p-value

- Mental Component Summary score

6 months

Intervention 15.7 (23.4), Control 10.4 (24.0)

  - **Treatment effect 5.4 (-**6 months
    Intervention 3.79 (95%CI, 1.05; 6.54), Control 1.64 (95%CI, 1.22; 4.51)
    Treatment effect 2.15 (95%CI -1.79; 6.09); p=0.20
  - 12 months
    Intervention 3.7 (13.4), Control 2.3 (12.6)
    Treatment effect 1.4 (-2.4;5.2), p=0.47
  - 24 months
    Intervention 3.1 (13.9), Control 1.1 (13.6)
    Treatment effect 2.0 (-2.2;6.2), p=0.36

- Physical Component Summary score
  - 6 months
    Intervention 5.6 (13.1), Control 6.2 (12.3)
    Treatment effect -0.6 (-4.1;3.0), p=0 .75
  - 12 months
    Intervention 9.5 (12.3), Control 8.4 (13.5)
    Treatment effect 1.1 (-2.7;4.9), p=0.56
  - 24 months
    Intervention 7.0 (14.6), Control 9.7 (13.9)
    Treatment effect -2.7 (-7.0; 1.7), p=0.22
- SF-36 vitality
  - 6 months
    Intervention 15.7 (23.4), Control 10.4 (24.0)
    Treatment effect 5.4 (-1.0;11.7), p=0.10
  - 12 months
    Intervention 18.9 (22.1), Control 14.1 (25.8)
    Treatment effect 4.8 (-1.9;11.5), p=0.16
  - 24 months
    Intervention 16.3 (22.2), Control 15.9 (26.89)
    Treatment effect 0.47 (-6.8; 7.7), p=0.91
- SF-36 physical functioning
  - 6 months
    Intervention 34.1 (36.0), Control 28.9 (32.1)
    Treatment effect 5.2 (-4.0;14.5), p=0.27
  - 12 months
    Intervention 40.6 (34.7), Control 35.4 (35.1)
    Treatment effect 5.2 (-4.7;15.1), p=0.30

- 24 months
  Intervention 34.0 (37.3), Control 35.4 (37.0)
  Treatment effect -1.4 (-12.4; 9.6), p=0.80

- SF-36 physical role function
  - 6 months
    Intervention 18.1 (39.3), Control 14.5 (39.0)
    Treatment effect 3.6 (-6.8;14.0), p=0.50
  - 12 months
    Intervention 28.0 (43.4), Control 16.8 (43.0)
    Treatment effect 11.2 (-0.8;23.2), p=0.07
  - 24 months
    Intervention 26.5 (44.2), Control 25.3 (46.0)
    Treatment effect 1.2 (-11.8; 14.3), p=0.85
- SF-36 bodily pain
  - 6 months
    Intervention -2.7 (40.8), Control 6.7 (41.2)
    Treatment effect -9.4 (-20.4;1.6), p=0.09
  - 12 months
    Intervention 7.1 (37.1), Control 13.4 (40.2)
    Treatment effect -6.3 (-17.2;4.6), p=0.26
  - 24 months
    Intervention -0.53 (41.6), Control 11.0 (41.9)
    Treatment effect -11.5 (-23.7; 0.7), p=0.07
- SF-36 general health perceptions
  - 6 months
    Intervention 2.1 (20.3), Control 2.2 (20.9)
    Treatment effect -0.1 (-5.6;5.4), p=0.97
  - 12 months
    Intervention 5.5 (23.4), Control 4.4 (22.5)
    Treatment effect 1.1 (-5.3;7.6), p=0.73
  - 24 months
    Intervention 2.9 (23.7), Control 1.6 (23.8)
    Treatment effect 1.3 (-5.7; 8.2), p=0.72
- SF-36 social role function
  - 6 months
    Intervention -1.1 (33.1), Control 3.3 (38.3)
    Treatment effect -4.4 (-14.1;5.2), p=0.36
  - 12 months
    Intervention 0.5 (33.4), Control 6.7 (38.9)

Treatment effect -6.2 (-16.5;4.0), p=0.23

- 24 months

  Intervention -0.8 (34.6), Control 6.5 (41.1)

  Treatment effect -.73 (-18.8; 3.9), p=0.20

- SF-36 emotional role function
  - 6 months

    Intervention 27.6 (55.2), Control 14.5 (55.2)

    Treatment effect 13.2 (-1.6;27.9), p=0.08
  - 12 months

    Intervention 27.4 (56.3), Control 19.6 (49.7)

    Treatment effect 7.8 (-7.1;22.7), p=0.30
  - 24 months

    Intervention 26.1 (56.4), Control 17.3 (54.1)

    Treatment effect 8.9 (-7.3; 25.0), p=0.28
- SF-36 mental health
  - 6 months

    Intervention 10.9 (21.3), Control 5.8 (24.9)

    Treatment effect 3.1 (-1.0;11.3), p=0.10
  - 12 months

    Intervention 12.8 (21.5), Control 7.1 (23.5)

    Treatment effect 3.2 (-0.6;11.9), p=0.08
  - 24 months

    Intervention 10.2 (23.2), Control 6.1 (23.9)

    Treatment effect 4.0 (-2.8; 10.9), p=0.25

- **Depression**

  Major Depression Inventory (MDI), MDI ranged from 0 to 50 (high score indicates high impairment)

  Intervention/Control [mean difference between follow-up (6 or 12 months baseline) and baseline (SD)].

  Treatment effect: difference between variation from baseline in both group (intervention – Control) (95%CI), p-value

  - 6 months

    Intervention -6.9 (10.3), Control -6.9 (10.7)

    Treatment effect -0.0 (-2.8;2.8), p=0.99
  - 12 months

    Intervention -8.8 (10.4), Control -7.4 (11.7)

    Treatment effect -1.4 (-4.5;1.7), p=0.36
  - 24 months

    Intervention -6.2 (11.9), Control -4.9 (13.2)

    Treatment effect -1.3 (-5.0; 2.4), p=0.48

• **PTSD**	Post-Traumatic Symptom Scale (PTSS-10), PTSS-10 ranged from 10 to 70 (high score indicates high impairment) Intervention/Control [mean difference between follow-up (6 or 12 months baseline) and baseline (SD)]. Treatment effect: difference between variation from baseline in both group (intervention – Control) (95%CI), p-value • 6 months Intervention -2.0 (11.0), Control -0.2 (11.2) Treatment effect -1.8 (-4.8;1.2), p=0.24 • 12 months Intervention -2.1 (12.9), Control 0.2 (10.9) Treatment effect -2.3 (-5.6;1.0), p=0.17 • 24 months Intervention -0.7 (12.1), Control 3.7 (11.8) Treatment effect -4.4 (-7.9; -0.8), p=0.002
• **Cognitive status**	Modified Telephone Interview for Cognitive Status (TICS-M), TICS-M ranged from 0 to 50 (high score indicates low impairment) Intervention/Control [mean difference between follow-up (6 or 12 months baseline) and baseline (SD). Treatment effect: difference between variation from baseline in both group (intervention – Control) (95%CI), p-value • 6 months Intervention 0.4 (3.9), Control 0.7 (4.0) Treatment effect -0.3 (-1.3;0.8), p=0.63 • 12 months Intervention 0.8 (4.1), Control 1.3 (4.5) Treatment effect -0.5 (-1.7;0.7), p=0.39 • 24 months Intervention 1.4 (5.0), Control 1.9 (5.2) Treatment effect -0.5 (-2.0; 1.0), p=0.49
• **Overall mortality**	Overall mortality • 6 month n=40 (13.7%) • 12 months n=53 (18.2%) • 24 months n=63 (21.7%)
• **Patient-Reported Functional Measures**	Intervention/Control [mean difference between follow-up (6 or 12 months baseline) and baseline (SD)] or median score [Q1;Q3] Treatment effect: difference between variation from baseline in both group (intervention – Control) (95%CI), p-value • Activities of Daily Living (ADL), median [Q1;Q3]; range 0-11 (high score indicates low impairment)

- 6 months

  Intervention 10 [7;11], Control 8 [6;11]

  Treatment effect 1.0 (0.2;1.8), p=0.03

- 12 months

  Intervention 10 [8;11], Control 10 [6;11]

  Treatment effect 0.9 (0.0;1.7), p=0.05

- 24 months

  Intervention 8.9 [8; 11], Control 8.8 [7; 11]

  Treatment effect 0.1 (-0.7; 0.9), p=0.94

- Short Musculoskeletal Function Assessment physical function (XSMFA-F), median [Q1;Q3]; range 0-100 (high score indicates high impairment)
  - 6 months

    Intervention 31 [12;58], Control 46 [17;76]

    Treatment effect -8.9 (-17.0;-0.7), p=0.04

  - 12 months

    Intervention 17 [6;54], Control 36 [9;61]

    Treatment effect -6.8 (-15.0;1.5), p=0.15

  - 24 months

    Intervention 20.8 [0; 29], Control 25 [0; 31]

    Treatment effect -2.5 (-10.9; 5.9), p=0.37

- Short Musculoskeletal Function Assessment disability (XSMFA-B), median [Q1;Q3]; range 0-100 (high score indicates high impairment)
  - 6 months

    Intervention 38 [12;69], Control 56 [25;81]

    Treatment effect -9.9 (-18.5;-1.2), p=0.03

  - 12 months

    Intervention 25 [6;50], Control 38 [11;69]

    Treatment effect -8.6 (-17.2;0.1), p=0.06

  - 24 months

    Intervention 18.75 [0; 62], Control 25 [6;62]

    Treatment effect -3.2 (-12.7; 6.4), p=0.46

- Neuropathic Symptom Score (NSS), mean difference (SD); NSS range 0 to 10 (high score indicates high impairment)
  - 6 months

    Intervention 0.6 (3.3), Control 0.6 (3.4)

    Treatment effect 0.0 (-0.9;0.9), p=0.98

  - 12 months

    Intervention 0.9 (3.5), Control 0.7 (3.5)

    Treatment effect 0.1 (-0.8;1.1), p=0.77

  - 24 months

Intervention 1.3 (3.7), Control 1.5 (3.7)

Treatment effect -0.1 (-1.2; 0.9), p=0.79

- Graded Chronic Pain Scale Disability Score (GCPS-DS), mean difference (SD); GCPS-DS range 0 to 100 (high score indicates high impairment)
  - 6 months

    Intervention -8.0 (36.9), Control -5.6 (40.5)

    Treatment effect -2.4 (-12.9;8.1), p=0.65
  - 12 months

    Intervention -14.8 (34.0), Control -7.6 (37.1)

    Treatment effect -7.2 (-17.3;2.8), p=0.16
  - 24 months

    Intervention -6.7 (40.0), Control -4.8 (37.5)

    Treatment effect -1.9 (-13.4; 9.6), p=0.74
- Graded Chronic Pain Scale Pain Intensity (GCPS-PI), mean difference (SD); GCPS-PI range 0 to 100 (high score indicates high impairment)
  - 6 months

    Intervention -6.8 (23.7), Control -7.7 (27.9)

    Treatment effect 1.0 (-6.0;7.9), p=0.78
  - 12 months

    Intervention -11.7 (22.1), Control -9.6 (28.9)

    Treatment effect -2.1 (-9.4;5.2), p=0.57
  - 24 months

    Intervention -6.0 (30.1), Control -10.1 (29.7)

    Treatment effect 4.1 (-4.7; 12.9), p=0.36
- Malnutrition Universal Screening Tool (MUST) >low risk, N (%)
  - 6 months

    Intervention 8 (7.3), Control 9 (8.8)

    Treatment effect OR (95%CI) 0.8 (0.3;2.5), p=0.80
  - 12 months

    Intervention 5 (4.7), Control 6 (6.4)

    Treatment effect OR (95%CI) 0.7(0.2;3.0), p=0.76
  - 24 months

    Intervention 2 (2.0), Control 3 (3.4)

    Treatment effect OR (95%CI) 1.7 (0.3; 13.1), p=0.67
- Body Mass Index BMI (kg/m²), mean difference (SD); BMI range 9 to 46 (high and low scores indicate high impairment)
  - 6 months

    Intervention -0.1(3.5), Control 5.8 (24.9)

    Treatment effect 0.7 (-0.2;1.7), p=0.14
  - 12 months

	Intervention 1.0 (3.1), Control 0.3 (3.5) Treatment effect 0.6 (-0.3;1.6), p=0.19 o 24 months Intervention 2.3 (4.2), Control 1.3 (3.7) Treatment effect 0.9 (-0.3; 2.1), p=0.13 • Regensburg Insomnia Scale (RIS), median [Q1;Q3]; range 0-40 (high score indicates high impairment) o 6 months Intervention 10 [7;14], Control 11 [7;18] Treatment effect -1.9 (-3.7;-0.1), p=0.14 o 12 months Intervention 9 [6;13], Control 12 [7;15] Treatment effect -1.8 (-3.5;-0.1), p=0.03 o 24 months Intervention 0.7 (7.9), Control 11.6 (8.1) Treatment effect -1.0 (-3.3; 1.3), p=0.36
Limitations and other comments	
• **Limitations and notes**	• Minimum sample size reached • Intervention integrity went as planned
• **Authors' conclusions**	Among sepsis survivors, a primary-care-focused team-based intervention did not improve mental HRQoL or impact PCP care compared with usual care One year after termination of a primary care management intervention (24 months after discharge from the ICU) there was no evidence of improved mental health-related quality of life or physical function among survivors of sepsis. An increase in late-onset PTSD symptoms in the control group suggests a possible protective effect of the intervention. Even 24 months after intensive care unit admission, sepsis survivors experienced mental and physical impairment and increased mortality.

Appendix 4.2.3. Diaries

Akerman 2018[70]	
Methods	
• **Design**	Descriptive and explorative cohort design
• **Source of funding and competing interest**	Funding: No grant from funding agencies Competing interest: the authors declared no conflict of interest
• **Setting**	4 Swedish mixed ICUs (two university and two county hospitals).
• **Sample size**	441 patients were included. It remained 419, 314 and 261 patients respectively at 2, 6 and 12 months
• **Duration and follow-up**	Duration: 1 year Follow-up: at 2, 6, and 12 months

• **Statistical analysis**	Descriptive statistics, Chi-squared tests, Mann-Whitney, Student's t-tests, general linear model Missing values on a question were replaced by using the series mean.
Patient characteristics	
• **Eligibility criteria**	≥18 y, ICU LOS ≥ 24 h, identified administrative database
• **Exclusion criteria**	Patients without address or living abroad
• **Patient & disease characteristics**	Number of participants : Follow-up visit (n = 239), No follow-up visit (n = 202), Diary (n = 183) No diary (n = 258) Age [mean (SD)] : *Follow-up visit* yes 63y (15.1) no 63y (15.8), p=ns – *Diary* yes 62y (14.8) no 64y (15.7), p=ns Gender (% of male): *Follow-up visit* yes 62% no 58%, p=ns – *Diary* yes 64% no 58%, p=ns Time on Ventilator [median, (Q1-Q3)]: *Follow-up visit* yes 41h (0–118) no 3,5h (0–43), p<0.001 – *Diary* yes 73.5h (18–186) no 0h (0–29), p<0.001 LOS in ICU (days) median, (Q1-Q3)b *Follow-up visit* yes 4 (2–8), no 2 (2–4), p<0.001 – *Diary* yes 6 (3–11) no 2 (1,5–3), p<0.001 EMRc mean, (SD±) *Follow-up visit* yes 33.7 (23.2) no 28.7 (22.4), p<0.05 – *Diary* yes 36.3 (23.8) no 28.0 (6), p<0.001 SAPS IIIc mean (SD±) *Follow-up visit* yes 57.1 (15.2) no 54.4 (13.9) 0.059, p=ns – *Diary* yes 58.4 (15.9) no 54 (13.4), p<0.002
Exposures	
• **Intervention group**	**Duration**: 12 months **Starting date:** 2 months post ICU discharge **Setting**: hospital **Frequency**: 3 follow-up visits **Content**: Patients were invited to follow-up where they were briefed on the content of the diary, what happened during their time in the ICU and in their recovery process.
• **Control group**	No diaries or no follow-up visit
Results	
• **Physical limitations**	3-set 4P questionnaire (score ranges from 0 to 4 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 1.97 (1.14) vs no follow-up visit 1.99 (1.22), p=ns o At 6 months Follow-up visit 2.18 (1.25) vs no follow-up visit 2.20 (1.29), p=ns o At 12 months

	Follow-up visit 2.33 (1.30) vs no follow-up visit 2.28 (1.32), p=ns • Diary [mean score (SD), p-value] o At 2 months Diary 1.88 (1.16) vs no diary 2.04 (1.19), p=ns o At 6 months Diary 2.12 (1.25) vs no diary 2.20 (1.29), p=ns o At 12 months Diary 2.28 (1.31) vs no diary 2.34 (1.30), p=ns
• **Physical condition**	3-set 4P questionnaire (score ranges from 0 to 2 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 1.12 (1.14) vs no follow-up visit 1.09 (1.22), p=ns o At 6 months Follow-up visit 1.20 (0.55) vs no follow-up visit 1.17 (0.56), p=ns o At 12 months Follow-up visit 1.15 (0.56) vs no follow-up visit 1.17 (0.47), p=ns • Diary [mean score (SD), p-value] o At 2 months Diary 1.09 (0.61) vs no diary 1.11 (0.52), p=ns o At 6 months Diary 1.20 (0.55) vs no diary 1.17 (0.56), p=ns o At 12 months Diary 1.19 (0.57) vs no diary 1.12 (0.48), p=ns
• **Change in appearance**	3-set 4P questionnaire (score ranges from 0 to 4 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 3.04 (0.78) vs no follow-up visit 3.19 (0.72), p<0.05 o At 6 months Follow-up visit 3.01 (0.91) vs no follow-up visit 3.32 (0.68), p<0.001 o At 12 months Follow-up visit 3.21 (0.77) vs no follow-up visit 3.40 (0.53), p<0.05 • Diary [mean score (SD), p-value]

	o At 2 months Diary 2.94 (0.85) vs no diary 3.23 (0.66), p<0.05 o At 6 months Diary 3.01 (0.91) vs no diary 3.32 (0.68), p<0.05 o At 12 months Diary 3.15 (0.81) vs no diary 3.41 (0.54), p<0.05
• **Mood**	3-set 4P questionnaire (score ranges from 0.25 to 6 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 4.97 (0.98) vs no follow-up visit 5.04 (1.05), p=ns o At 6 months Follow-up visit 4.97 (0.92) vs no follow-up visit 5.15 (0.86), p=ns o At 12 months Follow-up visit 4.79 (1.01) vs no follow-up visit 5.06 (0.98), p<0.05 • Diary [mean score (SD), p-value] o At 2 months Diary 4.90 (0.99) vs no diary 5.07 (1.01), p=ns o At 6 months Diary 4.95 (0.92) vs no diary 5.07 (0.94), p=ns o At 12 months Diary 4.74 (1.06) vs no diary 5.03 (0.92), p<0.05
• **Memory**	3-set 4P questionnaire (score ranges from 0.33 to 5 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 4.31 (0.92) vs no follow-up visit 4.40 (0.87), p=ns o At 6 months Follow-up visit 4.15 (1.05) vs no follow-up visit 4.47 (0.79), p<0.05 o At 12 months Follow-up visit 4.14 (1.03) vs no follow-up visit 4.59 (0.71), p<0.001 • Diary [mean score (SD), p-value] o At 2 months Diary 4.22 (0.98) vs no diary 4.42 (0.85), p<0.05 o At 6 months

	Diary 4.09 (1.06) vs no diary 4.48 (0.82), p<0.001 o At 12 months Diary 4.04 (1.13) vs no diary 4.57 (0.63), p<0.001
• **Social life**	3-set 4P questionnaire (score ranges from 0 to 3 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 0.73 (0.62) vs no follow-up visit 0.59 (0.54), p<0.01 o At 6 months Follow-up visit 0.79 (0.65) vs no follow-up visit 0.62 (0.52), p<0.05 o At 12 months Follow-up visit 0.90 (0.66) vs no follow-up visit 0.77 (0.68), p=ns • Diary [mean score (SD), p-value] o At 2 months Diary 0.79 (0.62) vs no diary 0.58 (0.55), p<0.001 o At 6 months Diary 0.71 (0.60) vs no diary 0.64 (0.55), p=ns o At 12 months Diary 0.93 (0.75) vs no diary 0.78 (0.57), p=ns
• **Sleep**	3-set 4P questionnaire (score ranges from 0 to 3 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 2.37 (0.65) vs no follow-up visit 2.39 (0.66), p=ns o At 6 months Follow-up visit 2.42 (0.68) vs no follow-up visit 2.40 (0.60), p=ns o At 12 months Follow-up visit 2.47 (0.62) vs no follow-up visit 2.45 (0.58), p=ns • Diary [mean score (SD), p-value] o At 2 months Diary 2.31 (0.66) vs no diary 2.43 (0.65), p=ns o At 6 months Diary 2.42 (0.67) vs no diary 2.46 (0.64), p=ns o At 12 months

	Diary 2.35 (0.60) vs no diary 2.49 (0.58), p=ns
• **Avoidance**	3-set 4P questionnaire (score ranges from 0 to 2 higher scores indicated fewer problems or fewer limitations) • Follow-up visits [mean score (SD), p-value] o At 2 months Follow-up visit 1.88 (0.28) vs no follow-up visit 1.87 (0.29), p=ns o At 6 months Follow-up visit 1.85 (0.33) vs no follow-up visit 1.86 (0.34), p=ns o At 12 months Follow-up visit 1.69 (0.50) vs no follow-up visit 1.76 (0.47), p=ns • Diary [mean score (SD), p-value] o At 2 months Diary 1.87 (0.28) vs no diary 1.87 (0.28), p=ns o At 6 months Diary 1.86 (0.32) vs no diary 1.86 (0.35), p=ns o At 12 months Diary 1.70 (0.48) vs no diary 1.73 (0.52), p=ns
Limitations and other comments	
• **Limitations and notes**	Cohort design so no randomisation leading in imbalance between groups Large sample size Multicentre design Not all patients completed the questionnaire at all 3 time points No multivariate analysis Combination effect of diaries and follow-up visits are not studied
• **Authors' conclusions**	The groups having follow-up or a diary after an ICU stay did not show significant positive effects on patients reported problems after ICU discharge.

Bäckman 2010[71]	
Methods	
• **Design**	Non-randomised, prospective study
• **Source of funding and competing interest**	Funding: No statement Competing interest: No statement

• **Setting**	Non-academic eight-bedded general ICU in Sweden
• **Sample size**	499 patients were enrolled in the study (459 in no diary group and 40 in diary group). After 36-month follow-up, 97 patients remained in the group without diary and 29 in the group with diary
• **Duration and follow-up**	Duration: between March 2002 and June 2004 Follow-up: 6, 12, 24 and 36 months
• **Statistical analysis**	Descriptive statistics, Pearson's Chi square, Student's t-test, multiple regression model adjusted for age, sex, presence of pre-existing disease, APACHE II score on admission, diagnostic category and duration of stay in hospital, MANOVA (longitudinal changes on HRQoL).
Patient characteristics	
• **Eligibility criteria**	>17 y, ICU LOS > 24 h, being alive 6 months after discharge from the hospital
• **Exclusion criteria**	None mentioned
• **Patient & disease characteristics**	Number of participants Diary group (n=38) No-diary group (n=224) at 6 months Gender (number of Male/female): Diary group 20/18, no-diary group 90/134, p=ns Age [mean (SD)]: Diary group 50.7y (17.2) , no-diary group 62.2y (17.8), p<0.001 Presence of concurrent disease: Diary group 58%, no-diary group 71%, p=ns APACHE II score [mean (SD)]: Diary group 18.7 (7.3) , no-diary group 14.1 (6.5), p<0.001 ICU admission diagnosis: Respiratory Diary group 37% no-diary group 17% – Gastrointestinal Diary group 18% no-diary group 22% – Multiple trauma Diary group 16% no-diary group 7% – Sepsis Diary group 5% no-diary group 6% – Other Diary group 24% no-diary group 48%, p<0.01 Mechanical ventilation: Diary group 89.5M , no-diary group 22.3%, p<0.001 Hours on ventilator [median (p25–p75)] : Diary group 216 (47–371) , no-diary group 19, 0 (0–0), p<0.001 Hours in ICU [median (p25–p75)] : Diary group 274 (126–499) , no-diary group 50 (35–93), p<0.001 Days in hospital [median (p25–p75)] : Diary group 14 (6–27) , no-diary group 8 (4–18), p<0.001
Exposures	
• **Intervention group**	**Duration**: 36 months **Starting date:** entries in the diaries started during the first 2 days after ICU admission **Setting**: Hospital **Frequency**: 1 patient visits **Content**: Diaries were done for patients with most severely ill intensive care and with a high likelihood of needing sedation and mechanical ventilation.

	A standard set of rules was followed to complete the patient diary using everyday language, a summary included the reason for admission, initial events on the ICU and the current state of the illness. Nurse, nurse assistant, physician, physiotherapist, relatives and close friends, was allowed to contribute to the patient's diary. Photographs of the patient were included in the ICU-diary. The diary was continued up to the time of discharge from hospital or death. Photographs were shown and explained during a follow-up visit 2–8 weeks after discharge from the ICU. As the ICU-diary was handed over to the patient at the end of the follow-up visit.
• **Control group**	No diary
Results	
• **HRQoL**	SF-36 at 6 months (number of participants Diary (n=38) and No-diary (n=224) • Physical functioning: Diary 64.4 (30.5) vs No-diary 59.7 (30.4), p=ns • Role physical: Diary 52.7 (44.8) vs No-diary 42.6 (42.7), p=ns • Bodily pain: Diary 67.5 (27.9) vs No-diary 59.3 (29.9), p=ns • General health: Diary 66.3 (23.4) vs No-diary 52.3 (24.2), p<0.001 • Vitality: Diary 63.2 (24.9) vs No-diary 51.7 (24.7), p<0.005 • Social function: Diary 75.0 (29.9) vs No-diary 69. 0 (27.9) p=ns • Role emotional: Diary 69.4 (41.7) vs No-diary 60.2 (43.6) p=ns • Mental health: Diary 72.4 (25.4) vs No-diary 69.4 (22.9) p=ns • Physical component score: Diary 42.4 (12.1) vs No-diary 38.0 (13.0), p<0.05 • Mental component score: Diary 47.2 (14.3) vs No-diary 44.8 (13.2), p=ns Changes over time in general health, vitality and the mental component score differed significantly between groups after controlling for age, APACHE II score, admission diagnosis and length of hospital stay (general health and vitality: p<0.05, mental component score: P<0.01; repeated measures MANOVA).
Limitations and other comments	
• **Limitations and notes**	• Selection bias : ICU-diaries were kept for a selected group of the most severely ill intensive care • Mono centre

	• No randomisation • Imbalance in baseline characteristics between group • No information about QoL before the ICU • Low response rate in the No-diary group potentially due to avoidance behaviour indicative of post-traumatic stress disorder • Small sample size in the diary group • Some data are reported only in graph
• **Authors' conclusions**	The use of an ICU-diary during critical illness together with a follow-up visit during the convalescent period was associated with higher scores in two health-related QoL dimensions (physical and mental well-being) during the 3-year period after discharge. The size of the difference, favouring the Diary group, was 45%, which is of clinical importance. The improvement, which was already noted 6 months after discharge, was sustained in both dimensions over the 3-year follow-up period.

Garrouste-Orgeas 2012[64]	
Methods	
• **Design**	Prospective open before after study
• **Source of funding and competing interest**	Funding: No statement Competing interest: No statement
• **Setting**	Medical-surgical ICU including 460-bed in Paris (France).
• **Sample size**	143 patients were included (48 in the pre-diary period, 49 in the diary period, and 46 in the post-diary period). After 3 months, 136 family members and 52 patients remained in the study. After 1y, 115 family members and 56 patients remained in the study.
• **Duration and follow-up**	Duration: between May 2008 and November 2009 Follow-up: at 3 and 12 months post-ICU
• **Statistical analysis**	Descriptive statistics, Kruskal-Wallis or chi-square test, logistic and linear regressions
Patient characteristics	
• **Eligibility criteria**	ICU LOS ≥ 4 days
• **Exclusion criteria**	death on day 4, unwillingness of the family to participate, patient and/or family not fluent in French, no visits from relatives on the discharge day (when family questionnaires were to be completed), and dementia
• **Patient & disease characteristics**	Prediary n = 48 Diary n = 49 Post-diary n = 46 p-value are ns unless mentioned **Patient characteristics** Age [mean (sd)]: Pre-diary 67.5y (13.5) vs Diary 65.4y (16.8) vs Post-diary 61.8y (15.9) Male:

Pre-diary 25/48 vs Diary 33/49 vs Post-diary 25/46

Treatments in the past 3 months: Antidepressant Pre-diary 6/48 vs Diary 2/49 vs Post-diary 8/46 – Anxiolytic Pre-diary 8/48 vs Diary 7/49 vs Post-diary 7/46

Previous psychiatric hospitalization: Pre-diary 3/48 vs Diary 2/49 vs Post-diary 6/46

Previous psychiatric outpatient care: Pre-diary 9/48 vs Diary 3/49 vs Post-diary 9/46

ICU admission characteristics

Simplified Acute Physiological Score II [mean (sd)]: Pre-diary 44.3 (13.9) vs Diary 41.2 (14.6) vs Post-diary 39.9 (15)

Logistic Organ Dysfunction score [mean (sd)]: Pre-diary 5.2 (2.4) vs Diary 4.4 (2.1) vs Post-diary 4.2 (2.5)

Admission category : Medicine Pre-diary 35/48 vs Diary 40/49 vs Post-diary 35/46

Unscheduled surgery: Pre-diary 8/48 vs Diary 5/49 vs Post-diary 6/46

Scheduled surgery: Pre-diary 5/48 vs Diary 4/49 vs Post-diary 5/46

Reason for admission: Septic shock and multiple organ failure Pre-diary 27/48 vs Diary 12/49 vs Post-diary 7/46 – Other shock Pre-diary 14/48 vs Diary 5/49 vs Post-diary 5/46 – Acute respiratory insufficiency Pre-diary 44/48 vs Diary 15/49 vs Post-diary 12/46 – Exacerbation of chronic obstructive pulmonary disease Pre-diary 14/48 vs Diary 0/49 vs Post-diary 5/46 – Acute renal insufficiency Pre-diary 5/48 vs Diary 1/49 vs Post-diary 3/46 – Coma Pre-diary 15/48 vs Diary 5/49 vs Post-diary 5/46 – Monitoring Pre-diary 24/48 vs Diary 10/49 vs Post-diary 9/46

ICU stay characteristics

Endotracheal mechanical ventilation: Pre-diary 38/48 vs Diary 38/49 vs Post-diary 31/46

Epinephrine/norepinephrine: Pre-diary 28/48 vs Diary 23/49 vs Post-diary 19/46

Dobutamine : Pre-diary 6/48 vs Diary 7/49 vs Post-diary 4/46

Dialysis : Pre-diary 14/48 vs Diary 6/49 vs Post-diary 8/46

Central venous catheter: Pre-diary 37/48 vs Diary 30/49 vs Post-diary 27/46

Arterial catheter: Pre-diary 31/48 vs Diary 28/49 vs Post-diary 18/46, $p< 0.05$

Events during the ICU stay

Cardiac arrest: Pre-diary 1/48 vs Diary 4/49 vs Post-diary 2/49

Self-extubation: Pre-diary 4/48 vs Diary 7/49 vs Post-diary 4/49

Extubation failure: Pre-diary 3/48 vs Diary 1/49 vs Post-diary 1/49

Ventral decubitus: Pre-diary 5/48 vs Diary 1/49 vs Post-diary 1/49

Treatment during the ICU stay, days [(n), mean ± sd]

Corticosteroids Pre-diary (32/48) 9.4 days± 9.2 vs Diary (16/49) 9.8 days ± 8.1 vs Post-diary (19/46) 7.2 days ± 5.8, $p<0.05$

Benzodiazepines Pre-diary (36/48) 6.6 days ± 6 vs Diary (31/49) 6.5 days ± 8.4 vs Post-diary (25/46) 5.1 days ± 4.3

	Morphine Pre-diary (37/48) 7.5 days ± 6.7 vs Diary (34/49) 7.6 days ± 10.1 vs Post-diary (28/46) 7 days ± 8.6 Neuromuscular blockers Pre-diary (23/48)) 3.7 days ± 4.2 vs Diary (23/49) 2.7 days ± 3 vs Post-diary (23/46) 3.3 days ± 4 Withdrawing and withholding decisions: Pre-diary 4/48 vs Diary 3/49 vs Post-diary 2/46 ICU stay length [mean ± sd]: Pre-diary 21.2 days ± 15.6 vs Diary 18.2 days ± 22.9 vs Post-diary 13 days ± 18, p<0.05 *Discharge characteristics* ICU mortality: Pre-diary 10/48, Diary 6/49, Post-diary 5/46 Post-ICU hospital stay length [mean ± sd): Pre-diary 35.1 days ± 67.1 vs Diary 19.5 ± 30.4 vs Post-diary 13.5 ± 18.7 Post hospital 3-month mortality: Pre-diary 7/48 vs Diary 9/49 vs Post-diary 8/46 **Characteristics of the relatives** Geographic origin: France Pre-diary 39/48 vs Diary 41/49 vs Post-diary 32/46 – Africa Pre-diary 5/48 vs Diary 2/49 vs Post-diary 8/46 – European countries other than France Pre-diary 2/48 vs Diary 5/46 vs Post-diary 1/46 – Other Pre-diary 2/48 vs Diary 1/49 vs Post-diary 5/46 Relationship with the patient: Spouses Pre-diary 13/48 vs Diary 22/49 vs Post-diary 18/46 – Grown children Pre-diary 16/48 vs Diary 14/49 vs Post-diary 7/46 – Siblings Pre-diary 9/48 vs Diary 4/49 vs Post-diary 7/46 – Parents Pre-diary 6/48 vs Diary 4/49 vs Post-diary 10/46 – Other family members Pre-diary 1/48 vs Diary 5/49 vs Post-diary 4/46 – Friends Pre-diary 3/48 vs Diary 0/49 vs Post-diary 0/46
Exposures	
• **Intervention group**	**Duration**: 12 months pot-ICU discharge **Starting date:** on the fourth calendar day after ICU admission **Setting**: at home **Frequency**: 2 phone calls at 3 and 12 months post-ICU **Content**: During the ICU stay, family members had an interview with the ICU physician shortly after admission to evaluate family distress, to exchange information about the patient, and to identify means of supporting the family. An information leaflet providing general explanations about the ICU is then given to the family. A senior or junior physician or the nurse in charge of the patient explained the study to the relatives. Format of the diary: first pages reported about the purpose of the diary and photos of the room with the equipment but no photographs of hospitalized patients. Following pages were completed by ICU staff and family. The ICU staff described medical events, procedures, and the information given to relatives in an everyday language. No other guidance was given to write in the diary except the avoidance of mentioning confidential matters. The patients received the diary when discharged to wards. Follow-up data on patients and relatives were collected over the phone 3 and 12 months after ICU discharge by the clinical research assistant.

	After 3 months, the study relative and the patient completed the HADS and the Peritraumatic Dissociative Experiences Questionnaire. A single relative per patient was included in the study. This relative was either the person who contributed most of the family diary entries or, when entries were made by many relatives, the closest relative (spouse, grown child, sibling, or other, in that order). At ICU discharge, the study relative completed the HADS.
• **Control group**	No diary
Results	
• **Peritraumatic dissociation at 3 months**	Peritraumatic dissociation was assessed using a questionnaire with 10 items to determine the degree of depersonalization, derealization, amnesia, out-of-body experiences, and alterations in time perception and body image. • Relatives o Mean (SD) Pre and post-diary periods 19.0 (7.9) vs diary period 16.8 (9.1), p=0.3 o Score >15, N (%) Pre and post-diary periods 53 (58.9) vs diary period 17 (37.0), p=0.07 • Patients o Mean (SD) Pre and post-diary periods 27.6 (9.8) vs diary period 22.5 (10.1), p=0.12 o Score >15, N (%) Pre and post-diary periods 25 (78.1) vs diary period 10 (66.7), p=0.3
• **PTSD at 12 months**	IES-R • Relatives o Total score - Mean (SD) Pre and post-diary periods 31.4 (13.6) vs diary period 21.6 (10.7), p=0.0003 - Score >22, N (%) Pre and post-diary periods 55 (74.3) vs diary period 13 (31.7), p<0.0001 o Intrusion [Mean (SD)] Pre and post-diary periods 13.1 (5.4) vs diary period 9.5 (5.1), p=0.002 o Avoidance [Mean (SD)] Pre and post-diary periods 12.3 (5.6) vs diary period 7.6 (4.2), p<0.0001 o Hyperarousal [Mean (SD)]

	Pre and post-diary periods 6 (4.9) vs diary period 4.4 (3.7), p=0.17 • Patients o Total score - Mean (SD) Pre and post-diary periods 32.1 (15.4) vs diary period 21.0 (12.2), p=0.004 - Score >22, N (%) Pre and post-diary periods 25 (69.4) vs diary period 10 (50), p=0.2 o Intrusion [Mean (SD)] Pre and post-diary periods 12.9 (6.1) vs diary period 9.1 (6.1), p=0.018 o Avoidance [Mean (SD)] Pre and post-diary periods 11.9 (6.0) vs diary period 6.8 (3.8), p=0.0005 o Hyperarousal [Mean (SD)] Pre and post-diary periods 7.2 (4.6) vs diary period 5.2 (4.6), p=0.095
• **Anxiety at 3 months**	HADS-A>8 [n (%)] • Relatives Pre and post-diary periods 56 (59.6) vs diary period 18 (38.3), p=0.08 • Patients Pre and post-diary periods 10 (30.3) vs diary period 2 (10), p=0.09
• **Depression at 3 months**	HADS-D>8 [n (%)] • Relatives Pre and post-diary periods 20 (22.0) vs diary period 10 (21.7), p=0.8 • Patients Pre and post-diary periods 13 (39.4) vs diary period 3 (15.8), p=0.07
Limitations and other comments	
• **Limitations and notes**	• Mono centre • Blinding of the assessor may be corrupted during the phone call • Small sample size • No randomisation
• **Authors' conclusions**	The intensive care unit diary significantly [and positively] affected posttraumatic stress–related symptoms in relatives and surviving patients 12 months after intensive care unit discharge.

Garrouste-Orgeas 2019[65]	
Methods	
• **Design**	Assessor-blinded, multicentre, randomized clinical trial
• **Source of funding and competing interest**	Funding: Fondation de France and Saint Joseph Hospital Network. Competing interest: Two authors reported grants from Fondation de France during the conduct of the study. Two authors reported grants from hospital groups (Centre Hospitalier de Troyes and Groupe Hospitalier Paris Saint Joseph). One author received consulting fees for methodology from ICUREsearch society. Finally, four authors received grants, personal fees, and nonfinancial support from device and pharmaceutical firms (MSD France, Pfizer, Sanofi, Astellas, LFB Biomédicament, AKSA, Medical Specialties Distributors, Nabriva and Biomerieux).
• **Setting**	35 French ICUs with physician leaders who were members of the French Society of Intensive Care or French Society of Anaesthesiology.
• **Sample size**	657 patients were randomized (332 patients and 332 family members of patients in intervention group and 325 patients and 325 family members in the control group). At 3 months, 164 patients and 281 family members remained in intervention group while 175 patients and 282 family members remained in control group.
• **Duration and follow-up**	Duration: October 2015 to July 2017. Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, χ2 test, Mann-Whitney test, generalized linear multivariable mixed model, logistic regression
Patient characteristics	
• **Eligibility criteria**	≥18y, mechanical ventilation ≥ 48h and initiated within 48h of ICU admission, have a family member present during the inclusion period and able to visit the patient during the ICU stay. Both the patient and family member had to have sufficient French-language skills for follow-up telephone interviews.
• **Exclusion criteria**	no visiting family members, under legal guardianship, psychosis or dementia, acute neurologic diseases, cardiac arrest at admission, mute or deaf, highly likely to lead to death or withdrawal of life support within 48h or included in another trial with a telephone interview after ICU discharge.
• **Patient & disease characteristics**	**Patients** *Baseline characteristics* Age [Median (IQR)]: Intervention group 66y (56-73), Control group 64y (54-72) Female gender (%): Intervention group 32.8%, Control group 36.0% Severity of illness on admission (Simplified Acute Physiologic Score [Median (IQR)]: Intervention group 57 (43-72), Control group 56 (42-69) Patient status (%): Medical patients Intervention group 76.2%, Control group 78.8% – Scheduled surgery Intervention group 3.9%, Control group 4% – Unscheduled surgery Intervention group 19.9%, Control group 17.2%

Main symptoms at admission (%):

Acute respiratory failure/COPD Intervention group 41.3%, Control group 44.9% – Shock and multi-organ failure Intervention group 41.3%, Control group 37.5% – Acute renal failure Intervention group 1.8%, Control group 0% – Coma Intervention group 9.6%, Control group 9.2% – Monitoring/ Scheduled Surgery Intervention group 1.5%, Control group 3.7% – Metabolic Intervention group 1.5%, Control group 1.5% – Trauma Intervention group 3%, Control group 3.1%

MacCabe score (subjective prognosis of co-morbid conditions at ICU admission):

No fatal illness Intervention group 65.1%, Control group 69.2% – Fatal illness within 5 years Intervention group 29.2%, Control group 23.4% – Fatal illness within 1 year Intervention group 5.7%, Control group 7.4%

Knaus score (presence or absence of limitation in daily activities): No limitation Intervention group 38.6%, Control group 40.9% – Moderate limitation Intervention group 42.2%; Control group 36.6% – Severe limitation Intervention group 16.9%, Control group 17.5% – Total dependency Intervention group 2.4%, Control group 4.9%

Treatment

Treatment [Median (IQR)]: Mechanical ventilation Intervention group 9 days (6-17), Control group 10 days (5-19) – Non-invasive ventilation Intervention group 0 days (0-2), Control group missing value days (0-1) – Fentanyl Intervention group 6 days (3-11) Control group 6 days (3-10) – Benzodiazepines Intervention group 4 days (2-8) Control group 4 days (2-8) – Propofol Intervention group 0 (0-3), Control group 1 (0-4)

ICU events: Self-extubation Intervention group 5.4%, Control group 5.5% – Weaning failure and re-intubation Intervention group 9%, Control group 11.7% – Unexpected cardiac arrest Intervention group 9.3%, Control group 8% – Episode of delirium Intervention group 25.6%, Control group 28.9% – Fall Intervention group 1.5%, Control group 0.6% – Physical constraints Intervention group 66%, Control group 69.5%

Outcome

Decisions to Forgo Life-Sustaining Treatments: None Intervention group 77.8%, Control group 77.9% – Withholding Intervention group 11.4%, Control group 13.5% – Withdrawal Intervention group 6.9%, Control group 4.6% – Withholding and withdrawing Intervention group 7.8%, Control group 4.0%

Duration of ICU stay [Median (IQR)]: Intervention group 13.5 days (8-23) Control group 15 days (9-25)

Duration of hospital stay [Median (IQR)]: Intervention group 22.5 days (12 (41.5) Control group 25 days (14-44)

Hospital mortality: Intervention group 37.0% Control group 30.8%

Families

Age [Median (IQR)]: Intervention group 55y (45-66), Control group 54y (44-66)

Female gender: Intervention group 72.9%, Control group 71.7%

Relationship with the patient: Spouse/ Partner Intervention group (53.6), Control group (55.9) – Children Intervention group (33.1), Control group

	(30.2) – Parents Intervention group (4.5), Control group (4.0) – Other Intervention group (8.7), Control group (9.9) Job occupation: Primary (agriculture) Intervention group 0, Control group 0% – Secondary (industries) Intervention group 5.0%, Control group 8.6% – Tertiary (commerce or activities related to administration or human health or public action) Intervention group 65.8%, Control group 64.4% – None Intervention group 9.0%, Control group 7.6% – Retired Intervention group 20.2%, Control group 19.4% Health occupation: Intervention group 12%, Control 10.7% Educational level: None Intervention group 0.6%, Control group 1.6% – Upper secondary education Intervention group 17.4%, Control group 14.8% – High school Intervention group 18.7%, Control group 19.6% – Technical college Intervention group 27.7%, Control group 31.8% – Associate degree Intervention group 10.0%, Control group 6.7% – Bachelor degree Intervention group 12.1%, Control group 15.4% – Master degree Intervention group 13.4%, Control group 10.0%
Exposures	
• **Intervention group**	**Duration**: during the ICU stay **Starting date:** at admission in ICU **Setting**: ICU **Frequency**: Entries should be made at least daily **Content**: The ICU diary was the same A4 notebook for all centres kept in the patient room available for physicians, nurses and family members. The first page was composed of a text describing the purpose of the diary and the persons who can use it. The following pages contained pictures of the ICU and of a patient room, and the list and phone numbers of the clinicians who may be in relation with the family members. The following pages are dedicated to entries from clinicians and family members. The first entry was written by physician or nurse and described the reason of ICU admission. Family members were encouraged by the healthcare professionals to write inside at will. Prior to ICU discharge, a concluding note was written by an ICU clinician The ICU diary was detailed to the patient in the ICU room a few days before discharge and was given to the patient. In cases of death in which the patient died, the diary was concluded with a condolence letter and mailed to the family.
• **Control group**	Usual ICU care without ICU diary.
Results	
Patient outcomes	
• **PTSD**	• Presence of PTSD symptoms (IES-R score>22) Risk difference (95% CI): −4 (−15 to 6), p=0.39 • IES-R score [median (IQR)] o Total score Difference (95% CI): −1.47 (−1.93 to 4.87), p=0.38 o Intrusion Difference (95% CI): −0.25 (−1.64 to 1.12),p=0.74 o Avoidance Difference (95% CI): −1.01 (−2.35 to 0.33), p=0.08 o Hyperarousal Difference (95% CI): −0.08 (−1.11 to 0.94), p=0.64

• **Anxiety and depression**	• HADS score [median (IQR)] o Total score Difference (95% CI): −0.75 (−2.27 to 0.78), p=0.30 o HADS-A score Difference (95% CI): −0.36 (−1.22 to 0.50), p=0.72 o HADS-D score Difference (95% CI): −0.39 (−1.29 to 0.52), p=0.66 • Symptoms of anxiety Risk difference (95% CI): 0.7 (−9 to 11), p=0.91 • Symptoms of depression Risk difference (95% CI): 5 (−5 to 13), p=0.35
• **Memories**	ICU memory tool questionnaire 3 months after ICU discharge. • Memories of the ICU stay o Factual memories Risk difference (95% CI): 0.4 (−7 to 8), p=0.90 Score difference (95% CI): −0.32 (−1.03 to 0.39), p=0.44 o Emotional memories Risk difference (95% CI): 4 (−6 to 13), p=0.45 Score difference (95% CI): −0.15 (−0.58 to 0.27), p=0.51 o Delusional memories Risk difference (95% CI): 0 (−11 to 11), p >0.99 Score difference (95% CI): (−0.35 to 0.22), p=0.57 • Memories of the hospital stay before ICU admission Risk difference (95% CI): 3 (−6 to 13), p=0.50 • Memory of being in the ICU Risk difference (95% CI): 6 (−4 to 17), p=0.23 • Memories of transfer from ICU to ward Risk difference (95% CI): −3 (−11 to 5), p=0.56 • Unexplained feelings of panic and apprehension Risk difference (95% CI): 2.7 (− 7 to 12), p=0.67 • Intrusive memories just before hospital admission Risk difference (95% CI): −2 (−12 to 8), p=0.67 • Discussion of ICU with family member Risk difference (95% CI): −2 (−10 to 7), p=0.71 • Discussion of ICU with friend Risk difference (95% CI): −5 (−16 to 7), p=0.41 • Discussion of ICU with nurse on the ward Risk difference (95% CI): −3 (−13 to 8), p=0.50 • Discussion of ICU with physician of the ward Risk difference (95% CI): −4 (−14 to 7), p=0.47

	• Discussion of ICU with family physician Risk difference (95% CI): −2 (−13 to 9), p=0.86
Family outcomes	
• **PTSD**	• Presence of PTSD symptoms (IES-R score>22) Risk difference (95% CI): 3 (−6 to 11), p=0.53 • IES-R score [median (IQR)] o Total score Difference (95% CI): 0.48 (−2.51 to 3.47), p=0.87 o Intrusion Difference (95% CI): 0.15 (−1.08 to 1.37), p=0.87 o Avoidance Difference (95% CI): 0.14 (−0.91 to 1.20), p=0.72 o Hyperarousal Difference (95% CI): 0.17 (−0.76 to 1.12), p=0.99 o Avoidance score 6 (2-11) 5 (2-11) 0.14 (−0.91 to 1.20), p=0.72
• **Anxiety and depression**	• HADS score [median (IQR)] o Total score Difference (95% CI): 0.33 (−0.96 to 1.63), p=0.45 o HADS-A score Difference (95% CI): 0.28 (−0.47 to 1.04), p=0.65 o HADS-D score Difference (95% CI): 0.05 (−0.67 to 0.78), p=0.96 • Presence of anxiety (HADS-A score >8) Risk difference (95% CI): 2 (−6 to 11), p=0.56 • Presence of depression (HADS-D score >8) Risk difference (95% CI): 1 (−6 to 8), p=0.77
Limitations and other comments	
• **Limitations and notes**	• Too short follow-up (3 months) • No baseline assessment of the outcomes • Variation in the completion of the diaries by the clinicians • No evaluation about how patients and families shared the diary
• **Authors' conclusions**	Among patients receiving mechanical ventilation in the ICU, the use of an ICU diary did not significantly reduce the percentage of patients who reported significant PTSD symptoms at 3months. These findings do not support the use of ICU diaries for preventing PTSD symptoms.

Jones 2010[72]	
Methods	
• **Design**	Non-blinded randomized control trial
• **Source of funding and competing interest**	Funding: Stanley Thomas Johnson Foundation; The Lundbeck Foundation and the Danish Health Insurance Foundation; Tryg Foundation, Aase & Ejnar Danielsen's Foundation, and Augustinus Foundation, Denmark, Regional Research fund of Västra, Götaland, Sweden and contributions from the various hospitals.

	Competing interest: The authors declare that they have no competing interests
• **Setting**	in 12 hospitals (6 general district hospitals and 6 university hospitals) in 6 European countries (Denmark, Italy, Norway, Portugal, Sweden and UK)
• **Sample size**	352 patients were randomised (177 intervention group and 175 controls). 333 completed their three-month follow-up questionnaires (162 intervention group and 160 controls): 11 patients lost to follow-up, 11 patients had an pre-existing PTSD and 8 patients died.
• **Duration and follow-up**	Duration: between 2006 to 2008 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, t tests and Mann Whitney U test, ANOVA, Scheffé post hoc test (for multiple comparisons), Fisher's exact test
Patient characteristics	
• **Eligibility criteria**	≥ 16y, ICU LOS ≥ 72 h and ventilated≥ 24 h
• **Exclusion criteria**	Not able to give informed consent, severe traumatic brain injury, schizophrenic, manic depression or diagnosed PTSD
• **Patient & disease characteristics**	*Patient characteristics at randomisation* Age [median (range)]: Control group 59y (18-82), Intervention group 60y (18-81), p=ns ICU stay [median (range)]: Control group 13 days (3-71), Intervention group 13 days (3-79) , p=ns Hours ventilated [median (range)]: Control group 240 (24-1200), Intervention group 212 (24-1500) , p=ns APACHE II severity score [median (range)]: Control group 18 (2-39), Intervention group 20 (5-46) , p=ns Total PTSS 14 score at 1 month [median (range)]: Control group 25 (13-65), Intervention group 22.5 (14-84) , p=ns Previous psychological problems: Control group 29%, Intervention group 29%, p=ns Previous traumatic experiences: Control group 22%, Intervention group 18%, p=ns Recall of delusional memories: Control group 52%, Intervention group 54% , p=ns Emergency admission to ICU: Control group 93%, Intervention group 89%, p=ns Gender (Male/female): Control group 104/71, Intervention group 123/54, p=0.045 Diagnostic groups: Respiratory failure Control group 23%, Intervention group 20%, p=ns – Sepsis Control group 19%, Intervention group 12%, p=ns – Circulatory failure Control group 13%, Intervention group 12%, p=ns – Multi-organ failure Control group 11%, Intervention group 17%, p=ns – Trauma Control group 14%, Intervention group 15%, p=ns – Combined (pulmonary/circulatory) Control group 10%, Intervention group 11%, p=ns – Gastrointestinal failure Control group 5%, Intervention group 8%, p=ns – Neurological failure Control group 3%, Intervention group 3%, p=ns – Other reasons Control group 2%,

	Intervention group 2%, p=ns – Planned Control group 0%, Intervention group 0.5%, p=ns
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** the diary started during ICU stay **Setting**: Outpatient setting at hospital, by phone or at patients' home (few patients only) **Frequency**: Daily record in ICU diary + 2 consultations (at 1 month and 3 months post-ICU). **Content**: ICU diary was hand written in everyday language by study nurses or physician. Family contributed to if they felt they could. Photographs were added. The reason of ICU admission is explained in the diary. Patients were randomised at 1 month post-ICU. Patients in intervention group received their diaries as soon as they wanted and the diary was discussed with the study nurse during the first consultation.
• **Control group**	The control group received the same intervention than those in intervention group but received their diaries only at 3 months post-ICU
Results	
• **New-onset PTSD**	Proportion of patients with PTSS-14 scores ≥ 45 Control group 13.1% vs intervention group 5%, p=0.02
• **ICU seen as traumatic**	Control group 47.5% vs intervention group 43.2%, p=0.36
• **Change in PTSD score over time**	Change in the PTSS-14 scores between 1 and 3 months • Overall sample no overall difference between the controls and interventions, p=0.737 (detailed data no showed) • Patients with PTSS-14 scores ≥ 45 [median difference between 1 and 3 months] Control group -2 vs intervention group -23, p=0.04
Limitations and other comments	
• **Limitations and notes**	• Multicentre and international RCT • Sample size calculation and minimal sample size was reached and low attrition rate was observed • More females in the control group and gender may influence the level of PTSD-related symptoms • Blinding of assessor was corrupted by some patients but blinding was kept for diagnosis of PTSD • PTSD Diagnostic Scale took one hour to be completed, it was probably long for some patients at 1 month post-ICU • Low number of patients for analysis for the sub-group analysis on patients with PTSS-14 scores ≥ 45
• **Authors' conclusions**	The provision of an ICU diary was associated with a reduction in the incidence of new-onset PTSD.

Kredentser 2018[73]	
Methods	
• **Design**	Single Centre, four-arm pilot randomized controlled trial
• **Source of funding and competing interest**	Funding: Manitoba Medical Service Foundation and Canadian Institutes of Health Research Foundation Competing interest: One authors disclosed that he was a consultant for UpTo- Date and has previously held Johnson and Johnson stock. Ms. Another author has received an unrestricted educational grant from Pfizer Canada Inc and honoraria from Mallickrodt Pharmaceuticals for work unrelated to this article.
• **Setting**	In a 10-bed tertiary ICU in Winnipeg (Canada)
• **Sample size**	58 patients/families were randomised (14 in usual care, 15 in ICU diaries, 14 in psychoeducation and 15 in ICU diaries + psychoeducation). At 30 days, 39 patients/families remained and at 90 days 37 patients/families remained (12 death, 5 withdrawals, 1 remained in ICU and 2 lost to follow-up)
• **Duration and follow-up**	Duration: Between May 30, 2014, and November 30, 2016 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, chi-square and Kruskal-Wallis/ Mann-Whitney U tests
Patient characteristics	
• **Eligibility criteria**	> 17y, mechanical ventilation > 24 hours, ICU LOS > 72h, English speaking.
• **Exclusion criteria**	no caregiver/family available, terminal illness with life expectancy < 6 months, pre-existing known cognitive impairment, or reason for admission involving suicide attempt/intentional toxic overdose, meningitis/encephalitis, status epilepticus, anoxic encephalopathy, traumatic brain injury, or coma due to another aetiology.
• **Patient & disease characteristics**	**Patient characteristics** Age [mean (sd)]: Usual care 49.9y (16.9), Psychoeducation 54.3y (17.7), Diary 59.3y (15.5), Diary + psychoeducation 55.7y (14.0), p=0.5 Male (n): Usual care 7/14, Psychoeducation 10/14, Diary 7/15, Diary + psychoeducation 11/15, p=0.3 Prior ICU admission (n): Usual care 3/14, Psychoeducation 3/14, Diary 2/15 Diary + psychoeducation 2/15 , p=0.9 Pre-existing comorbidities (n): Neurologic disease Usual care 4/14, Psychoeducation 5/14, Diary 3/15 Diary + psychoeducation 3/15, p=0.9 – Psychiatric disease Usual care 1/14, Psychoeducation 1/14, Diary 2/15, Diary + psychoeducation 2/15, p=0.9 – Respiratory disease Usual care 0/14 Psychoeducation 1/14 Diary 2/15 Diary + psychoeducation 2/15, p=0.5 – Renal disease Usual care 1/14 Psychoeducation 1/14 Diary 4/15 Diary + psychoeducation 0/15, p=0.3 – Drug abuse Usual care 5/14 Psychoeducation 2/14 Diary 1/15 Diary + psychoeducation 4/15,p=0.2 *Acute illness characteristics*

	Sequential Organ Failure Assessment score [mean (sd)]: Usual care 9.2 (3.5) Psychoeducation 8.6 (3.8) Diary 9.1 (3.7) Diary + psychoeducation 8.2 (4.8), p=0.9 Primary reason for admission (n): Respiratory failure Usual care 13/14 Psychoeducation 10/14 Diary 11/15 Diary + psychoeducation 10/15, p=0.4 – Cardiovascular Usual care 1/14 Psychoeducation 1/14 Diary 3/15 Diary + psychoeducation 2/15, p=0.7 – Sepsis Usual care 0/14 Psychoeducation 3/14 Diary 1/15 Diary + psychoeducation 3/15, p=0.2 ICU mortality (n): Usual care 4/14 Psychoeducation 2/14 Diary 2/15 Diary + psychoeducation 1/15, p=0.4 Hospital mortality (n): Usual care 4/14 Psychoeducation 3/14 Diary 2/15 Diary + psychoeducation 2/15, p=0.7 Sedation use duration [median (IQR)]: Duration of continuous sedation Usual care 9.5 days (8.5–12) Psychoeducation 2.5 days (0–12.25) Diary 5.0 days (2–7) Diary + psychoeducation 5.0 days (3–10), p=0.01 – Duration of continuous benzodiazepine Usual care 6.5 days (0.75–9.5) Psychoeducation 0.0 days (0–3.5) Diary 2.0 days (0–6) Diary + psychoeducation 2.0 days (0–6), p=0.2 – Duration of continuous narcotic Usual care 9.0 days (6.5–11.25) Psychoeducation 1.0 days (0–8.5) Diary 5.0 days (2–7) Diary + psychoeducation 5.0 days (2–9), p=0.03 – Duration of continuous propofol Usual care 6.0 days (1–8.25) Psychoeducation 1.5 days (0–3.25) Diary 1.0 days (0–3) Diary + psychoeducation 3.0 days (0–5), p=0.05 Ventilator duration [median (IQR)]: Usual care 14.0 days (8.5–22) Psychoeducation 6.0 day (3.75–18.5) Diary 7.0 days (3–11) Diary + psychoeducation 6.0 days (4–11), p=0.05 Coma duration [median (IQR)]: Usual care 8.0 days (5.5–13.25) Psychoeducation 2.0 days (0.75–4.25) Diary 4.0 days (0–7) Diary + psychoeducation 4.0 days (1–5), p=0.02 Delirium duration [median (IQR)]: Usual care 2.0 days (0.75–5.25) Psychoeducation 2.0 days (0–4) Diary 0.0 days (0–3), Diary + psychoeducation 2.0 days (1–5), p=0.9 ICU length of stay [median (IQR)] Usual care 19.0 days (9–24.5) Psychoeducation 10.5 days (6.75–23.75) Diary 9.0 days (7–13) Diary + psychoeducation 11.0 days (6–18), p=0.2 Hospital length of stay [median (IQR)]: Usual care 24.0 days (20–47.5) Psychoeducation 30.0 days (12–44.5) Diary 21.0 days (12–61) Diary + psychoeducation 23.0 days (9–48), p=0.8
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** diary is stated at 72h after ICU admission **Setting**: Hospital **Frequency**: 30 and 90 days **Content**: Prior to study commencement, approximately 75% of the ICU nurses attended an educational in-service on ICU diaries. In the “ICU diary” arm, diaries were created using a bound empty journal where family members and ICU staff were invited to write in the ICU diary at any time. The diary included photographs taken by staff. Diaries were reviewed with each participant by a member of our research team. Patients received their diary at 1 month post-ICU discharge. In the case of patient death, diaries were offered to their family.

	In the “psychoeducation” arm, participants and their follow-up physicians received a brochure described common ICU procedures and experiences (e.g., delirium); symptoms of PTSD, anxiety and depression; and follow-up/emergency resources. In the “ICU diary + psychoeducation arm,” participants benefited from both the ICU diary and psychoeducation interventions.
• **Control group**	No follow-up, psychological support or education was provided during “usual care”.
Results	
• **Acceptability of doing journal**	• Time per entry (n) o 1–5 min Family 17 (21.8) Friend 3/4 Nurse 64/98 Physician 9/12 Allied Health 2/6 o 5–10 min Family 28 (35.9) Friend 1/4 Nurse 31/98 Physician 2/12 Allied Health 4/6 o 15–20 min Family 15 (19.2) Friend 0/4 Nurse 3/98 Physician 0/12 Allied Health 0/6 o > 20 min Family 18 (23.1) Friend 0/4 Nurse 0/98 Physician 1/12 Allied Health 0/6 • Number of entries per day, mean (sd) Family & Friend 1.70 (1.74), Health professionals 1.50 (1.40) • Perceived burden to complete the last entry, mean (sd) assessed on a 10-point scale (0 = not burdensome to 10 = highly burdensome) Family 0.69 (1.39) Friend 2.0 (2.45) Nurse 1.6 (0.19) Physician 1.75 (1.48), p < 0.01 • Attitude toward completing diary entries, mean (sd) assessed on a 10-point scale (0 = very negative to 10 = very positive). Family 9.57 (1.46) Friend 7.33 (2.52) Nurse 8.12 (2.17) Physician 8.25 (1.49), p < 0.001
• **Anxiety**	HADS-A score • Different in medians across treatment arms o At 30 days Data reported in graph, p= 0.7 o At 90 days: Usual care 7.5 [IQR, 6–9] vs psychoeducation 8.0 [IQR, 8–11] vs diary 3.0 [IQR, 2–5] vs diary + psychoeducation 3.0 [IQR, 2–7]; p = 0.05 • Different in medians between 30 and 90 days by treatment arm (data reported in graph): Usual care p=0.2 Psychoeducation p=0.4

	Diary p=0.8 Diary + psychoeducation p = 0.9 • Significant anxiety symptoms (HADS-A ≥ 8) o At 30 days - Overall proportion: 20.5% of participants - Diaries 15.4% vs no diaries 30.8%, p = 0.3 - Psycho-education 26.3% vs no psycho-education 15.0%, p=0.3 o At 90 days - Overall proportion: 32.4% of participants - Diaries 19.2% vs no diaries 63.6%; p = 0.008 - Psycho-education 38.9% vs no psycho-education 26.3%, p=0.4 • Median HADS anxiety at 90 days o Diaries 3.0 [IQR, 2–6.25] vs no diaries 8.0 [IQR, 7–10], p = 0.01
• **Depression**	HADS-D score • Different in medians across treatment arms o At 30 days: Data reported in graph, p=0.7 o At 90 days: Usual care 4.5 [IQR, 2–7], psychoeducation 5.0 [IQR, 4–9]), diary 3.0 [IQR, 3–6], and diary + psychoeducation 2.0 [IQR, 1–3]; p = 0.06 • Different in medians between 30 and 90 days by treatment arm (data reported in graph): Usual care p=0.6 Psychoeducation p=0.6 Diary p=0.7 Diary + psychoeducation: 5.0 [IQR, 3–7] vs 2.0 [IQR, 1–3]; p = 0.03 • Significant depression symptoms (HADS-D ≥ 8) o At 30 days - Overall proportion: 20.5% of participants - Diaries 15.4% vs no diaries 30.8%, p = 0.3 - Psycho-education 7.7% vs no psycho-education 27.3%, p=0.1 o At 90 days - Overall proportion: 13.5% of participants - Diaries 7.7% vs no diaries 27.3%; p = 0.1 - Psycho-education 16.7% vs no psycho-education 10.5%, p=0.6 • Median HADS depression at 90 days

	o Diaries 3.0 [IQR, 1.75–5.25] vs no diaries 5.0 [IQR, 4–9]; p = 0.04
• **PTSD**	IES-R score • Different in medians across treatment arms o At 30 days: Data reported in graph, p=0.9 o At 90 days: Data reported in graph, p=0.6 • Different in medians between 30 and 90 days by treatment arm (data reported in graph): Usual care p=0.9 Psychoeducation p=0.9 Diary p=0.9 Diary + psychoeducation: p = 0.02 • Significant anxiety symptoms (IES-R ≥ 1.6) o At 30 days - Overall proportion: 12.8% of participants - Diaries 11.5% vs no diaries 15.4%, p = 0.7 - Psycho-education 5.3% vs no psycho-education 20.0%, p=0.2 o At 90 days - Overall proportion: 13.5% of participants - Diaries 11.5% vs no diaries 18.5%; p = 0.6 - Psycho-education 0.0% vs no psycho-education 26.3%, p=0.04
Limitations and other comments	
• **Limitations and notes**	Pilot RCT Monocentric design Small sample size (underpowered to assess between-group differences) Study completion rate 60% Some data are reported in graph Self-report symptom measures Limited generalizability because of inclusion criteria No blinding of the outcome assessors
• **Authors' conclusions**	The significant reduction in depression and anxiety symptoms at 90 days post ICU discharge in those who received the diary (with or without psychoeducation) is compelling and warrants further investigation of the two interventions in a larger trial.

Nielsen 2020[67]	
Methods	
• **Design**	Multicentre, block-randomised, single-blinded, controlled trial
• **Source of funding and competing interest**	Funding: Aarhus University, Denmark; the Department of Anesthesiology and Intensive Care, Regional Hospital West Jutland; and the Health Research Fund of Central Denmark Region Competing interest: No statement
• **Setting**	4 mixed medical-surgical ICUs (2 university hospitals and 2 regional hospitals) in Western Denmark.
• **Sample size**	116 cases were randomised (60 relatives and 36 patients in control group and 56 relatives and 39 patients in intervention group). At follow-up, 47 relatives and 22 patients in control group and 44 relatives and 26 patients in intervention group remained in the study. Four dyad patient-relative were excluded because patients did not meet the inclusion criteria. 43 patients and 23 relatives were lost to follow-up.
• **Duration and follow-up**	Duration: From 2015 to 2017 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, t-test, nonparametric tests
Patient characteristics	
• **Eligibility criteria**	Danish-speaking patient-relative dyads ≥18y, ICU LOS≥ 48 h, mechanical ventilation ≥24 h, having at least one close relative. Relatives continued in the study if the patient died or refused participation
• **Exclusion criteria**	Prior severe cognitive deficits or neurological damage, mechanical ventilation <24 h, ICU LOS <48 h
• **Patient & disease characteristics**	*No differences between groups were statistically significant except for gender and age in relatives.* **Patients** Sex Male/ Female (n): Intervention group 26/27 Control group 35/27 Age [median (range)]: Intervention group 70y (27-88) Control group 68y (18-89) ICU LOS [median (range)]: Intervention group 11.7 days (2.2-87.2) Control group 9.8 days (2.1-90.8) Time ventilated [median (range)]: Intervention group 6.0 days (1.4-78) Control group 6.9 days (1.2-83.0) Simplified Acute Physiology Score (SAPS) II (severity of illness) [median (range)]: Intervention group 52 (22-90) Control group 54 (16-99) Reason for admittance to ICU Medical/surgical: Intervention group 81%/19% Control group 80%/20% Educational level (n): No education Intervention group 10 Control group 13 – Short/middle/long education Intervention group 21 Control group 22 – Longer education Intervention group 1 Control group 0 – No response Intervention group 21 Control group 24

	Relatives Sex Male/ Female (n): Intervention group 12/41 Control group 12/77 Age [median (range)]: Intervention group 56y (25-79) Control group 48y (18-91) Relationship to patient n: Spouse/partner Intervention group 20 Control group 13 – Spouse living apart Intervention group 0 Control group 1 – Daughter/son Intervention group 22 Control group 29 – Parent Intervention group 6 Control group 5 – Friend Intervention group 1 Control group 1 – Other family Intervention group 4 Control group 10 (17%) Educational level (n): No education Intervention group 5 Control group 6 – Short/middle-long education Intervention group 38 Control group 46 – Longer education Intervention group 10 Control group 7 Days before inclusion[median (range)]: Intervention group 2 days (0-11) Control group 2 (0-16) Number of pictures in diary[median (range)]: Intervention group 2 (0-6) Control group -
Exposures	
• **Intervention group**	**Duration**: writing during the ICU stay evaluation at 3 months **Starting date:** at ICU admission **Setting**: home (reading the diary) ICU (for writing) **Frequency**: Every day **Content**: Recruitment: patients post ICU discharge and relative 1 to 3 days post ICU admission. Relatives' role: Relative were instructed by trained nurses on the purpose of diary for the patient and the relative, how to write a diary for the ICU patient and later share the diary with the patient (after the ICU-discharge). Relatives were cautioned that diary could be difficult to read to the patient and to wait the right moment to begin the reading. The instruction was pasted into the diary. The diary is brought back home and not left in the ICU. No additional support was offered to the patient or relative. Photographs: During the critical phase and at the turning point, photos of patient was taken by the nursing staff and included in the diary. Relatives will be permitted to be photographed, staff will not. Pictures were given to the patient by ICU nurses in a closed envelope with an explanation of what should be expected when looking at the pictures. The patient could refuse the photographs altogether. In this case, photographs were destroyed. In the case of death, photographs were not given to relatives.
• **Control group**	Usual care without diary
Results	
Patient outcomes	
• **PTSD at 3 months**	• Total PTSS-14 score, median (range) Intervention group 21 (14-75) vs Control group 28 (14-75), p=0.44 • PTSS-14 score > 31 Intervention group 8/26 Control group 9/22, RR (95% CI) 0.75 (0.35-1.62), p=0.55

• **Anxiety at 3 months**	HADS- A, score ≥ 11 (n) Intervention group 5/25 Control group 3/22, RR (95% CI) 1.47 (0.40-5.44), p=0.71
• **Depression at 3 months**	HADS-D, score ≥ 11 (n) Intervention group 2/25 Control group 2/22, RR (95% CI) 0.88 (0.14-5.73), p=1.0
• **HRQoL at 3 months**	SF-36 (mean scores) • Physical function Intervention group 45.8 Control group 38.6, p=0.46 • Role physical Intervention group 18.0 Control group 31.3, p=0.25 • Bodily pain Intervention group 62.6 Control group 52.7, p=0.26 • Global health Intervention group 53.2 Control group 47.0, p=0.36 • Vitality Intervention group 48.5 Control group 55.2, p=0.47 • Social function Intervention group 68.8 Control group 64.2, p=0.46 • Role emotional Intervention group 49.3 Control group 50.8, p=0.94 • Mental health Intervention group 74.5 Control group 74.0, p=0.76
• **Usage of diaries**	• Q1 – Was a diary written for you? p=0.00 Yes: Intervention group 22 Control group 5 No: Intervention group 3 Control group 16 Do not know: Intervention group 0, Control group 1 (5%) • Q2 – No of entries in your diary p=0.15 1-5: Intervention group 0 Control group 1 (20%) 6-10: Intervention group 4 Control group 1 (20%) >10: Intervention group 16 Control group 2 (40%) Do not know: Intervention group 2 (9%) Control group 1 (20%) • Q3 – No of times you read the diary p=0.89 Never: : Intervention group 3 Control group 2 1-2: Intervention group 11 Control group 1 3-6: Intervention group 4 Control group 0 >6: Intervention group 3 Control group 2 • Q4 – No of times talked about the diary, p=0.66 Never: : Intervention group 1 Control group 1 1-2: Intervention group 11 Control group 1 3-6: Intervention group 8 Control group 3 >6: Intervention group 8 Control group 1
Relative outcomes	
• **PTSD at 3 months**	• Total PTSS-14 score, median (range)

	Intervention group 26 (14-64) vs Control group 32 (14-77), p=0.01 • PTSS-14 score > 31 Intervention group 8/26 Control group 9/22, RR (95% CI) 0.65 (0.39-1.09), p=0.13
• **Anxiety at 3 months**	HADS- A, score ≥ 11 (n) Intervention group 5/41 Control group 7/46, RR (95% CI) 0.80 (0.28-2.33), p=0.76
• **Depression at 3 months**	HADS-D, score ≥ 11 (n) Intervention group 3/41 Control group 5/46, RR (95% CI) 0.67 (0.17-2.64), p=0.72
• **HRQoL at 3 months**	SF-36 (mean scores) • Physical function Intervention group 86.1 Control group 85.1, p=0.73 • Role physical Intervention group 73.7 Control group 68.5, p=0.20 • Bodily pain Intervention group 83.3 Control group 73.0, p=0.12 • Global health Intervention group 78.2 Control group 70.8, p=0.10 • Vitality Intervention group 65.8 Control group 56.3, p=0.06 • Social function Intervention group 81.4 Control group 79.4, p=0.48 • Role emotional Intervention group 73.5 Control group 70.4, p=0.79 • Mental health Intervention group 77.4 Control group 70.4, p=0.16
• **Usage of diaries**	• Q1 – Did you write a diary for the patient? p=0.00 Yes: Intervention group 40 Control group 8 No: Intervention group 4 Control group 39 • Q2 – Did nurses guide you? p=0.00 Yes: Intervention group 37 Control group 21 No: Intervention group 4 Control group 25 Do not know: Intervention group 2, Control group 0 • Q3 – No of entries made, p=0.03 1-5: Intervention group 3 Control group 3 6-10: Intervention group 8 Control group 2 >10: Intervention group 28 Control group 3 • Q4 – No of times you read the diary p=0.78 Never: : Intervention group 7 Control group 2 1-2: Intervention group 9 Control group 3 3-6: Intervention group 15 Control group 0 >6: Intervention group 8 Control group 3 • Q5 – No of times read about the diary with the patient, p=0.97 Never: : Intervention group 29 Control group 6 1-2: Intervention group 7 Control group 1

	3-6: Intervention group 3 Control group 1 >6: Intervention group 0 Control group 0 • Q6 – No of times talked about the diary with the patient, p=0.81 Never: : Intervention group 8 Control group 2 1-2: Intervention group 11 Control group 1 3-6: Intervention group 11 Control group 3 >6: Intervention group 9 Control group 2
Limitations and other comments	
• **Limitations and notes**	• Outcome assessors were blinded, no blinding possible for patients, relatives and health professionals. Allocation was not thus concealed. • Sample size calculation was not reached despite a long recruitment period. the study could have been underpowered to show differences in some outcomes. • Short follow-up period (3 months) and outcomes such as PTSD may occurred later in ICU patients • Cross contamination is observed because some patients received diaries in the control group • Intervention is provided by relatives (writing and reading the diaries). It may cause variation in the intensity of the intervention • As lower age and female gender are potential risk factors for development of PTSD, the possibility of an overestimation of the positive effect of the diary in relatives should at least be considered because difference in baseline characteristics are observed for these two variables.
• **Authors' conclusions**	A nurse-prompted diary written by relatives for the ICU patient may reduce the risk of posttraumatic stress symptoms in relatives but not in patients. The diary had no effect on anxiety and depression or health-related quality of life.

Svenningsen 2014[58]	
Methods	
• **Design**	Prospective observational multicentre study
• **Source of funding and competing interest**	Funding: The Novo Nordic Foundation, Foundation for Psychiatry, Risskov, The Health Science Research Fund of The Central Region of Denmark, Foundation of Research in Mental Disorders, Aarhus University; Danish Society for Nursing Research; Research Foundation at Hillerød Hospital, Aarhus Sygehus, Færgemans scholarship, Foundation of Psychiatry promotion and Lippmann Foundation. Competing interest: No conflict of interest declared
• **Setting**	3 multidisciplinary ICUs at 2 university hospitals in Denmark
• **Sample size**	360 patients were included. 325, 297 and 248 were remained at 1 week, 2 months and 6 months respectively. Number of lost to follow-up is unclear (data error in flowchart)

• **Duration and follow-up**	Duration: September 2009–July 2011 Follow-up: 6 months
• **Statistical analysis**	Descriptive statistics, Kruskal–Wallis test, chi-square test
Patient characteristics	
• **Eligibility criteria**	ICU LOS >48 hours, >17 y, and ability to communicate in Danish.
• **Exclusion criteria**	Severe brain damage restricting communication
• **Patient & disease characteristics**	Age [mean (SD)]: 61y (15) Gender [% of male]: 57% SAPSII mean (SD)]: 38 (16) Type of admission: Medical 41%, Surgical, n 59% Delirium: Positive 56%
Exposures	
• **Intervention group**	**Duration**: 6 months **Starting date:** A week after discharge **Setting**: at hospital and by phone **Frequency**: 3 interviews at 1 week, 2 months and 6 months post-ICU **Content**: Some patients benefited from diaries and/or follow-up visits.
• **Control group**	No control group
Results	
• **HRQoL**	SF-36 at six months • Diaries o General health perceptions [mean score (SD), p-value] Diary: 68.82 (23.68) vs without a diary 59.69 (25.78), p = 0.037. No difference among delirious and non-delirious patients (p = 0.723) receiving a diary. No difference between other sub-scales • The follow-up visit did not have an impact on SF-36 scores
Limitations and other comments	
• **Limitations and notes**	Observational study design Diary intervention and follow-up visit intervention are poorly described Effects of the mixed interventions (diary and follow-up visits) are not evaluated All data not shown for the effect of dairy and follow-visits
• **Authors' conclusions**	Short Form-36 might not be sensitive to delirium-related outcomes.

Appendix 4.2.4. Other interventions

Cox 2018[60]	
Methods	
• **Design**	Multicentre randomized clinical trial
• **Source of funding and competing interest**	Funding: Patient-Centered Outcomes Research Institute (PCORI) Competing interest: Despite grant from the funding institution, the authors declared not competing interests
• **Setting**	5 ICU at Duke University, University of Washington, University of North Carolina at Chapel Hill, and University of Pittsburgh (USA)
• **Sample size**	175 patients were randomised (86 patients and 39 family members in interventions and 89 patients and 47 family members in control group). At 3 months, 136 patients (65 in intervention and 71 in control group) and 69 family members (30 in intervention group and 39 in control group) remained. At 6 months, 131 patients (62 in intervention and 69 in control group) and 66 family members (29 in intervention group and 37 in control group) remained. In patient group, 14 patients withdrew because they were too ill, 12 died and 18 were lost to contact/ In family members, 5 were unable due to patient illness, 13 were lost to contact and 2 were unavailable.
• **Duration and follow-up**	Duration: Between December 2013 and April 2015 Follow-up: at 3 and 6 months
• **Statistical analysis**	Descriptive statistics and strata analyses
Patient characteristics	
• **Eligibility criteria**	Patients: ≥18 y, mechanical ventilation > 48 hours, and successful extubation before discharge. Patients without an available family member were still eligible Family members: ≥18 y, expected to provide significant post-discharge assistance
• **Exclusion criteria**	Patients: pre-existing or current cognitive impairment, treatment for severe mental illness during the 6 months preceding admission, residence at a location other than home immediately before admission, poor English fluency, ICU attending physician's expectation of patient survival less than 3 months, inability to complete study procedures as determined by study staff, and failure to return home from either a hospital or post-acute care facility within 3 months after discharge. Family members: history of cognitive impairment and poor English fluency.
• **Patient & disease characteristics**	Age, [mean (SD)]: Patients – Intervention group 49.7y (13.8) Control group 53.7y (13.5) / Family members – Intervention group 50.0y (14.9) Control group 52.9y (15.2) Female sex: Patients – Intervention group 38/86 Control group 37/89 / Family members – Intervention group 33/39 Control group 36/47 Marital status: Married or live with partner: Patients – Intervention group 44/86 Control group 45/89 / Family members – Intervention group 30/39 Control group 32/47 ; Divorced or separated: Patients – Intervention group 20/86 Control group 22/89 / Family members – Intervention group 2/39 Control group 3/47 ; Single: Patients – Intervention group 18/86 Control group 19/89 / Family members – Intervention group 7/39 Control

group 11/47 ; Widowed: Patients – Intervention group 4/86 Control group 3/89 / Family members – Intervention group 0/39 Control group 1/47

Highest level of education: High school graduate or less: Patients – Intervention group 37/86 Control group 36/89 / Family members – Intervention group 16 Control group 18/47 ; Trade, technical, or vocational school, some college: Patients – Intervention group 23/86 25/89 / Family members – Intervention group 9/39 Control group 10/47 ; College degree or higher : Patients – Intervention group 26/86 Control group 28/89 / Family members – Intervention group 13/39 Control group 19/47 ; Missing: Family members – Intervention group 1/39

Employment status prior to hospitalization: Working full-time: Patients – Intervention group 29/86 Control group 29/89 / Family members – Intervention group 17/39 Control group 14/47 ; Working part-time: Patients – Intervention group 6/86 Control group 6/89 / Family members – Intervention group 5/39 Control group 5/47 ; Unemployed, looking for work: Patients – Intervention group 3/86 Control group 7/89 / Family members – Intervention group 3/39 Control group 4/47 ; Homemaker full-time: Patients – Intervention group 2/86 Control group 2/89 / Family members – Intervention group 5/39 Control group 4/47 ; Student: Patients – Intervention group 2/86 Control group 1/89 / Family members – Intervention group 1/39 Control group 1/47 ; Retired: Patients – Intervention group 12/86 Control group 17/89 / Family members – Intervention group 5/39 Control group 16/47 ;Disabled: Patients – Intervention group 32/86 Control group 27/89 / Family members – Intervention group 3/39 Control group 3/47

Caring for young children at home: Patients – Intervention group 61/86 Control group 69/89 / Family members – Intervention group 27/39 Control group 35/47

Relationship to patient: Spouse or partner Intervention group 17/39 Control group 24/47 ; Parent Intervention group 7/39 Control group 5/47 ; Brother or sister Intervention group 4 Control group 3/47 ; Child Intervention group 3/39 Control group 3/47 ; Other family Intervention group 0/39 Control group 3/47 ; Friend Intervention group 2/39 Control group 1/47 ; Missing Intervention group 6/39 Control group 8/47

Insurance status of patients: Commercial Intervention group 39/86 38/89 ; Medicare Intervention group 25/86 30/89 ; Medicaid Intervention group 16/86 12/89 ; None Intervention group 4/86 7/89 ; Other Intervention group 2/86 2/89

Financial distress at randomization: Short on money and need more to pay bills: Patients – Intervention group 17/86 Control group 18/89/ Family members – Intervention group 8/39 Control group 8/47 ; Barely have enough to pay bills and for basic needs: Patients – Intervention group 19/86 Control group 1 /89 / Family members – Intervention group 10/39 Control group 6/47 ; Have enough money for just a few extra things: Patients – Intervention group 34/86 Control group 34/89 / Family members – Intervention group 12/39 Control group 16/47 ; Completely comfortable : Patients – Intervention group 16/86 Control group 27/89 / Family members – Intervention group 8/39 Control group 17/47

Treated for psychiatric condition in the3 months before admission*, n (%)

Depression: Patients – Intervention group 27/86 Control group 20/89 / Family members – Intervention group 9/39 Control group 5/47 ; Anxiety: Patients – Intervention group 24/86 Control group 17/89 / Family members – Intervention group 12/39 Control group 9/47 ; Post-traumatic stress disorder (PTSD): Patients – Intervention group 4/86 Control group

	6/89 / Family members – Intervention group 2/39 Control group 2/47 ; Other psychological condition: Patients – Intervention group 1/86 Alcohol abuse in the month before hospitalization: Intervention group 18/86 Control group 14/89 Drug abuse in the month before hospitalization: Intervention group 8/86 Control group 5/89 Chronic medical comorbidities [mean (SD)]: Intervention group 3.6 (2.8) Control group 3.8 (2.8) Treating ICU at time of eligibility: Medicine Intervention group 43/86 Control group 41/89 — General surgery Intervention group 14/86 Control group 20/89 — Cardiology Intervention group 12/86 Control group 9/89 — Trauma Intervention group 11/86 Control group 14/89 — Neurology and neurosurgery Intervention group 6/86 Control group 5/89 APACHE II score on day of enrolment [mean (SD)]: Intervention group 26.3 (7.7) Control group 25.4 (8.7) —
Exposures	
• **Intervention group**	**Duration**: Six weeks **Starting date:** within 3 weeks of patient arrival at home. **Setting**: at home by phone **Frequency**: weekly sessions **Content**: Coping skills training consisted telephone sessions (~30 minutes) including 1) introduction and relaxation exercise, 2) progressive muscle relaxation, 3) pleasant activities and activity–rest cycle, 4) communication, 5) cognitive restructuring and pleasant imagery, and 6) review and planning for sustainability. Psychologists guided participants through practice with feedback in the context of any self-reported ongoing stressors, helping participants plan how to apply the skill in real life, and highlighting relevant web-based content. In addition to learning skills themselves, family members coached patients in applying skills and using the web content on a day-to-day basis.
• **Control group**	**Duration**: Six weeks **Starting date:** within 3 weeks of patient arrival at home. **Setting**: at home by phone **Frequency**: 2 phone calls **Content**: Education programme consisted in 6 informational videos with accompanying web-based content. Participants were called 2 times during the study period to review materials and answer related questions.
Results	
Patients	
• **Anxiety and depression**	Difference between groups (95% CI) • HADS summary o At 3 months 1.3 (-0.9 to 3.4), p=0.24 o At 6 months -0.3 (-2.7 to 2.0), p=0.78

- HADS-A
  - At 3 months
    0.3 (-1.0 to 1.6), p=0.65
  - At 6 months
    -0.2 (-1.6 to 1.2), p=0.78
- HADS-D
  - At 3 months
    0.9 (-0.4 to 2.1), p=0.16
  - At 6 months
    -0.2 (-1.6 to 1.2), p=0.76

Sub-group analyse in patients with baseline HADS summary score > 14

- HADS summary
  - At 3 months
    0.02 (-3.71 to 3.75), p=0.99
  - At 6 months
    -4.63 (-8.61 to -0.64), p=0.02
- HADS-A
  - At 3 months
    -0.43 (-2.67 to 1.81), p=0.70
  - At 6 months
    -1.80 (-4.21 to 0.61), p= 0.14
- HADS-D
  - At 3 months
    -0.20 (-2.05 to 2.44), p=0.86
  - At 6 months
    -3.03 (-5.36 to -0.71), p=0.01

Sub-group analyse in patients with mechanical ventilation > 7 days

- HADS summary
  - At 3 months
    4.07 (0.05 to 8.08), p=0.047
  - At 6 months
    1.89 (22.61 to 6.40), p=0.41
- HADS-A
  - At 3 months
    1.29 (-1.11 to 3.69), p=0.29
  - At 6 months
    0.61 (-2.07 to 3.28), p=0.66
- HADS-D
  - At 3 months

	2.64 (0.21 to 5.08),p=0.03 o At 6 months 1.16 (-1.51 to 3.84), p=0.39
• **PSTD**	Difference in IES-R score between groups (95% CI) • At 3 months 3.1 (-1.9 to 8.1), p=0.22 • At 6 months 3.6 (-2.7 to 10.0), p=0.26 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months 2.50 (-6.60 to 11.60),p=0.54 • At 6 months 0 (-11.49 to 11.49), p=1.00 Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months 3.52 (-6.36 to 13.41),p=0.48 • At 6 months 4.28 (-8.59 to 17.14), p=0.51
• **Global physical health**	Difference in PROMIS score between groups (95% CI) [PROMIS: Patient-Reported Outcomes Measurement Information System) Global Short Form (range of each, 4 (worst) to 20 (best)] • At 3 months -0.3 (-1.3 to 0.6), p=0.53 • At 6 months 0.4 (-0.5 to 1.4), p=0.36 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months 0.3 (-1.5 to 2.0), p=0.78 • At 6 months 1.3 (-0.3 to 3.0), p=0.11 Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months -0.91 (-2.86 to 1.03), p=0.36 • At 6 months 0.39 (21.53 to 2.31), p=0.69
• **Global mental health**	Difference in PROMIS score between groups (95% CI) [PROMIS: Patient-Reported Outcomes Measurement Information System) Global Short Form (range of each, 4 (worst) to 20 (best)] • At 3 months

	-0.7 (-1.8 to 0.3), p=0.16 • At 6 months 0.08 (-0.9 to 1.1), p=0.88 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months 0.45 (-1.45 to 2.34), p=0.64 • At 6 months 2.26 (0.47 to 4.06), p=0.01 Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months - 2.18 (-4.21 to 20.15), p=0.04 • At 6 months -1.00 (-3.05 to 1.06), p=0.34
• **Quality of life**	Difference in EQ-5D score between groups (95% CI) • At 3 months - 3.0 (-9.6 to 3.6), p=0.37 • At 6 months 0.3 (-5.9 to 6.6), p=0.92 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months -2.65 (-15.04 to 9.74), p=0.67 • At 6 months 11.20 (0.02 to 22.37), p=0.0496 Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months -15.82 (-28.53 to -3.11), p=0.02 • At 6 months 2.40 (-10.89 to 15.69), p=0.72
• **Coping responses**	Difference in Brief COPE score between groups (95% CI) • At 3 months - 0.8 (-3.0 to 1.4), p=0.49 • At 6 months - 0.4 (-2.9 to 2.1), p=0.75 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months 2.12 (-1.97 to 6.21), p=0.31 • At 6 months 1.02 (-3.56 to 5.60), p=0.66

	Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months 1.27 (-3.22 to 5.76), p=0.58 • At 6 months 1.44 (-3.66 to 6.54) p=0.58
• **Self-efficacy**	Difference in score between groups (95% CI) [score from a four-item scale: item range, 1 (worst) to 10 (best)] • At 3 months 0.3 (-0.3 to 1.0), p=0.31 • At 6 months 0.4 (-0.2 to 1.0), p=0.23 Sub-group analyse in patients with baseline HADS summary score > 14 • At 3 months 0.72 (-0.48 to 1.91), p=0.24 • At 6 months 1.35 (0.23 to 2.47), p=0.02 Sub-group analyse in patients with mechanical ventilation > 7 days • At 3 months -0.36 (-1.73 to 1.02), p=0.61 • At 6 months -0.36 (-1.71 to 0.99), p=0.60
Family members	
• **Anxiety and depression**	Difference between groups (95% CI) • HADS summary o At 3 months 1.4 (-0.9 to 3.7), p=0.23 o At 6 months 1.1 (-0.9 to 3.2), p=0.26 • HADS-A o At 3 months 0.8 (-0.6 to 2.2), p=0.27 o At 6 months 0.8 (-0.6 to 2.2), p=0.26 • HADS-D o At 3 months 0.7 (-0.7 to 2.1), p=0.31 o At 6 months 0.5 (-1.0 to 1.9), p=0.52

• **PSTD**	Difference in IES-R score between groups (95% CI) • At 3 months -0.5 (-8.0 to 7.0), p=0.89 • At 6 months 3.8 (-4.4 to 12.0), p=0.36
• **Global physical health**	Difference in PROMIS score between groups (95% CI) [PROMIS: Patient-Reported Outcomes Measurement Information System) Global Short Form (range of each, 4 (worst) to 20 (best)] • At 3 months -0.1 (-1.0 to 0.8), p=0.79 • At 6 months -0.2 (-1.0 to 0.7), p=0.71
• **Global mental health**	Difference in PROMIS score between groups (95% CI) [PROMIS: Patient-Reported Outcomes Measurement Information System) Global Short Form (range of each, 4 (worst) to 20 (best)] • At 3 months -0.03 (-1.2 to 1.1), p=0.96 • At 6 months -0.7 (-1.8 to 0.4), p=0.20
• **Coping responses**	Difference in Brief COPE score between groups (95% CI) • At 3 months 1.1 (-2.0 to 4.2), p=0.47 • At 6 months -1.0 (-4.8 to 2.8), p=0.61
• **Self-efficacy**	Difference in score between groups (95% CI) [score from a four-item scale: item range, 1 (worst) to 10 (best)] • At 3 months 0.3 (-0.5 to 1.0), p=0.48 • At 6 months 0.3 (-1.2 to 0.6), p=0.47
Limitations and other comments	
• **Limitations and notes**	• Underpowered trial • High attrition rate due to patients' serious illnesses • Only university centres included. This may impair the results generalisation • Low adherence to intervention (63%) or control group (65%)
• **Authors' conclusions**	Among a general population of ICU survivors and their family members, a telephone- and web-based CST program did not improve symptoms of depression, anxiety, and PTSD compared with an education program. However, among patients with high baseline levels of distress, coping

	skills training improved symptoms of psychological distress compared with an education program at 6 months, whereas the education program improved distress at 3 months among those who received ventilation for 1 week or more.

Cox 2019[61]	
Methods	
• **Design**	Pilot randomized clinical trial
• **Source of funding and competing interest**	Funding: National Institutes of Health's National Center for Complementary and Integrative Health, Center of Innovation for Health Services Research in Primary Care (Durham VA Medical Center) Competing interest: No authors have either competing financial or non-financial interests in this research
• **Setting**	At Duke University Medical Center and the University of Washington / Harborview Medical Center (USA).
• **Sample size**	80 patients were randomized (31 in mobile mindfulness training, 31 in telephone mindfulness training and 18 in education program/control group). At 3 months, 66 patients remained (8 lost to contact, 4 withdrew, 1 time out in rehabilitation, 1 incarceration)
• **Duration and follow-up**	Duration: Between March 1, 2016 and February 6, 2017 Follow-up: 3 months (completed in June 2017)
• **Statistical analysis**	Descriptive statistics
Patient characteristics	
• **Eligibility criteria**	age ≥18, ICU management for ≥24 hours, and cardiorespiratory failure as defined by ≥1 of these criteria: mechanical ventilation via endotracheal tube for ≥12 hours; non-invasive ventilation for acute respiratory failure for ≥4 hours in a 24-hour period; high flow nasal cannula ≥15 Liters / minute or face mask oxygen with a fractional inspired oxygen content ≥ 0.5 for ≥4 hours; or use of vasopressors, inotropes, or an aortic balloon pump for shock for ≥1 hour
• **Exclusion criteria**	pre-existing or current cognitive impairment, treatment for severe mental illness within 6 months of current admission, hospitalized within 3 months of current admission, active substance abuse at admission, expected survival <6 months per ICU attending physician, ICU length of stay ≥30 days, expected discharge to a location other than home, complex medical care expected soon after discharge, poor English fluency, and lack of either a reliable smartphone with a data plan or internet plus telephone access
• **Patient & disease characteristics**	Age [mean (SD)]: Mobile mindfulness 48.7y (15.3), Telephone mindfulness 48.1y (16.1), Education program 53.3y (12.6) Female gender: Mobile mindfulness 12/31, Telephone mindfulness 15/31 Education program 8/18 Highest level of education high school or less: Mobile mindfulness 8/31, Telephone mindfulness 8/31, Education program 5/18

	Employment status in month prior to hospitalization: Working, homemaker, or student full time: Mobile mindfulness 14/31, Telephone mindfulness 18/31, Education program 7/18 – Working part time: Mobile mindfulness 4/31, Telephone mindfulness 3/31, Education program 3/18 – Unemployed: Mobile mindfulness 2/31, Telephone mindfulness 0/31, Education program 3/18 – Retired: Mobile mindfulness 8/31, Telephone mindfulness 7/31, Education program 4/18 – Disabled: Mobile mindfulness 3/31, Telephone mindfulness 3/31, Education program 1/18 Caring for children at home: Mobile mindfulness 6/31, Telephone mindfulness 10/31, Education program 7/18 Insurance status: Commercial or other: Mobile mindfulness 16/31, Telephone mindfulness 17/31, Education program 10/18 – Medicare: Mobile mindfulness 5/31, Telephone mindfulness 8/31, Education program 4/18 – Medicaid: Mobile mindfulness 8/31, Telephone mindfulness 4/31, Education program 3/18 – None: Mobile mindfulness 2/31, Telephone mindfulness 2/31, Education program 1/18 Financial distress: Mobile mindfulness 22/31, Telephone mindfulness 20/31, Education program 14/18 Chronic medical comorbidities [mean (SD)]: Mobile mindfulness 2.7 (2.7), Telephone mindfulness 2.9 (3.3), Education program 4.2 (4.3) Treating ICU at time of eligibility: Medicine: Mobile mindfulness 10/31, Telephone mindfulness 9/31, Education program 10/18 – Surgery: Mobile mindfulness 21/31, Telephone mindfulness 22/31, Education program 8/18 APACHE II score on day of enrolment [mean (SD)]: Mobile mindfulness 18.2 (6.7), Telephone mindfulness 16.9 (5.5), Education program 18.9 (8.9) Taking at the time of hospital admission: Antidepressants: Mobile mindfulness 6/31, Telephone mindfulness 7/31, Education program 3/18 – Anxiolytics: Mobile mindfulness 3/31, Telephone mindfulness 5/31, Education program 2/18 – Other psychiatric medication: Education program 1/18 – Narcotics: Mobile mindfulness 4/31, Telephone mindfulness 5/31, Education program 3/31 Prescribed at the time of hospital discharge: Antidepressants: Mobile mindfulness 6/31, Telephone mindfulness 5/31, Education program 5/18 – Anxiolytics: Mobile mindfulness 3/31, Telephone mindfulness 4/31, Education program 3/18 – Other psychiatric medication: Education program 1/18 – Narcotics: Mobile mindfulness 19/31, Telephone mindfulness 21/31, Education program 10/18
Exposures	
• **Intervention group**	**Intervention 1: telephone based mindfulness training** **Duration**: 1 month **Starting date:** within the first week of arrival home **Setting**: home by phone **Frequency**: each week **Content**: A trained psychologist delivered a ~30-minute-long telephone call composed o: brief discussion about participants' major current stressor(s); explanation of a didactic element and the rationale for its use; practice and review;, and discussion about participant's use of mindfulness skills, challenges in applying the skills, and how to maintain progress. The didactic elements included awareness of breathing, awareness of body systems, awareness of emotion and mindful

	acceptance, awareness of sound. Participants were able to access group-specific complementary video and audio resources on a password-protected study website, as well as a packet of printed information. **<u>Intervention 2: mobile mindfulness</u>** **Duration**: 4 weeks **Starting date:** within the first week of arrival home **Setting**: at home through mobile app **Frequency**: Once a week **Content**: A trained psychologist gave a brief mindfulness exercise. Thereafter, the mobile app delivered all the content of the telephone mindfulness program through a 4-session guided series of videos, audio files, and interactive text features. Each weekly session included a short (4–5 minutes) background video, a 6–8-minute guided mediation, and interactive suggestions for how to apply mindfulness within their daily routine (~10 minutes).
• **Control group**	**<u>Intervention 3: Education program</u>** **Duration**: 1 month **Starting date:** within the first week of arrival home **Setting**: at home **Frequency**: 6 times **Content:** Patients received educational information about the nature and treatment of critical illness, but none of the mindfulness training. The education information consisted in 6 videos (~10-15 minutes) regarding causes and diagnosis of acute respiratory failure, hospital and post-discharge treatment, neuromuscular weakness, exercise and critical illness, internet resources for ICU survivors and nutrition and critical illness. Handouts in PDF format were available for download that served to augment each session. Links to contact the study team were also present.
Results	
• **Depression**	PHQ-9 (Patient Health Questionnaire 9-item depression scale). Mean change between baseline and 3 months (95% CI) • Education program −3.0 (−5.3, −0.8) • Mobile mindfulness −4.8 (−6.6, −2.9) • Telephone mindfulness −3.9 (−5.6, −2.2)
• **Anxiety**	GAD-7 (Generalized Anxiety Disorder 7-item scale) Mean change between baseline and 3 months (95% CI) • Education program −0.6 (−2.5,1.3) • Mobile mindfulness

	−2.1 (−3.7, −0.5) • Telephone mindfulness −1.6 (−3.0, −0.1)
• **PTSD**	PTSS (Post-Traumatic Stress Scale- 10 items). Mean change between baseline and 3 months (95% CI) • Education program −3.5 (−8.0,1.0) • Mobile mindfulness −2.6(−6.3, 1.2) • Telephone mindfulness −2.2 (−5.6, 1.2)
• **Physical health**	PHQ-10 (Patient Health Questionnaire 10-item physical symptom scale). Mean change between baseline and 3 months (95% CI) • Education program −4.8 (−6.8, −2.7) • Mobile mindfulness −5.3 (−7.0, −3.7) • Telephone mindfulness −3.7 (−5.2, −2.2)
• **Quality of life**	QoL VAS (quality of life 100-point visual analogue scale). Mean change between baseline and 3 months (95% CI) • Education program 0.7 (−8.9, 10.1) • Mobile mindfulness −2.7 (−10.6, 5.1) • Telephone mindfulness 3.2 (−4.0,10.4)
• **Cognitive and Affective Mindfulness**	CAMS-R (Cognitive and Affective Mindfulness Scale-Revised Mindfulness instrument). Mean change between baseline and 3 months (95% CI) • Education program −1.3 (−4.1, 1.5) • Mobile mindfulness 0.7 (−1.7, 3.0) • Telephone mindfulness −0.9 (−3.1, 1.3)
• **Coping**	Brief COPE (Brief coping inventory).

	Mean change between baseline and 3 months (95% CI) • Education program −0.2(−2.0, 1.6) • Mobile mindfulness −0.5(−1.9, 1.0) • Telephone mindfulness 1.3(−0.03, 2.7)
Limitations and other comments	
• **Limitations and notes**	Participants are compensated for their participation (25$) Low sample size because pilot RCT Pilot study was not designed to evaluate efficacy Post-randomization dropout was higher in the mobile mindfulness group
• **Authors' conclusions**	A self-directed, four-session post-discharge mindfulness program for ICU survivors delivered by a mobile app demonstrated evidence for impact on psychological distress that was similar to a therapist-delivered mindfulness program.

Zhao 2017[63]	
Methods	
• **Design**	Non-blinded randomized clinical trial
• **Source of funding and competing interest**	Funding: no statement Competing interest: no statement
• **Setting**	in the Hefei NO.2 People Hospital (China)
• **Sample size**	332 patients were randomized (165 in control group and 167 in intervention group). At 3 months, 11 patients could not complete the second cognitive function assessment due to blindness and deafness, 10 patients died and 12 patients lost consciousness.
• **Duration and follow-up**	Duration: January 2013 to September 2013 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, one and two-way ANOVA
Patient characteristics	
• **Eligibility criteria**	No statement
• **Exclusion criteria**	No statement
• **Patient & disease characteristics**	Demographics Control group Cognitive intervention p-value Age [mean (SD)]: Control group 52y (31) Intervention group 50y (29), p=0.82 Gender (% of Female): Control group 51% Intervention group 55%, p=0.83

	Education [mean (SD)]: Control group 12y (5) Intervention group 12y (5), p=0.90 ICU duration [mean (SD)]: Control group 28 days (14.3) Intervention group 28 days (16.5), p=0.22 ICU type: Post-anaesthesia care unit Control group 63% Intervention group 66%, p=0.62 – Neurological intensive care unit Control group 22% Intervention group 22%, p=0.43 – Medical intensive care unit Control group 15% Intervention group 12%, p=0.87 Comorbidities: Diabetes Control group 8.1% Intervention group 10.0%, p=0.13 – Stroke Control group 5.3% Intervention group 6.0%, p=0.64 – Hypertension Control group 12.0% Intervention group 12.8%, p=0.89 – Brain tumour Control group 12.0% Intervention group 11.0%, p=0.55 – Multi-organ failure Control group 22.0% Intervention group 23.2%, p=0.88 – Anaemia Control group 6.2% Intervention group 6.0%, p=0.73 – Depression Control group 22.3% Intervention group 20.0%, p=0.34 Medication: Antidiabetics Control group 4.2% Intervention group 5.8%, p=0.35 – Direct vasodilators Control group 5.4% Intervention group 4.2%, p=0.12 – Thyroid Control group 12.4% Intervention group 13.6%, p=0.35 – Analgesics Control group 30.2% Intervention group 31.9%, p=0.54 – Sedatives Control group 28.0% Intervention group 29.3%, p=0.58 – Glucocorticoids Control group 10.3% Intervention group 9.8%, p=0.67 – Calcium channel blockers Control group 8.3% Intervention group 7.0%, p=0.68
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** not clear **Setting**: at hospital **Frequency**: Four days a week including 2 sessions by day during 30 minutes during 3 months **Content**: The intervention included of 4 components. Music playing: learning to play a simple song on an electronic musical keyboard with one hand (2x/week). Learn Spanish: Three new Spanish words has to be learned in 20 minutes by the patient and the words learned in previous sessions were also reviewed. None of the patients had a learning Spanish background. At the end of each month, an assessment of vocabulary knowledge was performed. (2X/week). Drawing a picture of clock: Patients had 10 minutes to observed picture of clock and remember as much details as possible to then reproduce it as closely as possible based on their memory (2X/week). Psychiatrist sessions: the purpose of the 30-minute sessions (2X/week) was to help alleviate any depression that might have occurred during the cognitive intervention and building optimism during discussion with the psychiatrist. Assessment by nurses using the Montreal Cognitive Assessment (MoCA) at 72h post-ICU discharge and at 3 months
• **Control group**	Patients in the control group did not undertake any cognitive training
Results	
• **Cognitive impairment**	Montreal Cognitive Assessment: cognitive impairment when score < 26 • Total average score at 3 months Control group 16.47 vs Intervention group 25.18, p=0.043

- Long-term cognitive impairment rate

  Control group 82% vs Intervention group 59%, p<0.05
- Subset dimension
  - Executive functions

    Results reported in graph in favour of intervention, p<0.05
  - Visuospatialability

    Results reported in graph in favour of intervention, p<0.05
  - Short-term memory

    Control group 2.01 vs Intervention group 3.95, p=0.012
  - Attention

    Results reported in graph in favour of intervention, p=0.021
  - Language

    Control group 2.53 vs Intervention group 4.22, p=0.045
  - Orientation

    Results reported in graph in favour of intervention, p<0.05
- Effect of intervention by type of intensive care
  - Post-anaesthesia care unit

    Mean difference between 72h post-ICU and 3 months in intervention group: + 2.20
  - Neurological intensive care unit

    Mean difference between 72h post-ICU and 3 months in intervention group: - 0.71
  - Medical intensive care unit

    Mean difference between 72h post-ICU and 3 months in intervention group: - 0.86
- Effect of intervention by age categories
  - Age [20-40[

    Mean difference between 72h post-ICU and 3 months

    Control group 1.02 vs Intervention group 3.21,, p<0.05

    Subset scores:
    - Executive functions

      Results reported in graph in favour of intervention, p<0.05
    - Visuospatialability

      Results reported in graph in favour of intervention, p<0.05
    - Language

      Results reported in graph in favour of intervention, p<0.05
    - Attention

      Results reported in graph in favour of intervention, p<0.05
    - Short-term memory

      Results reported in graph in favour of intervention, p<0.05

- Orientation

  Results reported in graph in favour of intervention, p<0.05

o Age [40-60[

Mean difference between 72h post-ICU and 3 months

Intervention group>control group, p<0.05

Subset scores:

- Executive functions

  Results reported in graph in favour of intervention, p<0.05

- Visuospatialability

  Results reported in graph in favour of intervention, p<0.05

- Language

  Results reported in graph in favour of intervention, p<0.05

- Attention

  Results reported in graph in favour of intervention, p<0.05

- Short-term memory

  Results reported in graph in favour of intervention, p<0.05

- Orientation

  Results reported in graph in favour of intervention, p<0.05

o Age [60-80]

Mean difference between 72h post-ICU and 3 months

Deterioration in intervention group < deterioration in control group, p<0.05

Subset scores:

- Executive functions

  Results reported in graph in favour of intervention, p<0.05

- Visuospatialability

  Results reported in graph in favour of intervention, p<0.05

- Language

  Results reported in graph in favour of intervention, p<0.05

- Attention

  Results reported in graph in favour of intervention, p<0.05

- Short-term memory

  Results reported in graph in favour of intervention, p<0.05

- Orientation

  Results reported in graph in favour of intervention, p<0.05

Limitations and other comments

- **Limitations and notes**
  - Only one centre
  - Incomplete results reporting means are provided without SD and some results are reported in graph only

	• Assessment of the intervention by patients and caregivers are done by 5-point scale. However mean results are higher than 5. • No blinding
• **Authors' conclusions**	In ICU survivors, cognitive intervention could significantly suppress the deterioration, or even promote the recovery, of cognitive function. Cognitive damage observed in Medical intensive care unit and Neurological intensive care unit survivors in the long-term can also be significantly attenuated by cognitive intervention. In comparison, cognitive intervention could sufficiently recover the cognitive impairments observed in post-anaesthesia care unit patients in the long-term. Furthermore, the younger sample was more likely than the older population to recover from acute cognitive impairments, especially those caused by anaesthesia and sedatives. Cognitive impairments observed among the older sample were multi-factorial and irreversible.

Appendix 4.2.5. PICS-F

Bohart 2019[69]	
Methods	
• **Design**	Multicentre, non-blinded, two-armed, pragmatic randomised controlled trial
• **Source of funding and competing interest**	Funding: The Novo Nordisk Foundation, the Danish Nursing Organization, and Nordsjællands Hospital, University of Copenhagen, Denmark Competing interest: No conflict of interest has been declared by the authors
• **Setting**	Ten intensive care units (level II-III) in four out of five regions in Denmark
• **Sample size**	181 adult relatives: intervention group (n = 87), control group (n = 94). At 3 months, 6 patients died and 36 lost to follow-up. At 12 months, 24 additional patients died and 46 addition lost to follow-up.
• **Duration and follow-up**	Duration: 2012–2015 Follow-up: at 3 and 12 months
• **Statistical analysis**	Descriptive statistics and unpaired t-test
Patient characteristics	
• **Eligibility criteria**	Danish speaking adults (>18 years) that were relatives of ICU patients who participated in the RAPIT-study (see Jensen 2016).
• **Exclusion criteria**	Relatives of died patients
• **Patient & disease characteristics**	<u>Characteristics of relatives</u> Age [median (IQR)]: Intervention group 57.4y (50–67), Control group 61.0y (41.75–69.0), p=ns Sex (male): Intervention group 22/87 30/94, p=ns

	Relation to ICU-patient: Spouses/cohabitant Intervention group 64/87, Control group 65/94 – Children Intervention group 13/87, Control group 18/94 –Other Intervention group 10/87, Control group 11/94 <u>Characteristics of ICU-patients of the recruited relatives</u> Age [Median (IQR)]: Intervention group 65y (57–73), Control group 67 (57–74.25), p=ns Sex (male) : Intervention group 56/87, Control group 65/94, p=ns Length of ICU stay [median (IQR)] : Intervention group 11 days (5–26), Control group 12 days (5–21.25), p=ns Mechanically ventilation [median (IQR)] : Intervention group 158.18h (96.82–443.6), Control group 188.42h (88.53–399.29), p=ns APACHE II score [median (IQR)] : Intervention group 25 (19–32), Control group 26 (20.5–32.5), p=ns Mini Mental State Examination [mean (IQR)] : Intervention group 27.5 (25–29), Control group 27 (24–29) (n = 93), p=ns Harvard Trauma Questionnaire [median (IQR)]: Intervention group 28 (24–35), Control group 28 (24–33.25), p=ns (81,6 missing) Pre-existing diseases, median (IQR) : Intervention group 2 (1–3), Control group 2 (1–3), p=ns Pre-existing diseases, (>1 disease) (%): Intervention group 76/87, Control group 81/94, p=ns Diagnostic groups (n): Respiratory: Intervention group 20/87, Control group 14/94 – Cardiovascular: Intervention group 16/87, Control group 17/94 – Sepsis: Intervention group 26/87, Control group 33/94 – Other: Intervention group 25/87, Control group 30/94
Exposures	
• **Intervention group**	**Duration**: 10 months post-ICU **Starting date:** at one month post-ICU **Setting**: at hospital and by phone **Frequency**: Three consultations conducted by specially trained study nurses **Content**: The first consultation was conducted with the patient and relatives at one to three months post-ICU and consisted in a dialogue on supporting the patient in constructing an illness narrative aided by photographs of the patient during the ICU-stay and revisiting ICU. The second and third consultations were conducted by telephone with patients at 5 and 10 months post-ICU and consisted in a dialogue focused on issues of importance to the patients.
• **Control group**	ICU discharge without follow-up.
Results	
Results are only reported in Intention to Treat (ITT). Results in per protocol (PP) led to the same conclusions	
• **HRQoL**	• SF-36 Mental Component Score o At 3 months after ICU Mean difference (95% CI): -0.13 (-4.23 to 3.99), p=0.95

	o At 12 months after ICU Mean difference (95% CI): 1.35 (-3.13 to 5.82), p=0.55 o Difference scores between 3 and 12 months after ICU Mean difference (95% CI): -0.73 (-5.16 to 3.70), p=0.75 • SF-36 Physical Component Score o At 3 months after ICU Mean difference (95% CI): 2.85 (-0.63 to 6.32), p=0.11 o At 12 months after ICU Mean difference (95% CI): 1.86 (-1.88 to 5.59), p=0.33 o Difference scores between 3 and 12 months after ICU Mean difference (95% CI): 0.24 (-2.40 to 2.88), p=0.86
• **Sense of coherence (SOC)**	*SOC was measured by 13 questions from Sense of Coherence Scale (SOC-13). The final score ranges from 13 to 91. Higher scores indicate stronger SOC.* • At 3 months after ICU Mean difference (95% CI): 1.52 (-3.22 to 6.26), p=0.53 • At 12 months after ICU Mean difference (95% CI): 2.21 (-3.37 to 7.80), p=0.43 • Difference scores between 3 and 12 months after ICU Mean difference (95% CI): 1.44 (-3.22 to 6.10), p=0.54
• **Anxiety**	HADS – A score • At 3 months after ICU Mean difference (95% CI): -0.40 (-1.89 to 1.1), p=0.43 • At 12 months after ICU Mean difference (95% CI): -0.73 (-2.18–0.72), p=0.99 • Difference scores between 3 and 12 months after ICU Mean difference (95% CI): -0.93 (-2.13–0.28), p=0.89
• **Depression**	HADS – D score • At 3 months after ICU Mean difference (95% CI): -0.75 (-1.95 to 0.45), p=0.97 • At 12 months after ICU Mean difference (95% CI): -0.68 (-1.89 to 0.54), p=0.16 • Difference scores between 3 and 12 months after ICU Mean difference (95% CI): -0.33 (-1.25 to 0.59), p=0.89
• **Posttraumatic stress**	*Harvard Trauma Questionnaire Part IV (HTQ-IV) consisting of items covering re-experience, avoidance, and arousal, corresponding to DMS-IV criteria for PTSD. The final score ranges from 18 to 72. Higher scores indicate greater symptoms of PTSD.* • At 3 months after ICU

	Mean difference (95% CI): -2.72 (-5.94 to 0.50), p=0.10 • At 12 months after ICU Mean difference (95% CI): -1.07 (-4.73 to 1.85), p=0.56 • Difference scores between 3 and 12 months after ICU Mean difference (95% CI): -0.25 (-2.05 to 2.55), p=0.83
Limitations and other comments	
• **Limitations and notes**	• Small sample size leading to underpowered outcomes • Large number of lost to follow-up
• **Authors' conclusions**	The recovery programme intended for intensive care survivors did not have an effect on the relatives. No statistically significant effect of the recovery programme on relatives' HRQOL, SOC, symptoms of anxiety, depression and PTSD at three or 12 months post-ICU was found.

Jones 2012[66]	
Methods	
• **Design**	Randomized clinical trial
• **Source of funding and competing interest**	Funding: Stanley Thomas Johnson Foundation, Bern, Switzerland Competing interest: no statement
• **Setting**	In general district hospitals in 2 European countries (UK and Sweden)
• **Sample size**	36 family members (18 in control group, 18 in intervention group) but 30 relatives (15 in control group, 15 in intervention group)completed the 3-month follow-up questionnaire
• **Duration and follow-up**	Duration: from January 2006 to September 2006 Follow-up: 3 months
• **Statistical analysis**	Descriptive statistics, Fisher exact test
Patient characteristics	
• **Eligibility criteria**	≥ 16y, ICU LOS ≥ 72 h and ventilated≥ 24 h
• **Exclusion criteria**	Not able to give informed consent, severe traumatic brain injury, schizophrenic, manic depression or diagnosed PTSD
• **Patient & disease characteristics**	*Characteristics at randomisation* **Patients** Age [median (range)]: Control group 58y (37-82), Intervention group 61y (19-74) ICU stay [median (range)]: Control group 13 days (4-50), Intervention group 15 days (4-49) Hours ventilated [median (range)]: Control group 240h (72-1172), Intervention group 264h (48-1097)

	APACHE II severity score [median (range)]: Control group 21 (9-37), Intervention group 18 (8-28) PTSS-14 score at 1 month [median (range)]: Control group 22 (15-65), Intervention group 26 (15-75) Emergency admission to ICU: Control group 15/15, Intervention group 13/15 Patient's sex, male/female: Control group 8/7, Intervention group 10/5 Diagnostic groups: Respiratory failure Control group 5/15, Intervention group 4/15 – Sepsis Control group 5/15, Intervention group 1/15 – Circulatory failure Control group 0/15, Intervention group 2/15 – Multi-organ failure Control group 1/15, Intervention group 3/15 – Trauma Control group 4/15, Intervention group 1/15 – Combined (pulmonary/circulatory) Control group 1/15, Intervention group 0/15 – Gastrointestinal failure Control group 1/15, Intervention group 2/15 – Neurological failure Control group 0/15, Intervention group 2/15 **Relatives** Sex (male/female): Control group 4/11, Intervention group 3/12 Memories recalled at 1 month by relatives from the time of critical illness (PTSS-14 part A): Nightmares Control group 5/15, Intervention group 5/15 – Severe anxiety/panic Control group 7/15, Intervention group 8/15 – Physical pain Control group 3/15, Intervention group 4/15 – Feelings of breathlessness Control group 4/15, Intervention group 4/15 PTSS-14 score [median (range)] at 1 month: Control group 26 (14-65), Intervention group 24 (14-54) PTSS-14 score [median (range)] at 3 months Control group 28 (14-38) , Intervention group 19 (14-28)
Exposures	
• **Intervention group**	**Duration**: 3 months **Starting date:** 1 month post-ICU **Setting**: Outpatient setting at hospital **Frequency**: at 1 month (baseline assessment) and at 3-month consultation **Content**: Family member was the patient's next of kin and was recruited to the study in the general care area about 1 week after ICU discharge. Patients received their ICU diary as soon as they wanted, as long as it was before 2 months. Patient's family members contributed to the writing of the diary if they felt they could. All relatives had read the ICU diary after the patient hospital discharge.
• **Control group**	The control group received the same intervention than those in intervention group but received their diaries only at 3 months post-ICU
Results	
• **Change in PTSD score over time in relative**	Median change in the PTSS-14 scores between 1 and 3 months Control group +5 vs intervention group -5, p=0.03
Limitations and other comments	
• **Limitations and notes**	• Small sample size

	• Centres proposed follow-up services for family of ICU-patients before the trials
• **Authors' conclusions**	Providing patients with diaries may reduce the level of PTSD-related symptoms for relatives of patients after critical illness.

Kentish-Barnes 2017[62]	
Methods	
• **Design**	Multicenter randomized clinical trial
• **Source of funding and competing interest**	Funding: Fondation de France, a non-profit institution Competing interest: No statement
• **Setting**	In 22 ICU in France (Paris, Le Chesnay-Versailles, Bordeaux, Brest, Lyon, Marseille, Dieppe, La Roche-sur-Yon, Montpellier, Argenteuil, La Rochelle, Poitiers, Nantes, Clermont Ferrand, Montfermeil, Corbeil-Essones, Amiens)
• **Sample size**	242 patients were randomised (123 in intervention group and 119 to the control group). At 1 month, 208 relatives were interviewed (107 in intervention group and 101 to the control group) and 190 relatives at 6 months (97 in intervention group and 91 to the control group). 19 relatives refused to answer to the interview and 31 did not respond.
• **Duration and follow-up**	Duration: December 2014 to December 2015 Follow-up: at 1 and 6 months
• **Statistical analysis**	Chi square test, Wilcoxon rank-sum test, Fisher test, multivariable logistic regression models
Patient characteristics	
• **Eligibility criteria**	≥18y, at least one family visit prior to death, ICU LoS ≥ 2 days, being the relative most involved with the ICU team
• **Exclusion criteria**	Being pregnant, family not fluent in French, do not consent to participate.
• **Patient & disease characteristics**	**Patients' characteristics** Age [median (IQR)]: Intervention group 61y (54–71) Control group 61y (54–66) Gender (% of female): Intervention group 33.3% Control group 37.0% At least one comorbidity: Intervention group 79.7% Control group 84.3% Intractable cancer: Intervention group 30.1% Control group 30.2% Dependent or bedridden: Intervention group 50.4% Control group 47.1% Dementia: Intervention group 9.7% Control group 8.4% Life support was withheld/withdrawn: Intervention group 80.5% Control group 86.5% Preferred role of relatives: Being only informed of the end-of-life decision Intervention group 25.3% Control group 34.4% – To actively share the end-of-life decision Intervention group 53.6% Control group 51.3% – Undetermined or unknown Intervention group 21.1% Control group 14.3%

	Patient intubated at the time of death: Intervention group 58.5% Control group 54.6% Patient sedated at the time of death: Intervention group 78.9% Control group 76.5% Extubation in the last 48 h of life: Intervention group 25.2% Control group 30.2% Family–clinician or intra-team conflicts: Intervention group 7.3% Control group 10.9% Bedside presence at the time of death: Nurses Intervention group 65.9% Control group 64.7% – Relatives Intervention group 61.0% Control group 59.7% – Physicians Intervention group 30.9% Control group 31.9% **Relatives' characteristics** Age [median (IQR)]: Intervention group 57y (46–65.5) Control group 56y (44–64.5) Gender (% of female): Intervention group 33.3% Control group 37.0% Relationship to the patient: Spouse: Intervention group 38.5% Control group 32.3% – Children: Intervention group 39.4% Control group 40.4% – Other: Intervention group 22.0% Control group 26.2% Live alone after patient's death: Intervention group 41.3% Control group 43.4% Rating of dying and death quality (CAESAR): Intervention group 66 [50–76] Control group 66 [52–78]
Exposures	
• **Intervention group**	**Duration**: 4 months after death **Starting date:** Within 3 days after the patient's death **Setting**: Home **Frequency**: at 1 and 6 months **Content**: During intensive care, all families talked with the clinicians daily and attended an end-of-life conference. The Family involvement was tailored to patient preferences and the family's preferred role. Symptom control, timing of communication at the end-of-life, and implementation of treatment-limitation decisions were at the clinician's discretion. A handwritten letter of condolence was prepared by physician and nurse in charge of the patient according a guidance describing the five domains that must be covered (recognize the death and name the deceased, mention a personal impression of the deceased, recognize the family member, offer help, and express sympathy). The clinicians recorded all reactions or feedback (telephone calls, letters, visits, or other) from the relatives within 4 months following death. Psychologists, sociologists, and research nurses contacted members 30 days and 6 months after the patient's death.
• **Control group**	**Duration**: 4 months after death **Starting date:** from the patient's death **Setting**: Hospital **Frequency**: at 1 and 6 months

	Content: During intensive care, all families talked with the clinicians daily and attended an end-of-life conference. The Family involvement was tailored to patient preferences and the family's preferred role. Symptom control, timing of communication at the end-of-life, and implementation of treatment-limitation decisions were at the clinician's discretion. A letter of condolence was not part of standard care in the participating. The clinicians recorded all reactions or feedback (telephone calls, letters, visits, or other) from the relatives within 4 months following death. Psychologists, sociologists, and research nurses contacted members 30 days and 6 months after the patient's death.
Results	
• **Anxiety and depression**	• HADS Median score (IQR) o At 1 month Intervention group 16 (10–22) Control group 14 (8–21), p=0.36 o At 6 months Intervention group 13 (6–19) Control group 9 (4–17), p=0.04 • HADS-D Median score (IQR) o At 1 month Intervention group 8 (4–12) Control group 6 (2–12), p=0.09 o At 6 months Intervention group 6 (2–10) Control group 3 (1–8), p=0.01 Mean difference (95% CI): 1.4 (−0.14 to +2.90), p=0.026 • Relatives with symptoms of depression (HADS-D ≥8) o At 1 month Intervention group 56.0% Control group 42.4%, p=0.05 o At 6 months Intervention group 36.6% Control group 24.7%, p=0.05 • HADS-A Median score (IQR) o At 1 month Intervention group 7 (4–11) Control group 7 (4–12), p=0.92 • Relatives with symptoms of depression (HADS-D ≥8) o At 1 month Intervention group 47.7% Control group 45.5%, p=0.97
• **PTSD**	• IES-R at 6 months [median score (IQR)] Intervention group 28 (15–38) Control group 20 (10–37), p=0.09 • Relatives with PTSD-related symptoms (IES-R ≥26) Intervention group 52.4% Control group 37.1%, p=0.03
• **Complicated Grief**	• Inventory of complicated grief (ICG) at 6 months [median score (IQR)] Intervention group 16 (8–30) Control group 13 (4–27), p=0.07

	• Relatives at high risk for complicated grief (ICG ≥25) Intervention group 37.6% Control group 27.0%, p=0. 11
• **Feedback professional on condolence letter**	Median score (IQR) *Number of respondents not mentioned* • In general, on a scale of 0 (very difficult) to 7 (very easy), writing this condolence letter was: 5 (3-5.5) • Emotionally, on a scale of 0 (very difficult) to 7 (not difficult), writing this letter was: 6 (5-6) • On a scale of 0 (very little time) to 7 (a great deal of time), did it take you long to write the letter?3 (2-4) • On a scale of 0 (not really) to 7 (a great deal), do you feel this letter will help the deceased's family member? 5 (3-6) • Did writing the letter help you (0 (not really) to 7 (a great deal))? 2 (0.5-4)
• **Risk factors**	Not reported see dedicated chapter
Limitations and other comments	
• **Limitations and notes**	• The study was adequately powered for the outcomes at 1 month, the compliance of intervention was very good and the design is multicentre • Psychological status of the relatives at the time they received the condolence letter was not unknown and may impact the effect of the intervention • Uncomplete reporting of some results such as HADS-A not reported at 6 months
• **Authors' conclusions**	A handwritten condolence letter sent 2 weeks after the death failed to alleviate grief symptoms. Unexpectedly, symptoms of depression and PTSD were worse with the intervention, albeit not significantly. Secondary outcomes, measured at 6 months, show a significant increased risk of developing depression and PTSD symptoms.

Appendix 4.4. Overview of meta-analyses

Intervention	Pooled estimate	Comments
Diaries in patients (Barreto 2019)[59]	**PTSD** • Pooling 1 (4 RCT)[65, 67, 72, 73] RR [95%CI] 0.70 [0.38;1.27], I²=22%, p=0.28 • Pooling 2 (4 RCT, one before-after study and observational study)[64, 65, 67, 72-74] RR [95%CI] 0.76 [0.43;1.34], I²=22%, p=0.28 Prediction interval [0.18;3.26] **Depression** • Pooling 1 (3 RCT)[67, 73, 75] RR [95%CI] 0.42 [0.12;1.46], I²=0%, p=0.65 • Pooling 2 (3 RCT and a before-after study)[64, 67, 73, 75] RR [95%CI] 0.41 [0.23;0.75], I²=0%, p=0.65 Prediction interval [0.12;1.36] **Anxiety** • Pooling 1 (3 RCT))[67, 73, 75] RR [95%CI] 0.48 [0.05;4.60], I²=0%, p=0.65 • Pooling 2 (3 RCT and a before-after study)[64, 67, 73, 75] RR [95%CI] 0.45 [0.13;1.51], I²=0%, p=0.65 Prediction interval [0.12;1.36]	**PTSD** • Pooling 1 was not appropriate Variations in interventions (handover of diaries with or without reading support by a professional) Variations in assessment tools (PTSS-14[67, 72] and IES-R[65, 73]) and variation in cut-off to define PTSD • Pooling 2 was not appropriate Same limits present in pooling 1 Variations in study design (RCT and non RCT) Prediction interval used inappropriately because number of study < 10[76] **Depression** • Pooling 1 was not appropriate Variations in interventions (handover of diaries with or without reading support by a professional) Variations in assessment timing (3 weeks[75] vs 3 months)[67, 73]) and variation in cut-off to define depression • Pooling 2 was not appropriate Same limits present in pooling 1 Variations in study design (RCT and non RCT) Prediction interval used inappropriately because number of study < 10[76] **Anxiety** • Pooling 1 was not appropriate Variations in interventions (handover of diaries with or

		without reading support by a professional) Variations in assessment timing (3 weeks[75] vs 3 months)[67, 73] and variation in cut-off to define anxiety • Pooling 2 was not appropriate Same limits present in pooling 1 Variations in study design (RCT and non RCT) Prediction interval used inappropriately because number of study < 10 [76]
	QoL • Pooling (2 RCT and 2 observational study)[58, 65, 67, 71] MD [95%CI] 10.29 [0.77;1.90], I^2=0%, p=0.50 Prediction interval [-29.52; 50.09]	**QoL** • Pooling was not appropriate Variations in study design (RCT and non RCT) Variations in assessment timing Prediction interval used inappropriately because number of study < 10 [76]
Diaries in patients (Geense 2019)[46]	**Depression** • Pooling (1 RCT and 1 before/after study)[64, 75] SMD [95%CI] 0.68 [0.14;1.21], I^2=15%, p_{eff}<0.01 **Anxiety** • Pooling (1 RCT and 1 before/after study)[64, 75] SMD [95%CI] 0.44 [0.01;0.87], I^2=0%, p_{eff}=0.05	**Depression** Variations in study design (RCT and non RCT) Variations in assessment timing **Anxiety** Variations in study design (RCT and non RCT) Variations in assessment timing
Diaries in patients (McIlroy 2019)[77]	**PTSD** • Pooling (1 RCT,1 before/after study and 1 prospective observational study)[64, 72, 74] RR [95%CI] 0.75 [0.33;1.73], I^2=66%, p_{eff}=0.5 **Depression**	**PTSD** Variations in study design (RCT and non RCT) Variation in interventions (usage of photo vs no photo, handover of diaries with or without reading support by a professional) Variation in assessment tools (PTSS-14, IES-R) Variations in assessment timing (2, 3 or 12 months)

	• Pooling (1 RCT and 1 before/after study)[64, 75] RR [95%CI] 0.39 [0.17;0.87], I^2=0%, p_{eff}=0.02 **Anxiety** • Pooling (1 RCT and 1 before/after study)[64, 75] RR [95%CI] 0.32 [0.12;0.86], I^2=0%, p_{eff}=0.02	**Depression** Variations in study design (RCT and non RCT) Variations in assessment timing **Anxiety** Variations in study design (RCT and non RCT) Variations in assessment timing
Diaries in patients (Nydahl)[78]	**PTSD** • Pooling (1 RCT[40, 42, 45, 47, 79, 80],1 before/after study and 2 prospective observational study)[81] OR [95%CI] 0.58 [0.24;1.42], I^2=51%, p_{eff}=0.23 * results of one study is reported in congress abstract[81] **Depression** • Pooling (1 RCT and 1 before/after study)[64, 75] OR [95%CI] 0.27 [0.09;0.77], I^2=0%, p_{eff}=0.02 **Anxiety** • Pooling (1 RCT and 1 before/after study)[64, 75] OR [95%CI] 0.23 [0.07;0.77], I^2=0%, p_{eff}=0.02	**PTSD** Variations in study design (RCT and non RCT) Variation in interventions (usage of photo vs no photo, handover of diaries with or without reading support by a professional) Variation in assessment tools (PTSS-14, IES-R) Variations in assessment timing (2, 3 or 12 months) **Depression** Variations in study design (RCT and non RCT) Variations in assessment timing **Anxiety** Variations in study design (RCT and non RCT) Variations in assessment timing
Diaries in relatives (Barreto 2019)[59]	**PTSD** • Pooling (3 RCT and 1 before/after study)[64-67] RR [95%CI] 0.68 [0.32;1.42], I^2=80%, p<0.01 Prediction interval [0.10;4.52]	**PTSD** • Pooling was not appropriate Variations in study design (RCT and non RCT) Variations in interventions (handover of diaries with or without reading support by a professional) Variation in control groups (in 1 study diaries are also given to patients of control relatives)[66] Variations in assessment tools (PTSS-14[66, 67] and IES-R[73])

	Depression • Pooling (2 RCT and 1 before/after study) [64, 65, 67] RR [95%CI] 1.02 [0.77;1.35], I^2=0%, p=0.82 Prediction interval [0.27; 3.78] **Anxiety** • Pooling (2 RCT and 1 before/after study) [64, 65, 67] RR [95%CI] 0.86 [0.41;1.80], I^2=65%, p=0.06 Prediction interval [0.03; 26.85]	and variation in cut-off to define PTSD Frequency of PTSD was not reported in Jones 2012 Prediction interval used inappropriately because number of study < 10[76] **Depression** • Pooling 1 was not appropriate Variations in study design (RCT and non RCT) Variation in cut-off to define depression Prediction interval used inappropriately because number of study < 10 [76] **Anxiety** • Pooling was not appropriate Variations in study design (RCT and non RCT) Variation in cut-off to define depression Prediction interval used inappropriately because number of study < 10 [76]
Diaries in relatives (Nydahl)[78]	**PTSD** • Pooling (1 RCT and 1 before/after study)[64, 66] OR [95%CI] 0.17 [0.08;0.38], I^2=0%, p<0.0001	**PTSD** Variations in study design (RCT and non RCT) Variations in assessment tools (PTSS-14[66] and IES-R[64]) Variation in interventions
Exercises (Geense 2019)[46]	**Depression** • Pooling (3 RCT and 1 non RCT)[38-40, 50] SMD [95%CI] 0.35 [-0.17;0.88], I^2=64%, p_{eff}=0.19 **Anxiety** • Pooling (3 RCT and 1 non RCT))[38-40, 50] SMD [95%CI] 0.29 [-0.41;1.00], I^2=83%, p_{eff}=0.41	**Depression** Variations in study design (RCT and non RCT) Variations in assessment timing Variation in interventions (exercise programme alone, or with educational session or with follow-up consultations) **Anxiety** Variations in study design (RCT and non RCT)

		Variations in assessment timing Variation in interventions (exercise programme alone, or with educational session or with follow-up consultations
	SF-36 MCS • Pooling (7 RCT)[40, 42, 45, 47, 79, 80] SMD [95%CI] 2.62 [0.92;4.32], I^2=65%, p_{eff}<0.001	**SF-36 MCS** Variations in assessment timing Variation in intervention timing (exercise programme starting from the ICU stay (some interventions stopped after ICU discharge) to starting of hospital discharge)
Exercises (Rosa 2019)[82]	**Depression** • Pooling (3 RCT and 1 non RCT)[38, 40, 44, 48] MD [95%CI] -1.21 [-2.31;-0.11], I^2=0%, p_{eff}=0.03	**Depression** Variations in study design (RCT and non RCT) Variations in assessment timing Variation in interventions (exercise programme alone, or with educational session or with nutritional supplement)
	Anxiety • Pooling (3 RCT and 1 non RCT))[38, 40, 44, 48] MD [95%CI] -0.66 [-1.81;0.54], I^2=0%, p_{eff}=0.28	**Anxiety** Variations in study design (RCT and non RCT) Variations in assessment timing Variation in interventions (exercise programme alone, or with educational session or with nutritional supplement)
	SF-36 PCS short term (0 to 3 months) • Pooling (4 RCT and 1 non RCT)[38, 40, 42, 44, 45] SMD [95%CI] 0.08 [-0.26;0.41], I^2=37%, p_{eff}=0.65	**SF-36 PCS short term (0 to 3 months)** Variations in study design (RCT and non RCT) Variation in interventions (exercise programme alone, or with educational session)
	SF-36 PCS medium term (>3 to 6 months) • Pooling (1 RCT and 1 non RCT)[38, 40, 42] SMD [95%CI] 0.02 [-0.25;0.30], I^2=0%, p_{eff}=0.30	**SF-36 PCS short medium (0 to 3 months)** Variations in study design (RCT and non RCT)
	SF-36 MCS short term (0 to 3 months) • Pooling (4 RCT and 1 non RCT)[38, 40, 42, 44, 45]	**SF-36 MCS short term (0 to 3 months)**

	SMD [95%CI] 0.26 [-0.02;0.51], I^2=6%, p $_{eff}$=0.04 **SF-36 MCS medium term (>3 to 6 months)** • Pooling (1 RCT and 1 non RCT)[38, 40, 42] SMD [95%CI] 0.15 [-0.13;0.42], I^2=0%, p $_{eff}$=0.30	Variations in study design (RCT and non RCT) Variation in interventions (exercise programme alone, or with educational session) **SF-36 MCS short medium (0 to 3 months)** Variations in study design (RCT and non RCT)
Follow-up consultations (Geense 2019)[46]	**Depression** • Pooling (1 RCT and 1 non RCT)[52, 53] SMD [95%CI] -0.01 [-0.20;0.19], I^2=0%, p $_{eff}$=0.67 **Anxiety** • Pooling (1 RCT and 1 non RCT)[52, 53] SMD [95%CI] -0.21 [-0.60;0.18], I^2=75%, p $_{eff}$=0.29 **SF-36 MCS** • Pooling (2 RCT)[41, 52] SMD [95%CI] -1.32 [-3.64;1.00], I^2=0%, p $_{eff}$<0.27	**Depression** Variations in study design (RCT and non RCT) Variation in intervention timing (follow-up during 3 months vs 10 months) Variation in intervention (usage of photos vs 2 ICU visits during the hospital stay) **Anxiety** Variations in study design (RCT and non RCT) Variation in intervention timing (follow-up during 3 months vs 10 months) Variation in interventions (usage of photos vs 2 ICU visits during the hospital stay) **SF-36 MCS** Variation in interventions (follow-up programme included exercises vs no exercises but usage photos)
Follow-up consultations (Rosa 2019)[82]	**Anxiety at short term (0 to 3 months)** • Pooling (3 RCT)[50, 75, 83] MD [95%CI] 0.08 [-1.36;1.53], I^2=42%, p $_{eff}$=0.91 **Anxiety at medium term (>3 to 6 months)** • Pooling (3 RCT)[41, 50, 83] MD [95%CI] -0.29 [-0.78;0.20], I^2=0%, p $_{eff}$=0.25 **Anxiety at long term (> 6 months)**	**Anxiety at short term (0 to 3 months)** Variation in interventions (usage of diary vs educational material+ education session during hospital stay vs educational material alone, ICU visit vs no ICU visit) **Anxiety at medium term (>3 to 6 months)** Variation in interventions (usage of educational material + education session during hospital stay vs exercises vs educational material alone, ICU visit vs no ICU visit)

	• Pooling (2 RCT)[41, 83] MD [95%CI] -0.56 [-1.63;0.52], I^2=0%, p $_{eff}$=0.31 **Depression at short term (0 to 3 months)** • Pooling (3 RCT)[50, 75, 83] MD [95%CI] -1.20 [-3.29;0.88], I^2=79%, p $_{eff}$=0.26 **Depression at medium term (>3 to 6 months)** • Pooling (3 RCT)[41, 50, 83] MD [95%CI] -0.07 [-0.53;0.39], I^2=0%, p $_{eff}$=0.76 **Depression at long term (> 6 months)** • Pooling (2 RCT)[41, 83] MD [95%CI] -0.11 [-1.15;0.93], I^2=0%, p $_{eff}$=0.83 **PTSD at short term (0 to 3 months)** • Pooling (2 RCT)[50, 83] SMD [95%CI] -0.21 [-0.65;0.24], I^2=74%, p $_{eff}$=0.36 **PTSD at medium term (>3 to 6 months)** • Pooling (3 RCT)[41, 50, 83] SMD [95%CI] -0.19 [-0.36;-0.01], I^2=0%, p $_{eff}$=0.04 **PTSD at long term (> 6 months)** • Pooling (2 RCT)[41, 83] SMD [95%CI] -0.17 [-0.49;0.15], I^2=62%, p $_{eff}$=0.31	**Anxiety at long term (> 6 months)** Variation in interventions (usage of educational material + education session during hospital stay vs exercises, ICU visit vs no ICU visit) **Depression at short term (0 to 3 months)** Variation in interventions (usage of diary vs educational material+ education session during hospital stay vs educational material alone, ICU visit vs no ICU visit) **Depression at medium term (>3 to 6 months)** Variation in interventions (usage of educational material + education session during hospital stay vs exercises vs educational material alone, ICU visit vs no ICU visit) **Depression at long term (> 6 months)** Variation in interventions (usage of educational material + education session during hospital stay vs exercises, ICU visit vs no ICU visit) **PTSD at short term (0 to 3 months)** Variation in interventions (usage of educational material + education session during hospital stay vs educational material alone, ICU visit vs no ICU visit) Variation in assessment tools (IES-R vs Davidson trauma scale) **PTSD at medium term (>3 to 6 months)** Variation in interventions (usage of educational material + education session during hospital stay vs educational material alone vs exercises, ICU visit vs no ICU visit) Variation in assessment tools (IES-R vs Davidson trauma scale)

SF-36 PCS at short term (0 to 3 months)

- Pooling (2 RCT)[83, 84]

SMD [95%CI] -0.14 [-0.47;0.18], I^2=62%, p_{eff}=0.38

SF-36 PCS medium term (>3 to 6 months)

- Pooling (3 RCT)[41, 54, 83]

SMD [95%CI] 0.09 [-0.22;0.05], I^2=0%, p_{eff}=0.22

SP-36 PCS at long term (> 6 months)

- Pooling (3 RCT)[41, 52, 54]

SMD [95%CI] 0.03 [-0.09;0.16], I^2=0%, p_{eff}=0.58

SF-36 MCS at short term (0 to 3 months)

- Pooling (2 RCT)[83, 84]

SMD [95%CI] -0.14 [-0.47;0.18], I^2=62%, p_{eff}=0.38

SF-36 MCS medium term (>3 to 6 months)

- Pooling (3 RCT)[41, 54, 83]

SMD [95%CI] 0.02 [-0.11;0.16], I^2=0%, p_{eff}=0.72

SP-36 MCS at long term (> 6 months)

- Pooling (2 RCT)
- [83, 84]

SMD [95%CI] 0.08 [-0.05;0.20], I^2=8%, p_{eff}=0.24

PTSD at long term (> 6 months)

Variation in interventions (usage of educational material + education session during hospital stay vs exercises, ICU visit vs no ICU visit)

SF-36 PCS at short term (0 to 3 months)

Variation in interventions (usage of educational material + education session during hospital stay vs case manager)

SF-36 PCS medium term (>3 to 6 months)

Variation in interventions (usage of educational material + education session during hospital stay vs exercises vs case manager + training of patients and GP , ICU visit vs no ICU visit)

SP-36 PCS at long term (> 6 months)

Variation in interventions (usage of photos vs exercises vs case manager + training of patients and GP, ICU visit vs no ICU visit)

SF-36 PCS at short term (0 to 3 months)

Variation in interventions (usage of educational material + education session during hospital stay vs case manager)

SF-36 PCS medium term (>3 to 6 months)

Variation in interventions (usage of educational material + education session during hospital stay vs exercises vs case manager + training of patients and GP, ICU visit vs no ICU visit)

SP-36 PCS at long term (> 6 months)

Variation in interventions (usage of photos vs exercises vs case manager + training of

		patients and GP, ICU visit vs no ICU visit)
Mental health interventions (Geense 2019)[46]	**Depression** • Pooling (3 RCT)[60, 61, 85] SMD [95%CI] -0.01 [-0.31;0.30], I^2=0%, p_{eff}=0.97 **Anxiety** • Pooling (2 RCT)[60, 61] SMD [95%CI] -0.03 [-0.29;0.34], I^2=0%, p_{eff}=0.86	**Depression** Variations in study design (RCT and non RCT) Variation in populations (all conditions vs focus on post cardiac surgery heart failure patients) Variation in interventions (cooping skill training vs mindfulness vs psychosocial support and education from an interdisciplinary team) Variation in assessment tools (BDI vs HADS-D, PHQ-9) **Anxiety** Variations in study design (RCT and non RCT) Variation in interventions (cooping skill training vs mindfulness) Variation in assessment tools (HADS-A, GAD-7)

All pooling are random effect, p_{eff} p-value of the effect, p= p-value of I^2, BDI Beck Depression Inventory

Appendix 4.5. List of ongoing trials

Status at 01/10/20	Study tittle	Conditions	Interventions	Localisations
• **PICS**				
Terminated	Feasibility of a Physiotherapy-led Follow-up Programme in Adult Critical Illness Survivors	Post Intensive Care Unit Syndrome	Physiotherapy-led follow-up programme	Kantonsspital Winterthur Winterthur, Zürich, Switzerland
Recruiting	Cytoflavin in the Rehabilitation of Post-intensive Care Syndrome in Stroke Survivors	Ischemic Stroke Post Intensive Care Unit Syndrome		Brain Institute Clinic Ekaterinburg, Sverdlovsk Region, Russian Federation
Active, not recruiting	Intensive Care Unit Recovery	Post Intensive Care Unit Syndrome Intensive Care Unit Acquired Weakness Critical Illness	Diagnostic Test: Venipuncture Diagnostic Test: Ultrasound Quadriceps Muscles	Medical Center Leeuwarden Leeuwarden, Friesland, Netherlands
Suspended	Intensive Care Unit (ICU) Diary Project	PTSD Post ICU Syndrome	Diary (blank journal) plus PTSD psycho-education vs PTSD psycho-education alone	Tulane University School of Medicine New Orleans, Louisiana, United States
Recruiting	ICU Diaries and Its Effects After the Unit Discharge	Post Intensive Care Unit Syndrome Intensive Care Unit Syndrome PTSD Anxiety Symptoms Depressive Symptoms	ICU Diaries	Juliana Mara Stormovski de Andrade Porto Alegre, RS, Brazil
Recruiting	Positive Suggestions Via MP3 Messages	Post Intensive Care Unit Syndrome Psychological Trauma Anxiety	Psychological Support Based on Positive Suggestion delivered via pre-recorded MP3 message	Mayo Clinic in Rochester Rochester, Minnesota, United State

		Depression PTSD		
Completed	Patterns of PTSD in Adult Patients After Intensive Care	Intensive Care Unit Syndrome	Post ICU recovery program	Holbæk Hospital Holbæk, Sjælland, Denmark
Recruiting	A Problem Solving Intervention for Post-ICU Cognitive Impairment in Older Adults	Critical Illness Mechanical Ventilation Complication Delirium Cognitive Impairment	Post-ICU Problem Solving	The Ohio State University College of Nursing Columbus, Ohio, United States
Active not recruiting	Assessing The Effects of Exercise, Protein, and Electric Stimulation On Intensive Care Unit Patients Outcomes	Muscle Weakness Critical Illness Sarcopenia	Dietary Supplement: MPR and High Protein Supplement (HPRO) and Neuromuscular Electric Stimulation (NMES)	U of Maryland, Baltimore, Professional Schools IRB Baltimore, Maryland, United State
Recruiting	A Problem Solving Intervention for Post-ICU Cognitive Impairment in Older Adults	Critical Illness Mechanical Ventilation Complication Delirium Cognitive Impairment	Post-ICU Problem Solving	The Ohio State University College of Nursing Columbus, Ohio, United States
Recruiting	Nursing Intervention in the Patient Being Discharged From the Intensive Care Unit	Anxiety Depression	Nursing Empowerment Intervention	Hospital de Bellvitge Hospitalet De Llobregat Hospital Clínic of Barcelona Hospital Vall d'Hebron (Barcelona, Spain)
• **PICS-F**				
Recruiting	Self-care App for Family Members of ICU Patients.	Post Intensive Care Unit Syndrome	Behavioral: App Intervention	Summa Health System Akron, Ohio, United States

• **PICS and PICS-F**				
Recruiting	Partnering With Family Members to Prevent, Detect and Manage Delirium in Critically Ill Patients.	Delirium Intensive Care Unit Delirium Post Intensive Care Unit Syndrome Post Intensive Care Unit Syndrome Family	Delirium Education, Prevention, and Management vs Standard Care	Peter Lougheed Centre Foothills Medical Centre Rockyview General Hospital South Health Campus (Calgary, Alberta, Canada)
Completed	The Effectiveness of a Post-ICU Recovery Program on Relatives	Intensive Care Unit Syndrome Relatives	Behavioral	Holbæk Hospital Holbæk, Sjælland, Denmark
• **PICS in COVID patients**				
Recruiting	The Usability, Feasibility, and Tolerability of Virtual Reality for Rehabilitation From COVID-19	Coronavirus Post Intensive Care Unit Syndrome	Device: Virtual Reality	Radboud university medical center. Nijmegen, Gelderland, Netherlands
Not yet recruiting	CoV-PICS: A Virtual Post-ICU Clinic	Post ICU Syndrome	Medical Record Review - Inpatient Treatment Online Questionnaires	Washington University School of Medicine
Recruiting	Early Care Program for the Management of Post-ICU Syndrome and Chronic Pain After COVID-19 Infection.	Post ICU Syndrome Chronic Pain Covid-19	Intervention program	Tomás Cuñat Barcelona, Spain
Recruiting	Optimizing Outcomes With Physical Therapy Treatment for IndividuALs Surviving an ICU Admission for Covid-19	Covid-19 Critical Illness Post Intensive Care Unit Syndrome Muscle Weakness	ICU Recovery + Physical Therapy	University of Kentucky Lexington, Kentucky, United States

Recruiting	Post Intensive Care Syndrome in COVID19 Patients	COVID19 Post Intensive Care Unit Syndrome	Diagnostic Test: Questionnaires	Corporació Parc Taulí Sabadell, Barcelona, Spain
• **PICS-F in COVID patients**				
Not yet recruiting	Psychological Symptoms and Families of COVID-19 Patients	Family Members Post Intensive Care Unit Syndrome Post Traumatic Stress Disorder	Behavioral: Written Summary of Rounds	Rush University Medical Center Chicago, Illinois, United States
Recruiting	Stress Related Disorders in Family Members of COVID-19 Patients Admitted to the ICU	Respiratory Failure SARS-CoV 2 Corona Virus Infection Post Intensive Care Unit Syndrome Family Members Post-Traumatic Stress Disorder Anxiety Depression		United States (Colorado, Louisiana, Massachusetts, New York, Pennsylvania, Vermont, Washington)

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Colophon

Title: Post intensive care syndrome in the aftermath of COVID-19 – Appendices

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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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