



## FOLLOW-UP SERVICES FOR IMPROVING LONG-TERM OUTCOMES IN INTENSIVE CARE UNIT (ICU) SURVIVORS – A COCHRANE REVIEW SUMMARY WITH COMMENTARY

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**The aim of this commentary is to discuss in a rehabilitation perspective the published Cochrane Review “Follow-up services for improving long-term outcomes in intensive care unit (ICU) survivors” known collectively as post-intensive care syndrome (PICS) by Schofield-Robinson et al. (1), under the direct supervision of the Cochrane Effective Practice and Organisation of Care Group. This Cochrane Corner is produced in agreement with the *Journal of Rehabilitation Medicine by Cochrane Rehabilitation*<sup>1</sup>.**

Key word: critical illness; intensive care units; rehabilitation; systematic review; post-intensive care syndrome

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### BACKGROUND

The number of Intensive Care Unit (ICU) survivors is increasing due to the ageing population and decreasing mortality for critical illness (2, 3). However, patients may present long lasting physical, cognitive and mental health impairments, leading to a decreased quality of life, return to work and life expectancy. These problems, including ICU-acquired weakness due to critical illness, neuro- and/or myopathy, have been described as the “Post-intensive care syndrome (PICS)” (2, 4). A systematic review performed by Ohtake et al. showed that during the first year following critical illness, individuals with PICS experienced physical

impairments in all three domains of the International Classification of Functioning, Disability and Health (ICF): body functions and structures, activity limitations and participation restrictions (5). Evidence on the effectiveness of interventions, to prevent or treat PICS, whether preformed during the ICU stay or after discharge are of growing importance. A Cochrane review has been published recently on “Follow-up services for improving long-term outcomes in intensive care unit (ICU) survivors” (1).

### FOLLOW-UP SERVICES FOR IMPROVING LONG-TERM OUTCOMES IN INTENSIVE CARE UNIT (ICU) SURVIVORS

(Oliver J Schofield-Robinson, Sharon R Lewis, Andrew F Smith, Joanne McPeake, Phil Alderson 2018)

### WHAT IS THE AIM OF THIS COCHRANE REVIEW?

The main aim of this Cochrane Review was to evaluate the effectiveness of follow-up services for ICU survivors that aim to identify and address unmet health needs related to the ICU period.

### WHAT WAS STUDIED IN THE COCHRANE REVIEW?

The population addressed in this review were adult patients, who had been discharged from hospital following an ICU stay. The primary objective was to assess the effectiveness of follow-up services for ICU survivors that aim to identify and address unmet health needs related to the ICU period using the following outcomes: health-related quality of life (HRQoL), mortality, depression and anxiety, post-traumatic stress disorder (PTSD), physical function, cognitive function, ability to return to work or education and adverse effects. The secondary objectives were to examine different models of follow-up services by exploring: the effectiveness of service organisation

<sup>1</sup>This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2018, Issue 11, Art. No.: CD012701, DOI: 10.1002/14651858.CD012701.pub4 (see [www.cochranelibrary.com](http://www.cochranelibrary.com) for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review. The views expressed in the summary with commentary are those of the Cochrane Corner author(s) and do not represent the Cochrane Library or Wiley.

(physician- versus nurse-led, face-to-face versus remote, timing of follow-up service); differences related to country (high-income versus low- and middle-income countries); and effect of delirium, which can affect cognitive function, and how follow-up services may have different effects for these participants.

### SEARCH METHODOLOGY AND UP-TO-DATENESS OF THE COCHRANE REVIEW?

For this review a search was performed in CENTRAL, MEDLINE, Embase and CINAHL on 7 November 2017. Clinical trials registers for ongoing studies were also searched, and backward and forward citation searching of relevant articles was performed. Selection criteria were randomised and non-randomised studies with adult participants, who had been discharged from hospital following an ICU stay. Studies that compared an ICU follow-up service using a structured programme and coordinated by a healthcare professional versus no follow-up service or standard care (which provided no follow-up service) were included.

### WHAT ARE THE MAIN RESULTS OF THE COCHRANE REVIEW?

The review included 5 studies (4 randomised studies with 1,297 participants; one non-randomised study with 410 participants) involving 1,707 ICU survivors in total with different illness severities and varying health conditions. The studies were all conducted in high-income countries: Denmark, Germany, Sweden, UK and US. Follow-up services were nurse-led in 4 or led by a multidisciplinary team in one of the studies. Face-to-face (at home or in a clinic) or telephone consultations or both were included in the studies with at least one consultation once a week, once a month or at 6 months in each study and up to 8 consultations in two studies. Each follow-up service included participants' needs assessment with different designs of consultations in studies and with referrals to specialists for support if needed.

The review found low-certainty evidence that follow-up services for improving long-term outcomes may make little or no difference to HRQoL at 12 months in ICU survivors [SMD (standardised mean difference)  $-0.0$ , 95% CI (confidence interval)  $-0.1$  to  $0.1$ ] (one study with 286 participants). Five studies showed moderate-certainty evidence that follow-up services probably also make little or no difference to all-cause mortality up to twelve months following discharge from ICU [RR (risk ratio)  $0.96$ , 95% CI  $0.76$  to  $1.22$ ; 4 studies with 1,289 participants) and in one non-randomised study 79/259 and 46/151 deaths in the intervention and the control group, respectively] and 4 studies showed low-certainty

evidence that they may make little or no difference to posttraumatic stress disorder (PTSD) (SMD  $-0.05$ , 95% CI  $-0.19$  to  $0.10$ ; 3 studies with 703 participants and one non-randomised study reported less chance of having PTSD when the intervention was used).

It is uncertain whether a follow-up service had an effect in reducing depression and anxiety [3 studies (two randomised and one non-randomised) with 843 participants], in improving physical function (4 studies with 1,297 participants), cognitive function (4 studies with 1,297 participants), or in increasing the ability to return to work or education (one study with 386 participants) (very low-certainty of evidence). No studies reported adverse effects.

The secondary objectives could not be assessed because insufficient studies were found to justify subgroup analysis.

### HOW DID THE AUTHORS CONCLUDE?

Because insufficient evidence was found, from a limited number of studies, it was not possible to determine whether ICU follow-up services are effective in identifying and addressing the unmet health needs of ICU survivors. Due to insufficient studies and limited data, the authors were unable to look at the differences between certain designs of follow-up services as to whether one design is better than another, or whether follow-up services are more effective for some individuals with varying health conditions. The authors found 5 ongoing studies which are not included in this review; these ongoing studies may increase certainty in the effect in future updates. They anticipate that future studies may also vary in design. They propose robustly designed preferably randomised studies for future research and consideration of only one variable (the follow-up service) compared to standard care which would increase confidence that the effect is due to the intervention studied rather than concomitant treatments.

### WHAT ARE THE IMPLICATIONS OF THE COCHRANE EVIDENCE FOR PRACTICE IN REHABILITATION?

The review discussed above was inconclusive on the effectiveness of ICU follow-up services. Follow-up services are one method to deal with PICS, but several preventive and treatment strategies are in use and have been studied. NICE produced a guideline on Rehabilitation after critical illness as early as 2009 (6). They recommend for example:

- For patients at risk of physical and non-physical morbidity, perform a comprehensive clinical assessment to identify their current rehabilitation needs. This

should include assessments by healthcare professionals experienced in critical care and rehabilitation.

- For patients at risk, agree short-term and medium-term rehabilitation goals, based on the comprehensive clinical assessment. The patient's family and/or carer should also be involved.

However, evidence to support these guidelines is currently still very limited. They did propose a list of research questions such as:

- Which therapeutic strategies are the most clinically and cost effective at reducing the prevalence and severity of critical illness-associated physical morbidity, psychological morbidity and cognitive dysfunction or at reducing the magnitude of critical illness-associated physical morbidity, psychological morbidity and cognitive dysfunction?

In the last decade, several Cochrane Reviews have been published regarding the prevention and treatment of critical illness neuro- and/or myopathy and PICS at large of which we give a short overview.

In 2014, a Cochrane Review on interventions for preventing critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) showed moderate-quality evidence suggesting a potential benefit – shorter duration of mechanical ventilation – of early rehabilitation on CIP/CIM. Very low-quality evidence suggested no effect of electrical muscle stimulation (7).

Two Cochrane Reviews were published in 2015 on rehabilitation for patients with critical illness. The first one focused on physical rehabilitation interventions for in- and outpatients with CIP/CIM, in the acute as well as the chronic phase. Unfortunately, the authors had to conclude that there were no published RCTs or quasi-RCTs that examine whether physical rehabilitation interventions improve activities of daily living for people with CIP/CIM (8). The second one assessed the effectiveness of exercise rehabilitation programmes, initiated after ICU discharge, for functional exercise capacity and HRQoL in adult ICU survivors (9). An overall result for the effects of exercise-based interventions could not be determined. Three studies reported improvement in functional exercise but 3 others found no effects of treatment. A third review published in 2018 studied the effects of early intervention (mobilization or active exercise), commenced in the ICU, provided to critically ill adults, on improving physical function or performance, muscle strength and HRQoL. Currently there was only low-quality evidence for the effect, more specifically (in one study) getting out of bed earlier and walking a greater distance, but no effect on number of daily activities they could perform (10). Another very recently published systematic review found that enhanced physical rehabilitation following ICU discharge may make little or no difference to quality of life or mortality (11). Two other non-Cochrane reviews concluded on positive effects

of early rehabilitation on muscle strength and functional status, even if they also advise further research to improve quality of evidence (12, 13).

Concerning psychological symptoms such as anxiety and depression a Cochrane Review from 2014 found minimal evidence from RCTs of the benefits or harms of patient diaries for patients and their caregivers or family members. A small study has described their potential to reduce post-traumatic stress symptomatology in family members. However, there is currently inadequate evidence to support their effectiveness in improving psychological recovery after critical illness for patients and their family members (14). The authors of a more recent Cochrane Review, from 2018, were uncertain of the effects of information or education interventions given to adult ICU patients and their carers, as the evidence in all cases was of very low-certainty (15).

So in summary, even though guidelines recommend early rehabilitation during as well as after a stay in the ICU for critically ill adults, robust evidence on the effectiveness is still lacking. This may change in future updates as several studies are ongoing. As Brown et al. (16) state, the complexity of the health states associated with PICS suggests that careful and rigorous evaluation of multidisciplinary, multimodality interventions – tied to the specific conditions of interest – will be required to address these important problems.

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