THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Exercise rehabilitation for recovery from critical illness (Protocol)

Citation for published version:

Geneen, L, Mercer, T, Salisbury, L, Walsh, T & Thomson, C 2010, *Exercise rehabilitation for recovery from critical illness (Protocol)*. John Wiley & Sons Inc.. <https://doi.org/10.1002/14651858.CD008632>

Digital Object Identifier (DOI):

[10.1002/14651858.CD008632](https://doi.org/10.1002/14651858.CD008632)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Publisher Rights Statement:

© Geneen, L., Mercer, T., Salisbury, L., Walsh, T., & Thomson, C. Exercise rehabilitation for recovery from critical illness (Protocol) 10.1002/14651858.CD008632

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Exercise rehabilitation for recovery from critical illness (Protocol)

Geneen L, Mercer TH, Salisbury L, Walsh T, Thomson CE

**THE COCHRANE
COLLABORATION®**

This is a reprint of a Cochrane protocol, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 8

<http://www.thecochranelibrary.com>

WILEY

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	2
METHODS	2
ACKNOWLEDGEMENTS	4
REFERENCES	5
APPENDICES	6
WHAT'S NEW	16
HISTORY	17
CONTRIBUTIONS OF AUTHORS	17
DECLARATIONS OF INTEREST	17
SOURCES OF SUPPORT	18

Exercise rehabilitation for recovery from critical illness

Louise Geneen¹, Tom H Mercer², Lisa Salisbury³, Tim Walsh⁴, Colin E Thomson⁵

¹Physiotherapy Dept, School of Health Sciences, Queen Margaret University, Edinburgh, UK. ²School of Health Sciences, Queen Margaret University, Edinburgh, Musselburgh, UK. ³School of Health in Social Sciences, Centre for Integrated Healthcare (CIHR), Edinburgh University, Edinburgh, UK. ⁴Edinburgh Royal Infirmary, Edinburgh, UK. ⁵School of Health Sciences, Queen Margaret University, Edinburgh, UK

Contact address: Louise Geneen, Physiotherapy Dept, School of Health Sciences, Queen Margaret University, Musselburgh, Edinburgh, EH21 6UU, UK. lgeneen@qmu.ac.uk.

Editorial group: Cochrane Anaesthesia Group.

Publication status and date: Edited (no change to conclusions), published in Issue 10, 2010.

Citation: Geneen L, Mercer TH, Salisbury L, Walsh T, Thomson CE. Exercise rehabilitation for recovery from critical illness. *Cochrane Database of Systematic Reviews* 2010, Issue 8. Art. No.: CD008632. DOI: 10.1002/14651858.CD008632.

Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The objective of this systematic review is to assess the effectiveness of exercise rehabilitation programmes, initiated after ICU discharge, on improving functional exercise capacity and quality of life in adult ICU survivors who have been mechanically ventilated for more than 24 hours.

We will compare an exercise intervention to any other intervention or a control or 'usual care' programme. Exercise includes any structured or taught programmes. Respiratory or inspiratory muscle training is excluded due to it being initiated within the ICU environment, for example with weaning from a ventilator, and not as post-discharge rehabilitation as required for this review.

BACKGROUND

Description of the condition

Critical Illness includes any condition that results in a stay in a critical care (CCU), intensive care (ICU), or high dependency unit (HDU) within a hospital, whether due to surgical complication, injury, trauma, exacerbated chronic illness, or acute onset of severe illness. It is often the case that critical care patients exhibit multiple pathologies and have a high risk of other comorbidities, including increased risk of a cardiac episode, respiratory weakness, and development of diabetes. The episode of critical illness is not limited to the period in intensive care but can continue to influence the

patients' and their families' lives for months and often years after hospital discharge ([Angus 1997](#); [Chaboyer 2003](#); [Eddleston 2000](#); [Elliott 2006](#); [Fletcher 2003](#); [Frank 2000](#)).

The traditional goal of intensive and critical care medicine has been to decrease short-term mortality ([Angus 2003](#)). In recent years, both technological and medical advancements have resulted in more and more patients surviving intensive care ([King 1998](#); [Lewis 2003](#)), leading to a need for greater patient turnover as ward beds need to be vacated for new admittances. Consequently, hospital discharge often occurs earlier, with a less prolonged implementation period to re-develop each patient's physical and psychological status.

Critical illness has a large weighting across the UK, and globally,

with a prolonged stay in ICU associated with high mortality, morbidity, and costs (Martin 2005).

The critical care population are a unique population in many ways, despite their heterogeneity (varied reasons for admission, large age range and background). As other ill populations look to maintain health or hinder the progression of the disease, many of those surviving intensive care have the opportunity to not simply maintain but improve and develop their strength, fitness, physical function, and quality of life.

Many factors can influence the individual experiences of ICU, irrespective of the admitting condition, but similar results are often observed by clinicians and researchers as survivors can suffer reduced physical function and independence, muscular atrophy and weakness, malnutrition and anaemia, and critical illness polyneuropathy and myopathy, all of which may negatively affect their quality of life. The majority of these contributing factors are associated with the admitting cause and the necessary treatment pathway prescribed by the medical staff, which cannot be greatly altered. It is, therefore, important to focus on prolonged and effective recovery and rehabilitation.

Description of the intervention

Regular exercise (physical activity) is known to improve the working function of many systems within the body, as well as to benefit muscular strength and size, improve balance and fitness, reduce the fear of falling in the elderly, and reduce the associated risk of hospital admission or re-admission. This has also been highlighted in other ill populations (reviewed by Kouidi 2002 for renal disease; Lavie 2009 for heart disease; and Puhan 2006 for pulmonary disease).

How the intervention might work

Older adults who regularly participate in physical training often gain significant improvements in both strength and aerobic power (Grimby 1986). Previously 'frail' older adults have greatly increased their functional ability (Gill 2002), helping to offset any decline and reducing the risk of illness. Older adults who regularly exercise are more resistant to chronic illness (Mazzeo 2001).

Clear evidence does exist linking muscle strength (assessed using hand grip strength) and muscle mass to mortality in the elderly (Miller 2002; Rantanen 2000). These measures can be used as factors in the prediction of long life in this population. There is a strong relationship between functional health status and mortality, as shown by Paffenbarger et al (Paffenbarger 1986) whose study into college alumni demonstrated a significantly lower result in all-cause mortality among those who regularly participated in physical activity. Investigations aimed at optimising and developing the strength and function of frail individuals have been successful when the individuals were trained over a prolonged period,

over three months (Brown 1990; Fiatarone 1994; Smith 2006), indicating that frailty and weakness are reversible and are largely affected by muscle inactivity. This can be potentially overcome by exercise training.

Evidence from quality of life and anxiety scores suggest that regular exercise also benefits mental health in the chronically ill (Iversen 2003; Yoshida 1999). This is vital as this population experiences a greater frequency of negative emotions and depressive symptoms (either arising from the medical condition or as a possible cause in the emergence of the condition) than their healthy counterparts (Baumgartner 1999; Krishnan 2002; Yoshida 1999).

Why it is important to do this review

There are some published trials demonstrating the advantages of prolonged in-patient and out-patient rehabilitation programmes following ICU admission, including passive movement (Wiles 2009), mobilisation (Schweickert 2009), bedside cycling (Burtin 2009); alongside anecdotal evidence and individual case studies of rehabilitation in practice (Stiller 2000; Storch 2008). No systematic reviews are yet available on this topic, to quantify the response. With many survivors of critical illness living with reduced function, often beyond a year after their discharge from hospital, it is important to establish whether exercise rehabilitation following critical illness can benefit survivors by improving function and quality of life. This review could help guide rehabilitation practice in the future.

OBJECTIVES

The objective of this systematic review is to assess the effectiveness of exercise rehabilitation programmes, initiated after ICU discharge, on improving functional exercise capacity and quality of life in adult ICU survivors who have been mechanically ventilated for more than 24 hours.

We will compare an exercise intervention to any other intervention or a control or 'usual care' programme. Exercise includes any structured or taught programmes. Respiratory or inspiratory muscle training is excluded due to it being initiated within the ICU environment, for example with weaning from a ventilator, and not as post-discharge rehabilitation as required for this review.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomized controlled trials (RCTs), quasi-RCTs, and controlled clinical trials (CCTs).

Types of participants

We will include all adults (aged 18 years or over) who are mechanically ventilated for 24 hours or more and admitted to an ICU or critical care environment.

We will exclude patients that are terminally ill or in palliative care; patients with head injury or involved in trauma, as a large number of subgroups are already addressed in a number of reviews published by the Cochrane Bone, Joint and Muscle Trauma Review Group; and studies examining cardiac surgery patients, as a review has already been published on this patient group (Jolliffe 2001) and this group of patients already have a very specific rehabilitation programme they can access.

Types of interventions

Our experimental intervention will be exercise rehabilitation or training where exercise includes any structured or taught programmes, but not respiratory or inspiratory muscle training (chest physiotherapy).

Our comparative intervention will be usual care, a non-exercise intervention, or no intervention.

Types of outcome measures

Primary outcomes

1. Functional exercise capacity (with physical objective assessment and subjective assessment): an individual's maximal ability to perform functional exercise that is beneficial in day-to-day living, for example, walking, stair climbing, sit-to-stand exercises, and strength.
2. Quality of life, as measured by reliable assessment scales.

Secondary outcomes

1. Withdrawal rates (withdrawal from the intervention or exercise programme)
2. Adherence (ability to adhere to the prescribed protocol within a single exercise session)
3. Mortality
4. Other adverse events

Search methods for identification of studies

The subject search will use a combination of controlled vocabulary and free text terms based on the search strategy for MEDLINE (in Appendix 1).

Electronic searches

We will search Ovid SP MEDLINE (1966 to present) (Appendix 1); Ovid SP EMBASE (1988 to present) (Appendix 2); the current issue of the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*) (Appendix 3); CINAHL via EBSCOhost (Appendix 4).

A search strategy will be developed for use in MEDLINE and revised appropriately for other databases in conjunction with the Cochrane Anaesthesia Review Group.

We will not impose any language or publication restrictions.

Searching other resources

We will identify trials by manually searching abstracts of journals including Critical Care, Critical Care Clinics, Physiotherapy, Nursing in Critical Care, and European Society of Intensive Care Medicine.

We will check the reference list of included studies and articles. We will attempt to contact relevant trial authors to identify any additional studies.

Data collection and analysis

Selection of studies

Authors will scan the titles and abstracts of reports identified through electronic and manual searches. We will retrieve and evaluate potentially relevant studies, chosen by at least one author, in full-text versions of the reports. Authors will independently select trials that meet the inclusion criteria using a purpose-designed checklist (LG, LS). A third author will act as arbitrator (CT) if the two authors cannot reach a consensus on the studies to be included.

Data extraction and management

Two authors will independently extract data using a standardized checklist (LG, LS). Any disagreement will be resolved by the third author (CT). Data will be collected manually on paper extraction forms and put into intermediate software (Microsoft Excel for Windows), ensuring accurate transference by using double entry, before being entered in to RevMan 5.0. This will allow for any necessary statistical conversions. We will review the data from included studies qualitatively and then, where possible, combine it quantitatively by population, intervention, and outcomes.

Assessment of risk of bias in included studies

Risk of bias will be independently assessed by at least two authors (LG, LS). A third author will arbitrate and resolve any disagreements (CT or TM). As recommended by the Cochrane Handbook (Higgins 2008), the domains to be assessed are:

- I - sequence generation;
- II - allocation concealment;
- III - blinding of participants, personnel, and outcome assessors (for assessment of each main outcome);
- IV - incomplete outcome data (for assessment of each main outcome);
- V - selective outcome reporting;
- VI - other sources of bias.

Each will be explicitly judged using 'yes' = low risk of bias, 'no' = high risk of bias, 'unclear' = either lack of information or uncertainty over the potential for bias.

For each study, a risk of bias graph and risk of bias summary figure will be constructed from the risk of bias table.

Measures of treatment effect

Where possible, for continuous data the weighted mean difference (WMD), or standardized mean difference (SMD), and 95% confidence interval (CI) will be used for summary statistics (functional exercise capacity, quality of life). Any dichotomous data will be extracted, analysed and reported as relative risk (RR) with 95% CI.

Unit of analysis issues

When different measurement scales are used, attempts will be made to contact lead authors for raw data (for conversion to a standard unit).

Dealing with missing data

Where available, data regarding intention to treat (ITT) will be extracted. If researchers did not perform an ITT analysis but sufficient raw data is available, then an ITT analysis will be conducted prior to data entry to Review Manager.

Initially, all data from all studies will be included in the meta-analysis. Secondly, a sensitivity analysis of all studies by excluding those with more than 20% of data missing from the study will be performed.

Assessment of heterogeneity

Heterogeneity will initially be assessed by visual assessment of forest plots from a meta-analysis of studies thought appropriate for pooling. The degree of statistical heterogeneity will be based on the value of the I^2 statistic and, if present, it will be explored through subgroup analysis. We will also undertake quality control

checks of data extraction and input, and review the clinical and methodological aspects of the study trials.

Assessment of reporting biases

To assess the level of publication bias, a funnel plot will be used (if we have greater than 10 studies) to make a visual assessment of whether small-study effects may be present in a meta-analysis.

Data synthesis

A fixed-effect Mantel-Haenszel model will be used for dichotomous and continuous data, with the assumption that between-trial variance is minimal. A random-effects model will be used if the I^2 statistic is greater than 50%. If the studies are sufficiently homogeneous, a meta-analysis will be performed and statistical heterogeneity will be assessed based on an intention-to-treat analysis, where possible.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis is only to be conducted if there are considerable differences in effects, based on: exercise type, intervention duration and frequency, age-related variation, or duration of the critical condition. We do not expect large numbers of studies at this time, in which case subgroup analysis would not be appropriate.

Sensitivity analysis

Sensitivity analysis will be conducted using the Cochrane Handbook definitions (Table 8.7a) of low, high, or unclear risk of bias to see if the level of risk of bias affects the estimate of effect.

Summary of findings table

We will assess the quality of the total body of evidence associated with our listed outcomes (functional exercise capacity as objective and subjective assessments, quality of life, withdrawal rate, adherence, mortality, and other adverse events) using the principles of the GRADE system (Guyatt 2008). We will construct a 'Summary of findings' (SoF) table using the GRADE software.

The GRADE approach appraises the quality of a body of evidence based on the extent to which one can be confident that an estimate of effect or association reflects the object being assessed. The quality of the evidence assessment considers: within study risk of bias (methodologic quality), directness of the evidence, heterogeneity of data, precision of effect estimates, and risk of publication bias.

ACKNOWLEDGEMENTS

We would like to thank Anna Lee (content editor), Nathan Pace (statistical editor), Tom Overend, Eric B Milbrandt (peer reviewers), Ann Fonfa (Cochrane Consumer Network) for their help and editorial advice during the preparation of this protocol.

REFERENCES

Additional references

Angus 1997

Angus, DC. Understanding the incidence and long-term outcomes of ARDS. In: Gullo, A editor(s). *Anaesthesia, pain, intensive care and emergency medicine: a scientific report*. Berlin Heidelberg New York: Springer, 1997:289–98.

Angus 2003

Angus DC, Carlet J, Brussels Roundtable 2002 Participants. Surviving intensive care: a report from the 2002 Brussels Roundtable. *Intensive Care Medicine* 2003;**29**(3):368–77. [PUBMED: 12536269]

Baumgartner 1999

Baumgartner WA, Walinsky PL, Salazar JD, Tseng EE, Brock MV, Doty JR, et al. Assessing the impact of cerebral injury after cardiac surgery: will determining the mechanism reduce the injury?. *The Annals of Thoracic Surgery* 1999;**67**(6):1871–3. [PUBMED: 10391329]

Brown 1990

Brown AB, McCartney N, Sale DG. Positive adaptation to weight-lifting in the elderly. *Journal of Applied Physiology* 1990;**69**(5):1725–33. [PUBMED: 2272965]

Burtin 2009

Burtin C, Clerckx B, Robbeets C, Ferdinande P, Langer D, Troosters T, et al. Early exercise in critically ill patients enhances short-term functional recovery. *Critical Care Medicine* 2009;**37**(9):2499–505. [PUBMED: 19623052]

Chaboyer 2003

Chaboyer W, Grace J. Following the path of ICU survivors: a quality improvement activity. *Nursing in Critical Care* 2003;**8**(4):149–55. [PUBMED: 12940690]

Eddleston 2000

Eddleston J, White P, Guthrie E. Survival, morbidity, and quality of life after discharge from intensive care. *Critical Care Medicine* 2000;**28**(7):2293–9. [PUBMED: 10921555]

Elliott 2006

Elliott D, McKinley S, Alison J, Aitken L, King M. Study protocol: Home-based rehabilitation for survivors of a critical illness. *Critical Care* 2006;**10**(3):R90. [PUBMED: 16792792]

Fiatarone 1994

Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. *New England Journal of Medicine* 1994;**330**(25):1769–75. [PUBMED: 8190152]

Fletcher 2003

Fletcher S, Kennedy D, Ghosh I, Misra V, Kiff K, et al. Persistent neuromuscular and neurophysiological abnormalities in long-term survivors of prolonged critical illness. *Critical Care Medicine* 2003;**31**(4):1012–6. [PUBMED: 12682465]

Frank 2000

Frank M, Schlapfer H, Otte B, Yasikoff N, Conzelmann M. Results of neurorehabilitation. An outcome study 20 months after stroke. *Praxis* 2000;**89**(44):1799–808. [PUBMED: 11109917]

Gill 2002

Gill TM, Baker DI, Gottschalk M, Peduzzi PN, Allore H, Byers A. A program to prevent functional decline in physically frail, elderly persons who live at home. *New England Journal of Medicine* 2002;**347**(14):1068–74. [PUBMED: 12362007]

Grimby 1986

Grimby G. Physical activity and muscle training in the elderly. *Acta Medica Scandinavica. Supplementum*. 1986; **711**:233–7. [PUBMED: 3535411]

Guyatt 2008

Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schunemann HJ, et al. What is “quality of evidence” and why is it important to clinicians?. *BMJ* 2008;**336**:995–8. [PUBMED: 18456631]

Higgins 2008

Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [updated September 2008]*. Available from www.cochrane-handbook.org: The Cochrane Collaboration, 2008.

Iversen 2003

Iversen MD, Fossel AH, Katz JN. Enhancing function in older adults with chronic low back pain: a pilot study of endurance training. *Archives of Physical Medicine and Rehabilitation* 2003;**84**(9):1324–31. [PUBMED: 13680569]

Jolliffe 2001

Jolliffe J, Rees K, Taylor RRS, Thompson DR, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews* 2001, Issue 1. [DOI: 10.1002/14651858.CD001800.]

King 1998

King J, Crowe J. Mobilisation practices in Canadian critical care units. *Physiotherapy Canada* 1998;**50**(3):206–11. [MEDLINE: 0346574]

Kouidi 2002

Kouidi E. Exercise training in dialysis patients: why, when, and how?. *Artificial Organs* 2002;**26**(12):1009–13. [PUBMED: 12460377]

Krishnan 2002

Krishnan KR, Delong M, Kraemer H, Carney R, Spiegel D, Gordon C, et al. Comorbidity of depression with other medical diseases in the elderly. *Biological Psychiatry* 2002;**52**(6):559–88. [PUBMED: 12361669]

Lavie 2009

Lavie CJ, Thomas RJ, Squires RW, Allison TG, Milani RV. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clinic Proceedings* 2009;**84**(4):373–83. [PUBMED: 19339657]

Lewis 2003

Lewis M. Intensive care unit rehabilitation within the United Kingdom: a review. *Physiotherapy* 2003;**89**(9): 531–8. [DOI: 10.1016/S0031-9406(05)60179-4]

Martin 2005

Martin M, Salim A, Murray J, Demetriades D, Belzberg H, Rhee P. The decreasing incidence and mortality of acute respiratory distress syndrome after injury: a 5-year observational study. *Journal of Trauma* 2005;**50**(5): 1107–13. [PUBMED: 16385287]

Mazzeo 2001

Mazzeo RS, Tanaka H. Exercise prescription for the elderly: current recommendations. *Sports Medicine* 2001;**31**(11): 809–18. [PUBMED: 11583105]

Miller 2002

Miller MD, Crotty M, Giles LC, Bannerman E, Whitehead C, Cobiac L, et al. Corrected arm muscle area: an independent predictor of long-term mortality in community dwelling older adults?. *Journal of the American Geriatrics Society* 2002;**50**(7):1272–7. [PUBMED: 12133024]

Paffenbarger 1986

Paffenbarger RS, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *New England Journal of Medicine* 1986;**314**(10):605–13. [PUBMED: 3945246]

Puhan 2006

Puhan MA, Busching G, Schunemann HJ, VanOort E, Zaugg C, Frey M. Interval versus continuous high-intensity exercise in chronic obstructive pulmonary disease:

a randomized trial. *Annals of Internal Medicine* 2006;**145**(11):816–25. [PUBMED: 17146066]

Rantanen 2000

Rantanen T, Harris T, Leveille SG, Visser M, Foley D, et al. Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *Journal of Gerontology. Series A: Biological Sciences and Medical Sciences* 2000;**55**(3):M168–73. [PUBMED: 10795731]

RevMan 5.0

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Schweickert 2009

Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;**373**(epub):1874–82. [PUBMED: 19446324]

Smith 2006

Smith TP, Kennedy SL, Smith M, Orent S, Fleshner M. Physiological improvements and health benefits during an exercise-based comprehensive rehabilitation program in medically complex patients. *Exercise Immunology Review* 2006;**12**:86–96. [PUBMED: 17201074]

Stiller 2000

Stiller K. Physiotherapy in intensive care: toward an evidence-based practice. *Chest* 2000;**118**(6):1801–13. [PUBMED: 11115476]

Storch 2008

Storch EK, Kruszynski DM. From rehabilitation to optimal function: role of clinical exercise therapy. *Current Opinion in Critical Care* 2008;**14**(4):451–5. [PUBMED: 18614911]

Wiles 2009

Wiles L, Stiller K. Passive limb movements for patients in an intensive care unit: A survey of physiotherapy practice in Australia. *Journal of Critical Care* 2009;**epub**:ahead of print. [PUBMED: 19819105]

Yoshida 1999

Yoshida T, Kohzuki M, Yoshida K, Hiwatari M, Kamimoto M, Yamamoto C, et al. Physical and psychological improvements after phase II cardiac rehabilitation in patients with myocardial infarction. *Nursing & Health Sciences* 1999;**1**(3):163–70. [PUBMED: 10894639]

* Indicates the major publication for the study

APPENDICES

Appendix I. MEDLINE (Ovid SP) search strategy

1 exp Exercise-Therapy/
2 exp Exercise/
3 exp Physical-Fitness/
4 exp Weight-Lifting/
5 exp Physical-Medicine/
6 exp Physical-Therapy-Modalities/
7 (rehabilitation adj3 (Exercise or Physical)).mp.
8 (Exercise or Physiatrics or Physiatry or Physiotherapy or mobilization).ti,ab.
9 Activit*.ti.
10 (movement adj3 (Active or Whole body)).mp.
11 (Exercise adj3 (training* or Progressive or therapy or intervention)).mp.
12 (training adj3 (Aerobic or endurance or Strength or resistance or weight or Fitness or Interval or Circuit)).mp.
13 (Physical therapy).mp. or (Weight lifting).mp.
14 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15 Critical-Care/ or exp Critical-Illness/
16 Intensive-Care/ or Intensive-Care-Units/
17 Atrophy/
18 Ventilator-Weaning/
19 Shock-Septic/
20 Sepsis/
21 (care adj3 (Critical or Intensive)).ti,ab.
22 (unit adj3 (Intensive care or High dependency or Intensive therapy or Intensive treatment)).mp.
23 (Critical adj3 (collapse or illness)).mp.
24 ((Critical illness) adj3 (neuropath* or myopath* or polyneuropath* or polyneuromyopathy)).mp.
25 (ICU or HDU or ITU or CIN or CIM or CIPN or CIPNM or ARDS).ti,ab.
26 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27 14 and 26
28 ((low back pain) or ((head or brain) adj3 injury) or pregnancy or stroke or (cardiac surg*)).mp.
29 27 not 28
30 CLINICAL-TRIAL.pt.
31 randomized.ab.
32 placebo.ab.
33 (clinical trials).sh.
34 randomly.ab.
35 trial.ti.
36 30 or 31 or 32 or 33 or 34 or 35
37 (animals not (humans and animals)).sh
38 36 not 37
39 29 and 38

Appendix 2. EMBASE (Ovid SP) search strategy

1 exercise therapy.mp.
2 exercise.mp.
3 physical fitness.mp.
4 Physical Medicine.mp.
5 Weight Lifting.mp.
6 physical therapy modalities.mp.
7 (exercise or physiatrics or physiatry or physiotherapy or mobili*ation).ti.
8 activit*.ti.
9 (physical therapy or weight lifting).mp.
10 (rehabilitation and (exercise or physical)).mp.
11 (movement and (active or whole body)).mp.
12 (exercise and (training* or progressive or therapy or intervention)).mp.
13 (training and (aerobic or endurance or strength or resistance or weight or fitness or interval or circuit)).mp.
14 (1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13).mp.
15 (critical care or critical illness).mp.
16 (intensive care or intensive care units).mp.
17 atrophy.mp.
18 Artificial Ventilation/
19 Septic Shock.mp.
20 sepsis.mp.
21 (care and (critical or intensive)).ti.
22 (unit and (intensive care or high dependency or intensive therapy or intensive treatment)).mp.
23 (critical and (collapse or illness)).mp.
24 (critical illness and (neuropath* or myopath* or polyneuropath* or polyneuromyopathy)).mp.
25 (ICU or HDU or ITU or CIN or CIM or CIPN or CIPNM or ARDS).mp.
26 (15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25).mp.
27 (14 and 26).mp.
28 (low back pain or ((head or brain) and injury) or pregnancy or stroke or cardiac surg*).mp.
29 (27 not 28).mp.
30 (crossover.mp. or multicenter.ab. or placebo.sh. or ((singl* or doubl* or tripl*) adj3 blind).mp. or controlled study.ab. or random*.ti.ab. or trial*.ti.ab.) not (animals not (humans and animals)).sh.
31 29 and 30

Appendix 3. CENTRAL search strategy

#1 MeSH descriptor Exercise Therapy explode all trees
#2 MeSH descriptor Exercise explode all trees
#3 MeSH descriptor Physical Fitness explode all trees
#4 MeSH descriptor Weight Lifting explode all trees
#5 MeSH descriptor Physical Medicine explode all trees
#6 MeSH descriptor Physical Therapy Modalities explode all trees
#7 (rehabilitation near (Exercise or Physical))
#8 (Exercise or Physiatrics or Physiatry or Physiotherapy or mobili?ation):ti,ab
#9 Activit*:ti
#10 (movement near (Active or Whole body))
#11 (Exercise near (training* or Progressive or therapy or intervention))
#12 (training near (Aerobic or endurance or Strength or resistance or weight or Fitness or Interval or Circuit))
#13 (Physical therapy) or (Weight lifting)
#14 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13)
#15 MeSH descriptor Critical Care explode all trees
#16 MeSH descriptor Critical Illness explode all trees

#17 MeSH descriptor Intensive Care explode all trees
 #18 MeSH descriptor Intensive Care Units explode all trees
 #19 MeSH descriptor Atrophy explode all trees
 #20 MeSH descriptor Ventilator Weaning explode all trees
 #21 MeSH descriptor Shock, Septic explode all trees
 #22 MeSH descriptor Sepsis explode all trees
 #23 (care near (Critical or Intensive)):ti,ab
 #24 (unit near (Intensive care or High dependency or Intensive therapy or Intensive treatment))
 #25 (Critical near (collapse or illness))
 #26 ((Critical illness) near (neuropath* or myopath* or polyneuropath* or polyneuromyopathy))
 #27 (ICU or HDU or ITU or CIN or CIM or CIPN or CIPNM or ARDS):ti,ab
 #28 (#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27)
 #29 (#14 AND #28)
 #30 (low back pain) or ((head or brain) near injury) or pregnancy or stroke or (cardiac surg*)
 #31 (#29 AND NOT #30)

Appendix 4. CINAHL (EBSCOhost) search strategy

S1 (MH "Therapeutic Exercise+")
 S2 exercise AND therap*
 S3 (MH "Exercise+")
 S4 (MH "Physical Fitness+")
 S5 (MH "Weight Lifting")
 S6 (MH "Physical Medicine")
 S7 (MH "Physical Therapy+")
 S8 rehabilitation N5 (exercise OR physical)
 S9 AB (exercise OR physiatrics OR physiatry OR physiotherapy OR mobili*ation)
 S10 TI activit*
 S11 movement N5 active
 S12 movement N5 "whole body"
 S13 training* OR progressive OR therapy OR intervention
 S14 exercise N5 S14
 S15 aerobic OR endurance OR strength OR resistance OR weight OR fitness OR interval OR circuit
 S16 training N5 S16
 S17 physical therapy OR weight lifting
 S18 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S15 OR S17
 S19 "critical care OR critical illness"
 S20 (MH "Intensive Care Units")
 S21 (MH "Atrophy+")
 S22 (MH "Ventilator Weaning") OR (MH "Ventilators, Mechanical")
 S23 (MH "Shock, Septic")
 S24 (MH "Sepsis+")
 S25 TI critical OR TI intensive
 S26 care N3 S25
 S27 intensive care OR high dependency OR intensive therapy OR intensive treatment
 S28 unit N3 S27
 S29 collapse OR illness
 S30 critical N3 S29
 S31 neuropath* OR myopath* OR polyneuropath* OR polyneuromyopath*
 S32 "critical illness" N5 S31
 S33 ICU OR HDU OR ITU OR CIN OR CIM OR CIPN OR CIPNM OR ARDS
 S34 S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S27 OR S29 OR S31 OR S33

S35 S18 AND S34
 S36 head OR brain
 S37 injury N5 S36
 S38 low* back pain OR pregnan* OR stroke OR cardiac surg*
 S39 S37 OR S38
 S40 S35 NOT S39
 S41 PT clinical trial
 S42 AB randomi?ed
 S43 AB placebo*
 S44 MW clinical trials
 S45 AB random*
 S46 TI trial*
 S47 S41 OR S42 OR S43 OR S44 OR S45 OR S46
 S48 animal*
 S49 human*
 S50 S48 AND S49
 S52 S48 NOT S50
 S53 S47 NOT S52
 S54 S40 AND S53

Appendix 5. Study selection, quality assessment and data extraction

CARG 172 Exercise Rehabilitation for recovery from Critical Illness

Study Selection, Quality Assessment & Data Extraction Form

First author	Journal/Conference Proceedings etc	Year

Study eligibility

RCT/Quasi/CCT (delete as appropriate)	Relevant participants adults, >= 18years old ICU/critical care admission with mechanical ventilation	Relevant interventions Exercise taught/structured/ supervised	Relevant outcomes Functional exercise capacity Quality of Life Withdrawal rates Adherence Mortality Other adverse events
Yes / No / Unclear	Yes / No / Unclear	Yes / No / Unclear	Yes / No* / Unclear

* Issue relates to selective reporting when authors may have taken measurements for particular outcomes, but not reported these within the paper(s). Reviewers should contact trial lists for information on possible non-reported outcomes & reasons for exclusion from

publication. Study should be listed in 'Studies awaiting assessment' until clarified. If no clarification is received after three attempts, study should then be excluded.

Do not proceed if any of the above answers are 'No'. If study to be included in 'Excluded studies' section of the review, record below the information to be inserted into 'Table of excluded studies'

Freehand space for comments on study design and treatment:

References to trial

Check other references identified in searches. If there are further references to this trial link the papers now & list below. All references to a trial should be linked under one *Study ID* in RevMan.

Code each paper	Author(s)	Journal/Conference Proceedings etc	Year
A	<i>The paper listed above</i>		
B	<i>Further papers</i>		

Participants and trial characteristics

Participant characteristics	
	Further details
Age (mean, median, range, etc)	
Sex of participants (numbers / %, etc)	

(Continued)

Disease status / type, etc (if applicable)	
Time on Mechanical Ventilation (mean, median, range, etc)	
Other	

Trial characteristics	
	Further details
Single centre / multicentre	
Country / Countries	
How was participant eligibility defined?	
How many people were randomized?	
Number of participants in each intervention group	
Number of participants who received intended treatment	
Number of participants who were analysed	
Treatment(s) used	
Dose / frequency of administration	
Duration of treatment (State weeks / months, etc, if cross-over trial give length of time in each arm)	
Median (range) length of follow-up reported in this paper (state weeks, months or years or if not stated)	
Time-points when measurements were taken during the study	
Time-points reported in the study	
Time-points you are using in RevMan	
Trial design (e.g. parallel / cross-over*)	
Other	

* If cross-over design, please refer to the Cochrane Editorial Office for further advice on how to analyse these data

Methodological quality

Allocation of intervention	
State here method used to generate allocation and reasons for grading	Grade (circle)
Note reason for allocation:	Adequate (Random)
	Inadequate (e.g. alternate)
	Unclear

Concealment of allocation Process used to prevent foreknowledge of group assignment in a RCT, which should be seen as distinct from blinding	
State here method used to conceal allocation and reasons for grading	Grade (circle)
Note reason for allocation:	Adequate
	Inadequate
	Unclear

Blinding	
Person responsible for participants care	Yes / No
Participant	Yes / No
Outcome assessor	Yes / No
Other (please specify)	Yes / No
Intention-to-treat	
An intention-to-treat analysis is one in which all the participants in a trial are analysed according to the intervention to which they were allocated, whether they received it or not	

(Continued)

All participants entering trial	
20% or fewer excluded	
More than 20% excluded	
Not analysed as 'intention-to-treat'	
Unclear	

Were withdrawals described? **Yes ?** **No ?** **not clear ?**

Discuss if appropriate

Data extraction

Outcomes relevant to your review	
	Reported in paper (circle)
Outcome 1 Functional capacity (subjective/objective) Including one or more of - Vo ₂ max and/or VO ₂ peak Muscle mass and/or morphology Body composition Strength and/or endurance tests Resting HR and/or BP	Yes / No Specify:
Outcome 2 Quality of Life	Yes / No
Outcome 3 Withdrawal rates	Yes / No
Outcome 4 Adherence	Yes / No
Outcome 5 Mortality	Yes / No
Outcome 6 Other adverse events	Yes / No

For Continuous data							
Code of paper	Outcomes	Unit of measurement	Intervention group		Control group		Details if outcome only described in text
			n	Mean (SD)	N	Mean (SD)	
A etc	Functional capacity subjective						
	Functional capacity objective						
	Quality of Life						
	VO ₂ max and/or VO ₂ peak						
	Muscle mass or morphology						
	Body composition						
	Strength test						
	Endurance test						
	Resting HR	Beats/min					
	Resting BP	mmHg systole/diastole					

For Dichotomous data			
Code of paper	Outcomes	Intervention group (n) n = number of participants, not number of events	Control group (n) n = number of participants, not number of events
	Withdrawal		
	Adherence		

(Continued)

	Mortality (i.e. deaths)		
	Adverse events (not death)		

Other information which you feel is relevant to the results

Indicate if: any data were obtained from the primary author; if results were estimated from graphs etc; or calculated by you using a formula (this should be stated and the formula given). In general if results not reported in paper(s) are obtained this should be made clear here to be cited in review

Freehand space for writing actions such as contact with study authors and changes

References to other trials

Did this report include any references to published reports of potentially eligible trials not already identified for this review?

First author	Journal / Conference	Year of publication
--------------	----------------------	---------------------

Did this report include any references to unpublished data from potentially eligible trials not already identified for this review? If yes, give list contact name and details

WHAT'S NEW

Date	Event	Description
9 August 2010	Amended	Typo in acknowledgement section corrected

HISTORY

Protocol first published: Issue 8, 2010

CONTRIBUTIONS OF AUTHORS

Conceiving the review: Louise Geneen (LG), Tom Mercer (TM)

Co-ordinating the review: LG

Undertaking manual searches: LG

Screening search results: LG, Lisa Salisbury (LS), Colin Thomson (CT)

Organizing retrieval of papers: LG, LS, CT, TM

Screening retrieved papers against inclusion criteria: LG, LS, CT

Appraising quality of papers: LG, LS, CT, TM

Abstracting data from papers: LG, LS, CT, TM

Writing to authors of papers for additional information: LG

Providing additional data about papers: LG

Obtaining and screening data on unpublished studies: LG, LS, TM, CT

Data management for the review: LG

Entering data into Review Manager ([RevMan 5.0](#)): LG, LS, CT

RevMan statistical data: LG, CT

Other statistical analysis not using RevMan: CT, LG

Double entry of data: (data entered by person one: LG; data entered by person two: CT/LS)

Interpretation of data: LG, CT, TM, LS, Tim Walsh (TW)

Statistical inferences: LG, CT

Writing the review: LG

Securing funding for the review: n/a

Performing previous work that was the foundation of the present study: TM, LS, TW

Guarantor for the review (one author): LG

Person responsible for reading and checking review before submission: LG, CT, TM, LS, TW

DECLARATIONS OF INTEREST

Prof Walsh is currently involved in clinical studies that are investigating potential strategies to improve recovery rates after critical illness and to evaluate patient outcomes.

Lisa Salisbury has been involved in the design and completion of a small pilot study to evaluate enhanced physical and nutritional rehabilitation after a prolonged intensive care stay. This may be eligible for inclusion in this Cochrane review. Ongoing work involves the design of a larger study evaluating enhanced physical and nutritional rehabilitation.

All other authors: none known.

SOURCES OF SUPPORT

Internal sources

- Queen Margaret University, Edinburgh, UK.

As part of an ongoing research education programme.

External sources

- No sources of support supplied