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Effectiveness of rehabilitation interventions on the secondary consequences of surviving a cardiac arrest: a systematic review and meta-analysis

Vicky L Joshi ,[1] Jan Christensen,[2] Esben Lejsgaard,[1] Rod S Taylor,[3] Ann Dorthe Zwisler,[1] Lars H Tang[4,5]

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For numbered affiliations see end of article.

Correspondence to
Mrs Vicky L Joshi;
victoria.louise.joshi@rsyd.dk

ABSTRACT

Aim The aim of this systematic review was to assess the effectiveness of rehabilitation interventions on the secondary physical, neurological and psychological consequences of cardiac arrest (CA) for adult survivors.

Methods A literature search of electronic databases (MEDLINE, Allied and Complementary Medicine Database, Cumulative Index to Nursing and Allied Health Literature, Excerpta Medica database, Psychological Information Database, Web of Science and Cochrane Central Register of Controlled trials) was conducted for randomised controlled trials (RCTs) and observational studies up to 18 April 2021. The primary outcome was health-related quality of life (HRQoL) and main secondary outcome was neurological function with additional secondary outcomes being survival, rehospitalisation, safety (serious and non-serious adverse events), psychological well-being, fatigue, exercise capacity and physical capacity. Two authors independently screened studies for eligibility, extracted data and assessed risk of bias.

Results Three RCTs and 11 observational studies were included (total 721 participants). Study duration ranged from 8 weeks to 2 years. Pooled data from two RCTs showed low-quality evidence for no effect on physical HRQoL (standardised mean difference (SMD) 0.19, (95% CI: −0.09 to 0.47)) and no effect on mental HRQoL (SMD 0.27 (95% CI: −0.01 to 0.55)).

Regarding secondary outcomes, very low-quality evidence was found for improvement in neurological function associated with inpatient rehabilitation for CA survivors with acquired brain injury (SMD 0.71, (95% CI: 0.45 to 0.96)) from five observational studies. Two small observational studies found exercise-based rehabilitation interventions to be safe for CA survivors, reporting no serious or non-serious events.

Conclusions Given the overall low quality of evidence, this review cannot determine the effectiveness of rehabilitation interventions for CA survivors on HRQoL, neurological function or other included outcomes, and recommend further high-quality studies be conducted. In the interim, existing clinical guidelines on rehabilitation provision after CA should be followed to meet the high burden of secondary consequences suffered by CA survivors.

Strengths and limitations of this study

- ► This is the first systematic review and meta-analysis to assess the effectiveness of rehabilitation interventions for cardiac arrest (CA) survivors.
- ► Comprehensive literature searches were conducted with the inclusion of both randomised controlled trial and observational studies, and a wide range of outcomes relevant to CA survivors.
- ► High heterogeneity in intervention design and outcome measures limited the possibility for meta-analysis of study results.
- ► Quality of evidence was generally low with the majority of studies having small or very small sample sizes and insufficient description of the rehabilitation interventions.

PROSPERO registration number CRD42018110129.

INTRODUCTION

The number of people surviving a cardiac arrest (CA) to hospital discharge is increasing due to improvements in postcardiac arrest systems of care.[1] In the USA, survival to hospital discharge is now 11.4% translating to 70 000 new CA survivors each year with this number expected to increase.[1 2] However, after survival, multiple research studies have documented the secondary physical, neurological and psychological consequences for CA survivors.[1 3–6] Rehabilitation helps people to achieve and maintain optimum functioning in interaction with their environments.[7] Rehabilitation interventions have shown benefits for the secondary consequences of brain injury or cardiac events[8 9] indicating the same may be true for CA survivors. Rehabilitation after surviving a CA is recommended in consensus-based international clinical guidelines[1 10 11] but, to date, there has not been a

systematic assessment of the effectiveness of rehabilitation interventions for CA survivors.[12] In previous consensus building research with survivors, relatives and clinicians, quality of life and neurological function were identified as important outcomes after CA.[4 13]

The aim of this systematic review and meta-analysis was to assess the effectiveness of rehabilitation interventions for adult CA survivors. The primary outcome was health-related quality of life (HRQoL) and main secondary outcome was neurological function. Additional secondary outcomes were survival, rehospitalisation, safety (serious and non-serious adverse events), psychological well-being, fatigue, exercise capacity and physical capacity.

METHODS

Protocol and registration

This systematic review and meta-analysis is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (online supplemental file 1).[14]

Eligibility criteria

Studies using randomised controlled trials (RCTs) using individual or cluster randomisation in a parallel or crossover design, pilot studies, non-RCTs and prospective/retrospective observational studies were included. Studies using a case series or case report design were excluded.

The parameters for the systematic review were defined using the Population, Intervention Comparator, Outcome (PICO) framework. The question being: What is the effectiveness among adult (≥18 years) CA survivors (P), of rehabilitation interventions (I) on HRQoL and neurological function (O)? Comparator was defined as no treatment, active control, usual care, additional intervention or no comparator (C). No restriction on publication date, language or length of follow-up was made.

Studies that included both CA survivors and people with cardiac disease without CA were eligible for inclusion if subgroup data for CA survivors were presented or if these specific data could be obtained by contacting the study authors. If separate subgroup data for CA survivors could not be acquired, studies were eligible for inclusion if at least 50% of participants were CA survivors. Studies with mixed CA survivors and non-CA survivors acquired brain injury populations were treated in the same way.

Rehabilitation can be defined as: 'A set of measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimum functioning in interaction with their environments'.[7] To align with this broad definition of rehabilitation and ensure inclusion of all possible rehabilitation interventions, interventions were included if they were not primarily pharmacologically or surgically based or involved invasive technology. Interventions in the emergency room or critical care unit setting were excluded.

The primary outcome was HRQoL. HRQoL outcome measures could include generic or disease-specific patient-reported outcome measures and could be either a single item or multi-item outcome measure. The main secondary outcome was neurological function, defined as measuring the level of disability after a neurological event. Measures may primarily test cognitive ability or may combine cognitive and physical ability hence measuring global disability. Additional secondary outcomes were survival, rehospitalisation, safety (serious and non-serious adverse events), psychological well-being, fatigue, exercise capacity and physical capacity. Measures may be patient reported, clinician reported, observer reported or performance based. The primary and main secondary outcomes were chosen as, alongside survival, HRQoL and neurological function have been identified as important core outcome domains after CA by survivors, relatives and clinicians.[4 13] Choice of secondary outcomes was informed by existing evidence on the secondary consequences of CA[1 3 5 6] and inspired by outcomes in previous systematic reviews on rehabilitation with other cardiac disease populations.[8 15]

Information sources

Preliminary searches were conducted to identify relevant search terms and subject headings. The final systematic search for eligible studies was conducted in the online databases: The National Library of Medicine (MEDLINE), Allied and Complementary Medicine Database, Cumulative Index to Nursing and Allied Health Literature, Excerpta Medica database, Psychological Information Database, Web of Science, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled trials were initially searched on 2 December 2019 and updated on 18 April 2021. Abstracts from the 'postcardiac arrest conferences' 2013–2019 were hand searched, and bibliographies of articles included at the full-text stage were reviewed to identify possible additional studies. Ongoing trials were identified by searching clinical trial registries (International Standard Randomised Controlled Trial Number, WHO International Clinical Trials Registry Platform and ClinicalTrials.gov).

Searches

The search matrix consisted of a combination of keywords and synonyms for: (1) CA and (2) non-pharmacological/surgical/invasive technology rehabilitation interventions. The complete search strategy and detailed search matrix is outlined in online supplemental table 1.

Study selection

Using the technology platform Covidence, two authors (VLJ and EL) independently screened all identified studies, first by title and abstract, and then after reading the full-text articles. First and last authors of studies were contacted where full-text articles were unavailable or CA survivors subgroup data were required. Any disagreements in the screening process were discussed between the two authors and if necessary a third author was consulted (JC).

Data collection process

Data were extracted from the included studies independently by two review authors (VLJ and LHT) using a predefined standardised data extraction form. Any inconsistencies between authors in the data extraction process were resolved by discussion and if necessary a third author was consulted (JC).

Data items

Extracted data items included: study characteristics (author, year of publication, country, number of groups, number of participants, inclusion and exclusion criteria, setting, method of recruitment, aim of study, study design, length of study), characteristics of participants (mean age, gender, ethnicity, cause of CA, and comorbidities), description of intervention (duration, timing after CA, provider of intervention, description of control if relevant), theory or mechanism of intervention, outcomes (measured at baseline, hospital discharge, 3 months and final follow-up point and, if present, mortality, rehospitalisation, serious and non-serious adverse events) and results (sample sizes, baseline and all follow-up points, mean, estimate of effect, CI, SD, p value).

Risk of bias in individual studies

Two researchers independently assessed risk of bias for the included studies. RCTs were assessed using the RoB 2: a revised tool for assessing risk of bias in randomised trials,[16] and observational studies were assessed using the National Institutes of Health Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group.[17]

Summary measures

For continuous data, the effectiveness of the rehabilitation interventions was expressed either as mean difference (MD) or as standardised MD (SMD) with 95% CI. For time-to-event outcomes (survival, rehospitalisation), hazard ratios were pooled if presented.

Synthesis of results

If more than one study reported an outcome related to the outcomes of interest, the clinical heterogeneity (similarity in CA survivors population, rehabilitation interventions and outcomes) was assessed. If studies were considered clinically comparable, data were pooled using a random effects meta-analysis. SMD was calculated where the same outcome was reported but using different measurement tools with values of 0.2, 0.5 and 0.8 interpreted as small, medium and large effect sizes, respectively. Separate analyses were conducted for RCTs and observational studies. Study heterogeneity was examined using the Cochran Q test and quantified with I^2 statistic (statistical heterogeneity indicated by χ^2 test, $p<0.10$ and an I^2 statistic >50%). All analyses were conducted using STATA V.16 (StataCrop) statistical software.

Results from the Short Form Health Survey (SF-36 or SF-12) can be reported as either two component scores, (physical/mental) or as eight subscales. To allow synthesis of results, where results were reported as the eight subscales they were transformed into the two component scores following the method used by Matcham *et al*.[18]

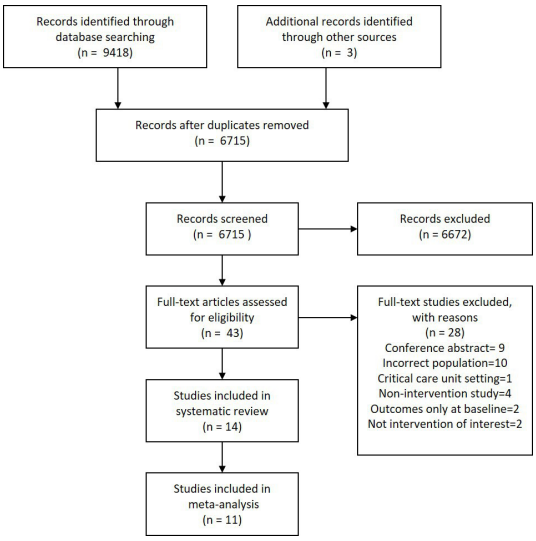

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram describing study selection.

Risk of bias and quality of evidence across studies

Grades of Recommendation, Assessment, Development and Evaluation system (GRADE)[19] was used to assess the overall quality of evidence across studies separately for the primary and main secondary study outcomes.

Additional analyses

If possible, subgroup and stratified analyses, meta-regression and assessment of small study bias will be investigated as prespecified in the protocol (online supplemental file 1).

Patient and public involvement

The need for the systematic review of rehabilitation interventions, and identification of important outcomes for the systematic review, were developed from a patient and public involvement event involving survivors, relatives and clinicians.[13]

RESULTS

Study selection

The search identified 6715 unique articles. After screening titles and abstracts, 43 full-text articles were screened, of which 14 studies were included for analysis.[20–34] Studies excluded at the full-text stage are listed with reasons in online supplemental table 2. Figure 1 presents the study flow chart and reasons for exclusion in the full text screening. Two registered ongoing trials were identified.[35 36]

Study characteristics

Study characteristics of the 14 included studies are described in online supplemental table 1.

Three RCTs (total 393 participants) and 11 observational studies (total 328 participants) were included. Nine studies

A

Study author, year	Risk of bias domains: Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Cowan, 2001	-	?	-	?	?	-
Dougherty, 2004	+	?	+	-	?	-
Moulaert, 2015	+	+	+	+	?	?

+ = Low risk; ? = Some concerns; - = High risk

B

Study Author, year	Quality assessment domains: Research question	Eligibility criteria	Representativeness of participants	Eligible participants enrolled	Sample size	Intervention	Outcome measures	Blinding of outcome assessors	Loss to follow-up	Statistical measures	Multiple outcome measures taken	Group level statistical analysis
Burke, 2005	+	-	+	-	-	-	+	-	+	-	-	?
Dougherty, 2008	+	+	+	-	-	+	+	-	+	+	-	?
Dougherty, 2019	+	+	+	+	+	+	+	-	+	+	+	?
Fertl, 2000	+	+	+	+	-	-	+	-	?	+	-	?
Howell, 2013	+	+	+	+	+	-	+	-	?	+	-	?
Kim 2014	+	+	+	?	-	+	+	-	+	+	-	?
Kim, 2016	+	+	+	-	-	+	+	-	+	+	-	?
Mion 2019	-	-	+	?	-	+	+	-	+	+	-	?
Schmidt, 1997	+	+	+	-	-	-	+	-	+	+	-	?
Shah 2007	+	+	+	+	-	-	+	-	+	-	-	?
Tazopoulou, 2016	+	+	+	?	-	-	+	-	+	+	-	?

+ = Yes; ? = Cannot determine, not applicable, not reported; - = No

Figure 2 Quality assessment and risk of bias, review authors judgements about quality assessment and risk of bias for each included study. (A) Summary based on 'RoB 2: a revised tool for assessing risk of bias in randomised trials'. (B) Summary based on 'Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group'.

investigated outpatient or community-based rehabilitation interventions of which three were RCTs. Five studies investigated inpatient rehabilitation for acquired brain injury, all were observational studies. Considering the very different CA survivor populations and intervention settings, the results for outpatient or community-based rehabilitation studies and inpatient rehabilitation for acquired brain injury are presented separately. Study follow-up period ranged from 1 to 24 months. One study[25] had CA survivors in both arms of the RCT receiving the same intervention, hence, data from both arms were combined and treated as one observational study (data obtained from study authors).

Risk of bias within studies

Risk of bias assessments are summarised in figure 2A,B. Of the three included RCTs,[21–23 31] Moulaert *et al*[31] was assessed as having 'some concerns' and the two other studies[21–23] were assessed having a 'high risk' of bias in the overall risk of bias assessment. Ten of the 11 observational studies had multiple high risk of bias domains.

Results of individual studies

A summary of the results of the individual studies is reported in online supplemental table 1.

Synthesis of results

Health-related quality of life

In total, two RCTs[22 23 31] and four observational studies[24 25 30 34] measured HRQoL.

HRQoL meta-analysis

Two RCTs[22 23 31] evaluated the effectiveness of a rehabilitation intervention compared with standard care. The

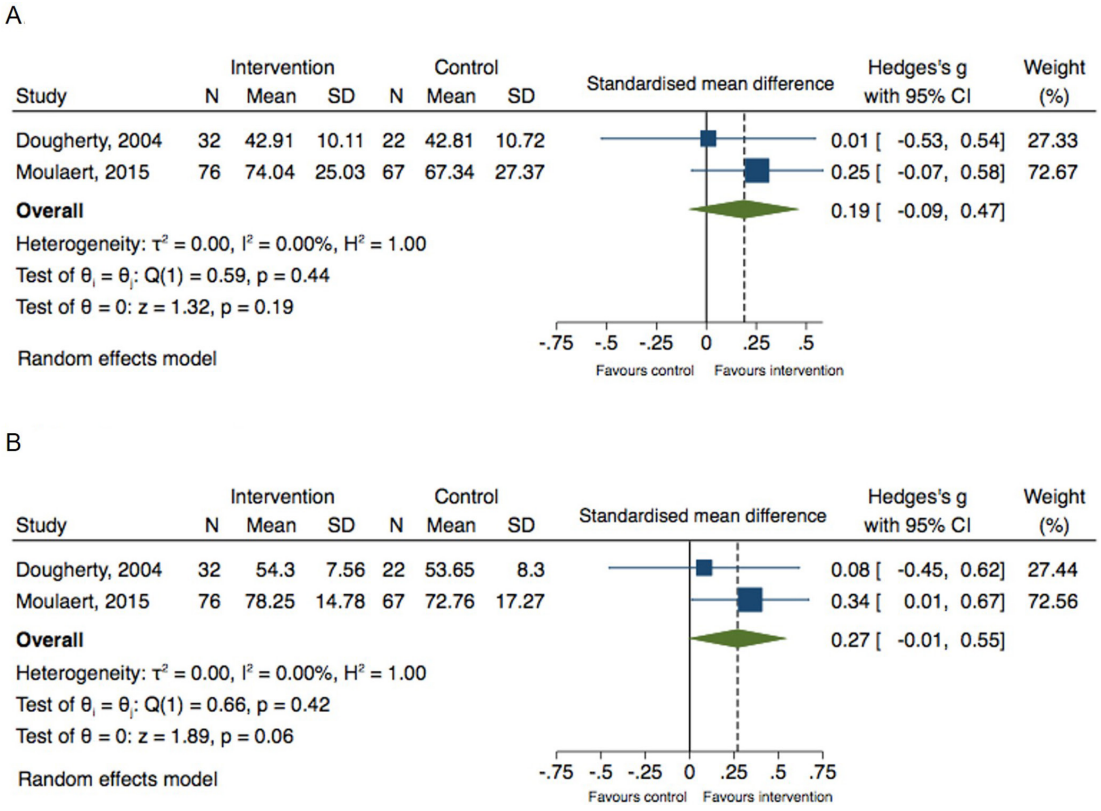

Figure 3 Forest plots for outpatient/community-based rehabilitation for cardiac arrest survivors compared with standard intervention, effect on health-related quality of life as measured by SF-12 or SF-36 (Short Form Health Survey) at 12 months follow-up. (A) Physical Component Score, (B) Mental Component Score

random effects meta-analyses showed from baseline to 12 months follow-up, no statistically significant effectiveness of rehabilitation interventions in physical HRQoL, overall SMD 0.19, (95% CI: −0.09 to 0.47, p=0.19), I^2=00.0% or mental HRQoL, overall SMD 0.27, (95% CI: −0.01 to 0.55, p=0.06), I^2=0.00% (figure 3A,B).

Two observational studies[25 30] could be pooled and a significant improvement in physical HRQoL was observed 6 months after baseline assessment, overall SMD 0.95, (95% CI: 0.64 to 1.27, p<0.001), I^2=0.00%, p<0.001 (figure 4A), however, no improvement in mental HRQoL was observed with an overall SMD 0.80, (95% CI: −0.45 to 2.05, p=0.21), I^2=90.17% (figure 4B).

HRQoL studies not included in meta-analysis

Due to clinical heterogeneity, two observational studies[24 34] reporting on HRQoL were not included in the meta-analysis. One study,[24] involving exercise-based rehabilitation, showed a non-significant increase in physical HRQoL at 8 weeks follow-up (44.33 points (SD 10.77) to 47.19 (SD 9.11), p=0.19) and mental HRQoL (51.33 (SD 11.68) to 55.03 (SD 8.04), p=0.48). A second observational study[34] involving a community-based rehabilitation intervention for CA survivors with acquired brain injury showed a significant increase in HRQoL at 2 months follow-up (Quality of Life after Traumatic Brain Injury Satisfaction scale mean score, 82.25–89.95 points, p=0.015).

Neurological function

Neurological function was used as an outcome in one RCT[31] and six observational studies.[20 26 27 32–34]

The RCT[31] showed an outpatient rehabilitation intervention had no significant effectiveness in improving cognitive function on performance-based cognitive tests compared with standard care at any follow-up point.

Neurological function meta-analysis

Five observational studies[20 26 27 32 33] were included in a meta-analysis. This showed rehabilitation significantly increased clinician-reported function, overall SMD 0.71, (95% CI: 0.45 to 0.96, p<0.001), I^2=17.36%, between admission and discharge for CA survivors with acquired brain injury (figure 5). Howell *et al*[27] was removed in a sensitivity analysis as the population were all in a vegetative or minimally conscious state with the lowest possible Functional Independence Measure (FIM) score of 18. This resulted in a larger overall SMD 0.89, (95% CI: 0.56 to 1.22, p<0.001), I^2=0.00 (online supplemental figure 1). In an analysis with the three observational studies[20 32 33] using FIM as their outcome, rehabilitation interventions showed an improvement in total FIM, overall MD of 28.24 points (95% CI: 16.33 to 40.15, p<0.001), I^2=0.00%, between admission and discharge (figure 6).

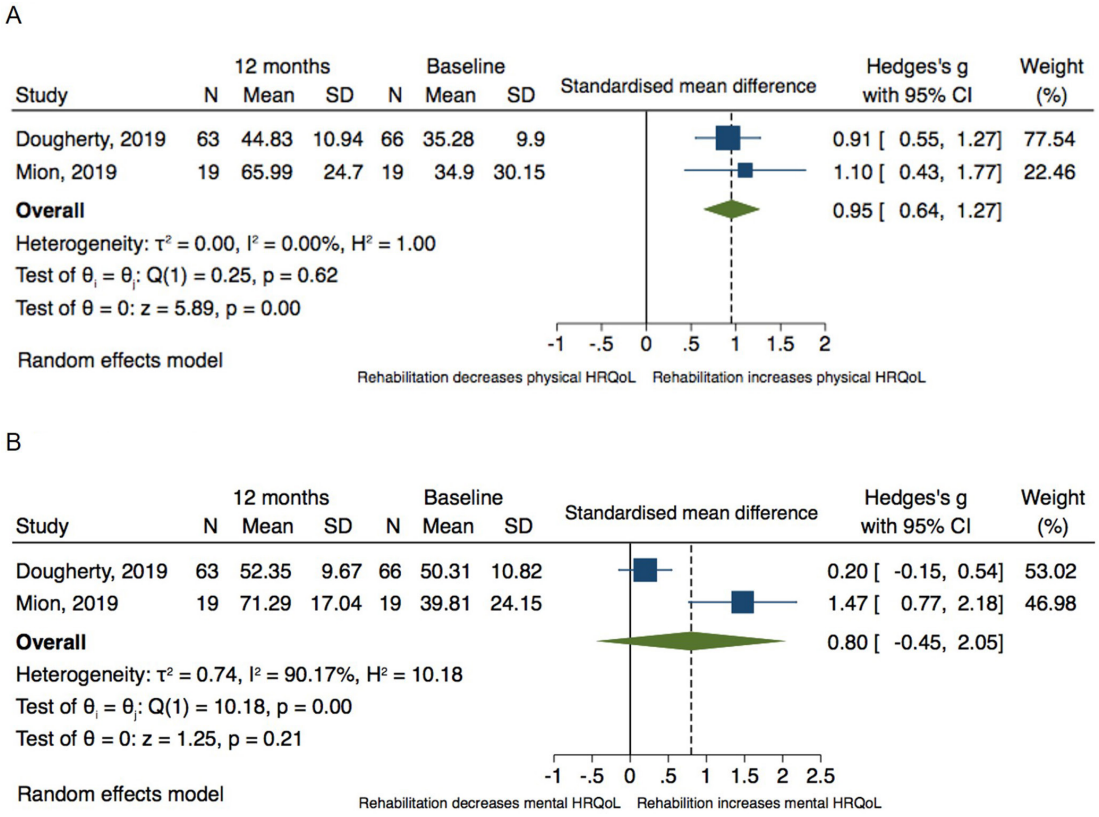

Figure 4 Forest plots for outpatient/community-based rehabilitation for cardiac arrest survivors, effect on health-related quality of life (HRQoL) as measured by SF-12 or SF-36 (Short Form Health Survey) between baseline and 6 months follow-up (A) Physical Component Score, (B) Mental Component Score.

Neurological function data not included in meta-analysis

One observational study[34] showed no significant change in neurological function after a community-based rehabilitation intervention for acquired brain injury. Further, Howell *et al*[27] found by discharge, 6.2% of CA survivors with acquired brain injury in a vegetative or minimally conscious state achieved a good neurological functional outcome (defined as Glasgow Outcome Scale category 4–5). Cognition, specifically executive function, is the primary outcome in one ongoing trial,[36] with results due in 2024.

Survival

Survival was used as an outcome in one RCT.[21] The study found no statistically significant reduction in risk of all-cause mortality (62% risk reduction, p=0.13, CI not stated). However, a statistically significant decrease in risk of cardiovascular death was found in favour of those who were allocated to the rehabilitation intervention (86% risk reduction, HR=0.14; p=0.03, CI not stated) one death in the intervention group due to stroke, six out of seven deaths in control group due to CA.

Rehospitalisation

No study reported on rehospitalisation.

Safety (serious and non-serious adverse events)

Reported in two observational studies[24 28] involving exercise-based rehabilitation. No serious or non-serious events were reported in either study.[24 28]

Psychological well-being

Psychological well-being was reported in one RCT[31] and three observational studies.[24 25 34] No meta-analysis was

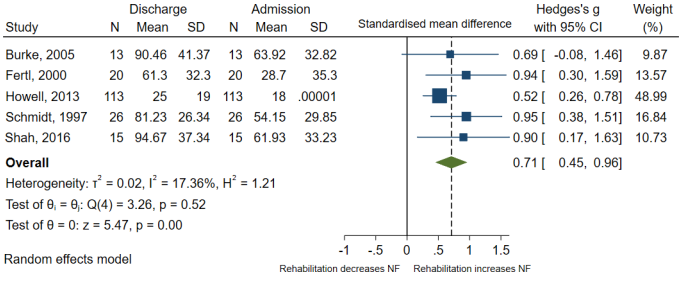

Figure 5 Forest plot for effect of inpatient rehabilitation on neurological function (NF) between admission and discharge.

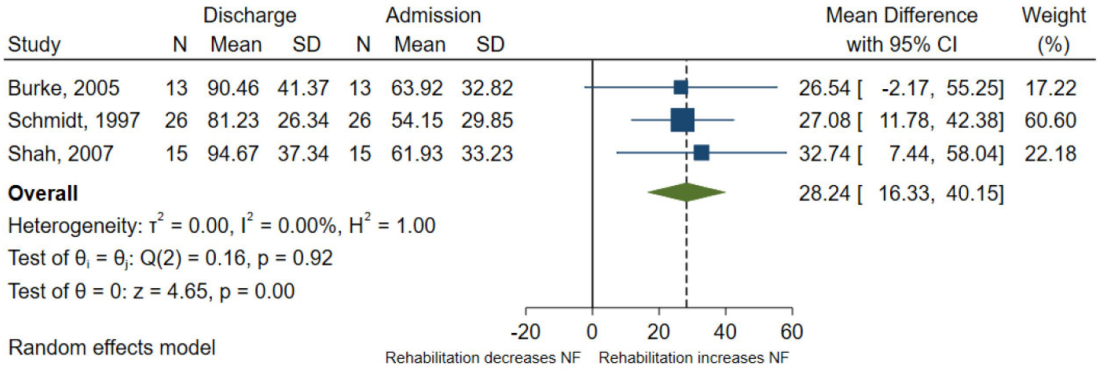

Figure 6 Forest plot for effect of inpatient rehabilitation for cardiac arrest survivors with acquired brain injury on neurological function (NF) between admission and discharge as measured by the Functional Independence Measure (scale: 18–126 points, with higher scores indicating better function).

possible due to clinical heterogeneity between studies. All studies used self-reported symptom measurements and not a medical diagnosis of psychological well-being.

The RCT[31] found that education-based rehabilitation had a positive effect on total anxiety and depression (p=0.002) and anxiety subscale (p<0.001) compared with standard care at 1-year follow-up.

An observational study[25] found that an education/psychological support-based intervention had a reduction in anxiety (32.10 points (SD 11.03) to 28.57 (SD 9.65)) and depression (5.46 points (SD 4.37) to 3.7 (SD 3.89)) between baseline and 3 months. This was maintained at 12 months follow-up (28.87 (SD 10.62) and 3.36 (SD 4.29), respectively). An exercise-based rehabilitation intervention observational study[24] found a non-significant reduction in anxiety (31.56 (SD 11.83) to 28.22 (SD 9.68), p=0.06) and depression (11.00 (SD 13.08) to 9.22 (SD 11.88), p=0.46) from baseline to 8 weeks follow-up . An observational study involving a community-based rehabilitation intervention for acquired brain injury showed no statistically significant change in anxiety or depression from baseline to 2 months follow-up.[34]

Fatigue

One observational study[29] found between baseline and study end (3–5 weeks) of an energy conservation and problem solving therapy intervention, a significant decrease in self-reported total (p<0.001), physical (p=0.001) and cognitive (p=0.006) fatigue, with small to moderate effect sizes (r=0.23–0.25). Fatigue is the primary outcome in one ongoing trial,[35] with results due in 2021.

Exercise and physical capacity

Reported in two observational studies.[24 28] Meta-analysis of the two studies found that an 8-week exercise-based rehabilitation intervention significantly increased exercise duration (MD 3.72 min (95% CI: 0.49 to 6.95, p=0.02), I^2=42.61% but not exercise capacity, overall SMD 0.41, (95% CI: −0.23–1.04, p=0.32), I^2=0.00% (online supplemental figures 2 and 3).

Daily activity was reported in one observational study.[28] Measured by RT3 accelerometer, it increased after an 8-week exercise-based rehabilitation intervention and continued to increase at 6-month follow-up (baseline 143.02 vector magnitude/minute (vm/min) (SD 41.44), 8 weeks 230.0 vm/min (SD 121.78), 6 months 289.89 vm/min (SD 8.99), p=0.17).

Risk of bias and quality of evidence across studies

Quality of evidence (GRADE) for both the primary and main secondary outcomes, HRQoL and neurological function, was assessed as low for the RCTs and very low for the observational studies. Reasons for downgrading of evidence are described in the Summary of findings tables (online supplemental tables 3 and 4).

Heterogeneity between studies

Possibility for meta-analyses in this study was limited due to the heterogeneity in CA survivors populations, rehabilitation interventions and outcomes (online supplemental table 1).

Additional analyses

A priori, we planned several univariate meta-regression analyses,[37] subgroups analyses and investigation of small study bias (see protocol, online supplemental file 1). However, due to the limited number of included studies, all of these analyses were not conducted, as recommended in the Cochrane Handbook for Systematic Reviews of Interventions.[37]

DISCUSSION

This study systematically investigated the effectiveness of rehabilitation interventions for CA survivors. Overall, quality of the body of evidence of these interventions is low or very low. Eleven of the 14 studies were observational and cannot determine the cause and effect of an intervention, but can only show the associated change in outcomes between one time point and another. The overall risk of bias of the three included RCTs ranged from ‘some concerns’ to ‘high risk of bias’ (figure 2A).

Analysis of these RCTs showed no significant effect on HRQoL or neurological function with one RCT showing a positive effect on anxiety and depression (psychological well-being). The included observational studies suggested some associated positive change in outcomes, but the quality of the body of evidence was generally low (figure 2B) with the majority having small or very small sample sizes and insufficient description of the content of the rehabilitation interventions. Hence, all of the findings should be interpreted with caution as additional evidence is needed and could substantially impact the interpretation of the results.

The meta-analysis of RCTs found no significant effect for rehabilitation interventions on HRQoL. However, it should be noted that only two RCTs[22 23 31] were included in this pooled analysis. The RCT by Moulaert *et al*,[31] taken on its own, reported a significant effect on HRQoL compared with control in three out of eight SF-36 domains (online supplemental table 1). Our findings on HRQoL, being mindful of the low number of included RCTs, are largely in agreement with an earlier systematic review of similar education-based rehabilitation interventions for patients with coronary heart disease.[15] While the review authors found some evidence for greater HRQoL in some domain scores, overall, they found no definite evidence for better HRQoL after education in comparison to control.

A meta-analysis of two observational studies[25 30] showed a significant associated increase in physical HRQoL. However, as is inherent to the study design, neither of the studies had a control group. From the control arms in the two RCTs,[22 23 31] we see that CA survivors receiving standard care also seem to improve over time (mean 12.8 points improvement in physical HRQol, online supplemental table 3). Thus, demonstrating the importance of using control group trial designs to determine the real effectiveness of rehabilitation interventions in this population.

Our main secondary outcome was neurological function. The only RCT[31] to report neurological function found no effect of an outpatient intervention compared with usual care on cognitive function, however, Moulaert *et al*[31] state that this was expected as the intervention did not include cognitive training. In the observational studies, inpatient rehabilitation was associated with improvements in neurological function for CA survivors with acquired brain injury (figure 5). Three of the studies[20 32 33] reported total FIM (figure 6). The total FIM minimal clinically important difference (MCID) has not been described for CA survivors, but in patients who had a stroke, the MCID has been shown to be an improvement of ≥22 points.[38] Hence, the pooled mean improvement of 28.24 points found in this study would indicate inpatient rehabilitation provides a clinically significant improvement in neurological function for CA survivors. However, none of the studies had control arms, and all had several high risk of bias domains including insufficient description of intervention or small sample sizes. This review found very few studies aimed at improving neurological function including cognition for CA survivors. However, one ongoing RCT was found investigating a computer-based intervention to improve executive function with results due in 2024.[36]

Survival was only reported in one study[21] that was judged to be of high risk of bias with missing data, therefore, no conclusions on the effect of rehabilitation on survival can be made. By definition, rehabilitation helps people to achieve and maintain optimum functioning in interaction with their environments.[7] Hence, survival would not seem to be a primary outcome for rehabilitation for CA survivors.

Two small observational studies[24 28] reported exercise-based rehabilitation interventions as safe for CA survivors. The reporting of no serious or non-serious events is in agreement with earlier studies exploring safety during moderate or high intensity exercise training for people with cardiovascular disease[39–41] or implantable cardioverter defibrillators.[42] However, both included studies had very small populations (8 and 10 participants) and much larger study populations are needed to establish the safety of exercise for CA survivors.

Psychological interventions have been shown to reduce anxiety and depression in patients with coronary heart disease.[43] The RCT by Moulaert *et al*[31] found a reduction in total anxiety and depression although their intervention provided primarily education and screening for cognitive/emotional problems rather than psychological focused interventions. Education on the consequences of CA along with insight into their cognitive/emotional problems may have led to the participants' improved psychological state. Alternatively, participants in the intervention group could be referred for additional specialist support. However, we do not know what proportion of participants received additional specialist psychological support or how this may have influenced the results.

This is the first systematic review and meta-analysis to assess the effectiveness of rehabilitation interventions for CA survivors. Its strengths lie in the comprehensive literature searches, inclusion of both RCTs and observational studies, and the included wide range of outcomes relevant to CA survivors. Nevertheless, there are a number of limitations. In order to pool the HRQoL data, the SF-36 scores from two studies[30 31] were transformed from subscales to component scores. Some overlap in physical/mental domains between the eight subscales has been noted when using this transformation method.[18] Therefore, transformed scores may not completely represent the original study results.[18] We included two studies with populations of CA survivors and people with anoxic brain injury due to other causes (45%[34] and 42%[32] participants with anoxic brain injury other causes) where CA survivors subgroup data were not available. Including non-CA survivors may have influenced the results, however, we deemed the inclusion of these studies as important considering the paucity of data available. The effect of including studies with mixed populations on this review's

results is difficult to determine without greater examination of the aetiology and secondary consequences of the other non-CA causes of anoxic brain injury. However, Schmidt *et al*[32] showed a similar change in FIM to two of the studies[20 33] that only included CA survivors (figure 6).

Our primary outcome, HRQoL, is an important outcome in rehabilitation research.[7] However, the choice of generic or disease-specific HRQoL measures may influence the results as generic measures of HRQoL can be crude with important details lost and large sample sizes required to demonstrate effect.[4 44 45] In this review, all studies except one[34] used generic measures of HRQoL.

Another element that potentially influenced our findings may be the standard care received by the RCT control groups. Two[21–23] of the included RCTs provided educational elements to both the intervention and control groups and in a third[46] participants could have received cardiac rehabilitation.

The high heterogeneity found between studies, limiting meta-analysis, may be explained by the wide range of physical, neurological and psychological problems suffered by CA survivors.[1 3–6] Most CA survivors will have a new or ongoing cardiac condition,[1] and therefore, be eligible for cardiac rehabilitation.[47] Neurological rehabilitation has been recommended to meet the 'brain' aspect of CA recovery.[3 48] This can be mild cognitive impairments in self-caring CA survivors[49] or more severe brain injury needing long-term residential care.[3] Hence, different CA survivor populations lead naturally to the selection of different rehabilitation interventions and study outcomes.

Implications for future research and clinical practice

The majority of studies found by this systematic review were observational. Given their potential risk of bias and no control group, we recommend no further observational studies focusing on the question of effectiveness are conducted but instead there is a need for high-quality RCTs comparing rehabilitation interventions for CA survivors to standard care alone. Considering the small population of CA survivors, multicentre RCTs should be considered to achieve a sufficient sample size to determine an effect on specific outcomes. In view of the wide range of potential consequences after CA, future studies might also consider investigating interventions that target a single consequence of CA, for example, fatigue, or whether interventions should be multicomponent. A minimum outcome set for these future rehabilitation RCTs should include those recommended by COSCA (Core Outcome Set for Cardiac Arrest),[4] HRQoL and neurological function, and consider including disease-specific outcomes. However, more research is needed to identify outcomes and measurement tools that reflect the range of rehabilitation needs of CA survivors. Agreement on a CA survivors' rehabilitation core outcome set would facilitate subsequent meta-analysis of study results providing a stronger body of evidence on rehabilitation after CA. Further, it is essential future RCTs use agreed reporting guidelines such as CONSORT (Consolidated Standards of Reporting Trials)[50] or TIDieR (Template for Intervention Description and Replication)[51] to detail the complex rehabilitation interventions under investigation. This systematic review has focused primarily on impairment and function outcomes and less on activity and participation. Hence, future systematic reviews on this subject could consider including these outcomes.

Based on the low quality of the body of evidence, clinical rehabilitation guidelines should continue to be consensus based.[1 10 11] In clinical practice, rehabilitation interventions should be offered based on these consensus-based recommendations with ongoing monitoring of clinical outcomes. The documented secondary physical, neurological and psychological consequences of CA for survivors are so comprehensive[1 3–6] that we as clinicians must meet these needs in current clinical practice.

CONCLUSIONS

Given the overall low quality of evidence, this review cannot determine the effectiveness of rehabilitation interventions for CA survivors on HRQoL, neurological function or other included outcomes, and recommend further high-quality studies are conducted. In the interim, existing clinical guidelines on rehabilitation provision after CA should be followed to meet the high burden of secondary consequences suffered by CA survivors.

Author affiliations
[1]REHPA, The Danish Knowledge Centre for Rehabilitation and Palliative Care, Odense University Hospital, Odense, Denmark
[2]Department of Occupational- and Physiotherapy, Copenhagen University Hospital, København, Denmark
[3]3MRC/CSO Social and Public Health Sciences Unit & Robertson Centre for Biostatistics, Institute of Health and Well Being, University of Glasgow, Glasgow, UK
[4]Department of Physiotherapy and Occupational Therapy, Slagelse Hospital, Slagelse, Sjaelland, Denmark
[5]The Department of Regional Health Research, University of Southern Denmark, Odense, Syddanmark, Denmark

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Contributors Conception of study: VLJ, RST, ADZ and LHT. Preparation of protocol: VLJ, JC, RST, ADZ and LHT. Study selection: VLJ, JC, EL and LHT. Data extraction, data analysis and risk of bias assessment: VLJ, JC and LHT. Writing of the manuscript, review and editing: VLJ, JC, EL, RST, ADZ and LHT. The final manuscript was approved by all authors.

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ORCID iD

Vicky L Joshi http://orcid.org/0000-0003-3524-1990

REFERENCES

1 Sawyer KN, Camp-Rogers TR, Kotini-Shah P, *et al*. Sudden cardiac arrest survivorship: a scientific statement from the American heart association. *Circulation* 2020;141:e654–85.
2 Benjamin EJ, Muntner P, Alonso A, *et al*. Heart disease and stroke Statistics-2019 update: a report from the American heart association. *Circulation* 2019;139:E56–28.
3 Boyce LW, Goossens PH. Rehabilitation after cardiac arrest: integration of neurologic and cardiac rehabilitation. *Semin Neurol* 2017;37:094–102.
4 Haywood K, Whitehead L, Nadkarni VM, *et al*. COSCA (core outcome set for cardiac arrest) in adults: an Advisory statement from the International liaison Committee on resuscitation. *Resuscitation* 2018;127:147–63.
5 Wilder Schaaf KP, Artman LK, Peberdy MA, *et al*. Anxiety, depression, and PTSD following cardiac arrest: a systematic review of the literature. *Resuscitation* 2013;84:873–7.
6 Elliott VJ, Rodgers DL, Brett SJ. Systematic review of quality of life and other patient-centred outcomes after cardiac arrest survival. *Resuscitation* 2011;82:247–56.
7 Cantista P, Ceravolo MG, Christodoulou N, *et al*. White book on physical and rehabilitation medicine (PRM) in Europe. Chapter 1. definitions and concepts of PRM. *Eur J Phys Rehabil Med* 2018;54:156–65.
8 Anderson L, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2014;12:CD011273.
9 Turner-Stokes L, Pick A, Nair A, *et al*. Multi-Disciplinary rehabilitation for acquired brain injury in adults of working age. *Cochrane Database Syst Rev* 2015;29:CD004170.
10 The Scottish Government. *Out-of-Hospital Cardiac Arrest - A Strategy for Scotland*, 2015: 1–58.
11 Nolan JP, Soar J, Cariou A, *et al*. European resuscitation Council and European Society of intensive care medicine 2015 guidelines for post-resuscitation care. *Intensive Care Med* 2015;41:2039–56.
12 Joshi V, Tang L, Long L. Report on rehabilitation and palliative care in the management of cardiovascular diseases: the evidence and the gaps, 2018. Available: https://hjerteforeningen.dk/wp-content/uploads/sites/17/2018/02/2018.01-dhf-report-on-rehabilitation-and-palliative-care-final.pdf
13 Tang LH, Zwisler A-D. Rehabilitation after cardiac arrest - we can surely do better! *Cardiologisk Forum* 2019;30:30–7.
14 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62:1006–12.
15 Anderson L, Brown JP, Clark AM, *et al*. Patient education in the management of coronary heart disease. *Cochrane Database Syst Rev* 2017;6:CD008895.
16 Sterne JAC, Savović J, Page MJ, *et al*. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
17 National Institutes of Health. Quality assessment tool for before-after (pre-post) studies with no control group. Available: http://wwwnhlbinihgov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/before-after
18 Matcham F, Scott IC, Rayner L, *et al*. The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2014;44:123–30.
19 Guyatt GH, Oxman AD, Schünemann HJ, *et al*. Grade guidelines: a new series of articles in the Journal of clinical epidemiology. *J Clin Epidemiol* 2011;64:380–2.
20 Burke DT, Shah MK, Dorvlo ASS, *et al*. Rehabilitation outcomes of cardiac and non-cardiac anoxic brain injury: a single institution experience. *Brain Inj* 2005;19:675–80.
21 Cowan MJ, Pike KC, Budzynski HK. Psychosocial nursing therapy following sudden cardiac arrest: impact on two-year survival. *Nurs Res* 2001;50:68–76.
22 Dougherty CM, Pyper GP, Frasz HA. Description of a nursing intervention program after an implantable cardioverter defibrillator. *Heart Lung* 2004;33:183–90.
23 Dougherty CM, Thompson EA, Lewis FM. Long-Term outcomes of a telephone intervention after an ICD. *Pacing Clin Electrophysiol* 2005;28:1157–67.
24 Dougherty CM, Glenny R, Kudenchuk PJ. Aerobic exercise improves fitness and heart rate variability after an implantable cardioverter defibrillator. *J Cardiopulm Rehabil Prev* 2008;28:307–11.
25 Dougherty CM, Thompson EA, Kudenchuk PJ. Patient plus partner trial: a randomized controlled trial of 2 interventions to improve outcomes after an initial implantable cardioverter-defibrillator. *Heart Rhythm* 2019;16:453–9.
26 Fertl E, Vass K, Sterz F, *et al*. Neurological rehabilitation of severely disabled cardiac arrest survivors. Part I. course of post-acute inpatient treatment. *Resuscitation* 2000;47:231–9.
27 Howell K, Grill E, Klein A-M, *et al*. Rehabilitation outcome of Anoxic-ischaemic encephalopathy survivors with prolonged disorders of consciousness. *Resuscitation* 2013;84:1409–15.
28 Kim C, Jung H, Choi HE, *et al*. Cardiac rehabilitation after acute myocardial infarction resuscitated from cardiac arrest. *Ann Rehabil Med* 2014;38:799–804.
29 Kim YJ, Rogers JC, Raina KD, *et al*. An intervention for cardiac arrest survivors with chronic fatigue: a feasibility study with preliminary outcomes. *Resuscitation* 2016;105:109–15.
30 Mion M, Al-Janabi F, Islam S, *et al*. Care after resuscitation: implementation of the United Kingdom's first dedicated multidisciplinary follow-up program for survivors of out-of-hospital cardiac arrest. *Ther Hypothermia Temp Manag* 2020;10:53–9.
31 Moulaert VRM, van Heugten CM, Winkens B, *et al*. Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: a randomised controlled trial. *Int J Cardiol* 2015;193:8–16.
32 Schmidt JG, Drew-Cates J, Dombovy ML. Anoxic encephalopathy: outcome after inpatient rehabilitation. *Neurorehabil Neural Repair* 1997;11:189–95.
33 Shah MK, Carayannopoulos AG, Burke DT, *et al*. A comparison of functional outcomes in hypoxia and traumatic brain injury: a pilot study. *J Neurol Sci* 2007;260:95–9.
34 Tazopoulou E, Miljkovitch R, Truelle J-L, *et al*. Rehabilitation following cerebral anoxia: an assessment of 27 patients. *Brain Inj* 2016;30:95–103.
35 Joshi VL. Rehabilitation for survivors of cardiac arrest focused on fatigue: U.S. National library of medicine clinical Trials.gov, 2019. Available: https://ClinicalTrials.gov/show/NCT04114773
36 Christensen H. Computer-Assisted Self-training to improve executive function (COMPEX) clinical Trials.gov, 2020. Available: https://clinicaltrials.gov/ct2/show/NCT042290562021
37 Higgins JPT, Thomas J, Chandler J. *Cochrane Handbook for systematic reviews of interventions*. version 60: Cochrane, 2019.
38 Beninato M, Gill-Body KM, Salles S, *et al*. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Arch Phys Med Rehabil* 2006;87:32–9.
39 Wewege MA, Ahn D, Yu J, *et al*. High-Intensity interval training for patients with cardiovascular Disease-Is it safe? A systematic review. *J Am Heart Assoc* 2018;7:e009305.
40 Hannan AL, Hing W, Simas V, *et al*. High-Intensity interval training versus moderate-intensity continuous training within cardiac rehabilitation: a systematic review and meta-analysis. *Open Access J Sports Med* 2018;9:1–17.
41 Rognmo Øivind, Moholdt T, Bakken H, *et al*. Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. *Circulation* 2012;126:1436–40.
42 Alswyan AH, Liberato ACS, Dougherty CM. A systematic review of exercise training in patients with cardiac implantable devices. *J Cardiopulm Rehabil Prev* 2018;38:70–84.
43 Richards SH, Anderson L, Jenkinson CE, *et al*. Psychological interventions for coronary heart disease. *Cochrane Database Syst Rev* 2017;4:CD002902.
44 Haywood K. Survival and quality of life following a cardiac arrest: capturing what really matters to survivors. *Resuscitation* 2019;135:221–3.
45 Bohm M, Lilja G, Finnbogadóttir H, *et al*. Detailed analysis of health-related quality of life after out-of-hospital cardiac arrest. *Resuscitation* 2019;135:197–204.

46 Moulaert V, van Heugten C, Winkens B, *et al*. New psychosocial intervention improves quality of life after cardiac arrest: results of a randomised controlled trial. *Resuscitation* 2013;84:S1–2.
47 Tang LH, Joshi V, Egholm CL, *et al*. Are survivors of cardiac arrest provided with standard cardiac rehabilitation? - Results from a national survey of hospitals and municipalities in Denmark. *Eur J Cardiovasc Nurs* 2021;20:115–23.
48 Maciel CB, Barden MM, Greer DM. Neurologic recovery after cardiac arrest: a multifaceted puzzle requiring comprehensive coordinated care. *Curr Treat Options Cardiovasc Med* 2017;19:52.
49 Lilja G, Nielsen N, Friberg H, *et al*. Cognitive function in survivors of out-of-hospital cardiac arrest after target temperature management at 33°C versus 36°C. *Circulation* 2015;131:1340–9.
50 Eldridge SM, Chan CL, Campbell MJ, *et al*. Consort 2010 statement: extension to randomised pilot and feasibility trials. *Pilot Feasibility Stud* 2016;2:64.
51 Hoffmann TC, Glasziou PP, Boutron I, *et al*. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687.

Supplementary data 1

PROSPERO Protocol

Citation

Vicky Joshi, Jan Christensen, Esben Lejsgaard, Ann-Dorthe Zwisler, Rod Taylor, Jørgen Feldbæk Nielsen, Lars Tang. Non-pharmacological rehabilitation interventions for survivors of cardiac arrest: a systematic review and meta-analysis. PROSPERO 2018 CRD42018110129 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018110129

Review question

What is the effectiveness of non-pharmacological rehabilitation interventions on adult cardiac arrest survivors?

Searches

The following electronic databases will be searched: MEDLINE, EMBASE, CINAHL, PsycINFO, AMED, The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled trials (CENTRAL) and Web of Science (up to April 2021 without any restriction in publication date or language).

Trial registries ISRCTN and the WHO ICTRP search portal, and the database ClinicalTrials.gov will be used to search ongoing trials relevant to the review, identify unpublished work, and describe upcoming publications within the studied area. The Cochrane Database of Systematic Reviews will be searched to identify former reviews that identify possible studies for inclusion. These will be screened for eligibility in the same manner as all other studies identified during the database searches.

The search matrix will consist of a combination of relevant indexed terms (e.g. MeSH, Subject Headings or Thesaurus terms), keywords and synonyms for: 1) cardiac arrest, and 2) non-pharmacological rehabilitation interventions.

Title and abstracts from the following conferences will be hand searched: 'European Resuscitation Council Congress', 'American Heart Association' and American College of Cardiology (all from 2009), and the 'Post-cardiac arrest conference' (from 2013).

To identify studies that were not captured by the search matrix, forward and backward citation searching will be conducted on all papers included after full-text screening by two authors (VLJ and MA). Backward citation searching involves screening the references in papers identified after full-text screening. Forward citation searching, searches papers that have cited any papers found after full test screening. References will be hand-searched and citations will be searched for via Web of Science. Titles will be screened for eligibility. Abstracts of possible eligible studies will be screened for eligibility as per all other studies identified during the original database searches.

The first and last authors of unobtainable studies or studies with missing data will be contacted.

Types of study to be included

Included:

- Randomised controlled trials using individual, cluster or any design including parallel group, cross overallocation trials, including pilot studies. - Non-randomised controlled trials

- Prospective and retrospective observational studies with or without a control group.

Excluded:

- Case reports

Condition or domain being studied

The number of people surviving a cardiac arrest is increasing due to improvements in bystander resuscitation and acute hospital care. However, following a cardiac arrest up to half of survivors experience cognitive, psychological and physical problems. These secondary problems plus the underlying cardiac condition present in the majority of cardiac arrest survivors may impact on survivors' well-being and healthrelated quality of life. Non-pharmacological rehabilitation interventions have been recommended in international guidelines but the effect of these interventions remains unknown. A recent investigation into the outcomes for testing effectiveness of interventions for cardiac arrest survivors, by the COSCA initiative (core outcome set for cardiac arrest), recommended three measures be used: survival at 30 days or hospital discharge, neurological function and health-related quality of life (1).

For reference list, see additional information section.

Participants/population

Studies investigating adults, over the age of 18, of both sexes, and all ethnicities who have survived a cardiac arrest will be eligible for inclusion.

Studies that include both survivors of cardiac arrest, and people with cardiac disease without cardiac arrest will be managed in the following way; all trials that present data for cardiac arrest survivors in a subgroup will be included. Where data is not presented in a sub-group, we will contact trial authors to ascertain separate data on the survivors of cardiac arrest. If it is not possible to ascertain subgroup data and only pooled data is available, the study will only be included if at least 50% of participants were survivors of a cardiac arrest.

Intervention(s), exposure(s)

Studies investigating any non-pharmacological rehabilitation intervention for survivors of cardiac arrest, will be considered eligible for inclusion. Non-pharmacological interventions refers to interventions that are not primarily surgically or pharmacologically based or do not involve invasive technology. There will be no restrictions related to length of intervention, timing of intervention or timing of follow-up. The intervention may be a single session or a series of sessions. It may be provided one-to-one or in a group of survivors. Most cardiac arrest survivors have an underlying cardiac condition and hence cardiac rehabilitation intervention studies that include cardiac arrest survivors will be considered as a non-pharmacological intervention and included in this review. The cardiac rehabilitation may be exercise-based, psychological-based, education based or comprehensive in nature.

Exclusion criteria:

1. All studies reporting on effectiveness of medical, surgical or invasive technology interventions will be excluded.

2. Interventions in the emergency room or critical care unit will be excluded.

3. Studies that do not report results at baseline and at minimum one follow-up point after intervention.

Comparator(s)/control

Comparator can include no treatment, active control, usual care, or where the intervention is in addition to another non-pharmacological intervention (for example, as an add on to exercise rehabilitation) or no comparator.

Context

The intervention may take place in any setting: in the hospital (but not while in the emergency room/critical care unit), outside the hospital, at survivors' home or may start in hospital and continue following discharge from hospital or via telemedicine.

Main outcome(s)

The outcomes are based on the those recommended by the COSCA initiative (1). The primary outcome will be health-related quality of life. Measures of health-related quality of life outcomes will include generic or disease-specific patient reported outcome measures. The outcome measure can be a single-item tool (e.g. 'How would you rate your overall quality of life?') or a multi item tool (examples include 36-item Short Form Health survey and EuroQoL five dimensions questionnaire). For multi component/dimensional outcome measures a subscale which contains health-related quality of life will be favoured over the overall score of the measurement even if the overall score reflects health-related quality of life.

Main secondary outcome: neurological function. Measures of neurological function measure the level of disability after a neurological event. Included measures may primarily test cognitive ability (for example the Mini-mental state examination) or may combine cognitive and physical ability hence measuring global disability (for example the Modified Rankin Scale). Measures may be clinician reported (for example the Cerebral Performance Category or Glasgow Outcome Scale –Extended) or observer reported (for example the Informant Questionnaire on Cognitive Decline in the Elderly, completed by relatives or carers) or patient reported (for example Two-simple questions).

Measures of effect

It has been suggested that outcomes for cardiac arrest survivors evolve over time and survivors should be reassessed at 30-days, 60-days and one-year after arrest (1, 2). Hence, data will be extracted at all time points that are the nearest possible to the recommended follow-up points (1) (survival at 30 days or hospital discharge, three-month follow-up and longest follow up point) to discern if outcomes change over time.

Additional outcome(s)

Secondary outcomes:

1. Survival at 30 days or hospital discharge (if both are reported, survival at 30 days will be favoured over survival at hospital discharge), and one year. Mortality due to any cause, but if proportion due to cardiac cause is available this will be reported.

2. Re-hospitalization (all cause and the proportion due to cardiac cause if available)

3. Serious adverse events: defined as resulting in death or re-hospitalization causing significant disability ,including cardiovascular complications such as cardiac arrest or any arrhythmia with hemodynamic compromise.

4. Non-serious adverse events for example musculoskeletal injury, palpitations, or dizziness.

5. Psychological well-being: measured by patient reported symptoms of anxiety, depression, post-traumatic stress disorder or stress. The outcome measure can be a single-item tool (for example 'How would you rate your overall psychological well-being?') or a multi item tool (for example the Hospital Anxiety and Depression Scale).

6. Fatigue outcomes: measured by patient reported outcomes such as the Fatigue impact scale. Measures may be disease specific or generic and multi-component/dimensional. For multi component/dimensional outcome measures a sub-scale which contains fatigue will be favoured over the overall score of the measurement even if the overall score reflects fatigue.

7. Exercise capacity: measured by aerobic fitness. This will include any objective measure of the ability of the heart and lungs to get oxygen to the muscles where it can be consumed. This could be maximal or peak oxygen consumption. A change of the aerobic fitness could be an increase in peak oxygen consumption (VO2peak) obtained from a maximal cardiopulmonary exercise test or as a decrease in sub-maximal oxygen uptake at a given work load, or a decrease of sub-maximal heart rate at a given work load.

8. Physical capacity: measured by self-reported questionnaires, single item questions or objectives measures for example activity monitors or step counters.

Data extraction (selection and coding)

Selection of studies will be done by merging all search results into the technology platform, Covidence. Duplicates will be removed before two authors (VLJ and MA) will independently screen titles and abstracts followed by full-text screening of potentially eligible studies. Any disagreements will be discussed and resolved with a third review author (JC). For randomised controlled crossover trials data will be handled as it would have been a randomised controlled trial and therefore data will be extracted for baseline and from the assessment of effect from the first period (data from after the cross-over will not be extracted).

A standardised pre-piloted form will be used to extract data from all the included studies.

The following data will be extracted if it is relevant in terms of study design (observational vs randomised controlled studies) by two independent reviewers (VLJ & MA):

1. Source of study and author contact details

2. Study design, study duration, setting and country.

3. Participant characteristics: age, sex, cause of cardiac arrest, place of cardiac arrest, cardiac arrest circumstances, health-status of participants including details of any ongoing cardiac condition (for example myocardial infarction), in hospital interventions and whether they received targeted temperature management and/or an implantable cardioverter defibrillator.

4. Number of groups and number of participants in each study, and study arm.

5. Description and components of rehabilitation intervention and any control, length of intervention, dose and frequency.

6. Theory or mechanism of the study intervention.

7. Which primary and secondary outcomes as defined above are present and time points of outcomes.

8. For each outcome of interest: sample size, estimate of effect and confidence interval; p value and subgroup analyses.

9. Information for assessment of risk of bias.

Any discrepancies in data extraction will be investigated and discussed, then if necessary resolved with a third review author (JC).

Risk of bias (quality) assessment

Two review authors (VLJ & MA) will independently assess the risk of bias in included studies. RoB 2.0 tool for randomised controlled trials ROBINS-I (risk of bias in non-randomised Studies – of Interventions) will be used to assess risk of bias in observational studies.

Risk of bias will be assessed for each outcome within each study. While some items are generic across outcomes, where potential differences may occur (for example between subjective and objective measures), outcomes will be assessed separately and may be judged at a different level of bias within the same study.

Any disagreements between review authors will be discussed and resolved with a third review author (JC).

Strategy for data synthesis

Results from the different study designs will be presented and pooled separately.

We will undertake a meta-analysis where two or more trials are similar enough clinically and statistically for pooling of trials to be appropriate. Where there is high heterogeneity between studies or inappropriate quantitative reporting of outcomes, a narrative synthesis of outcomes from included studies will be provided.

If it is possible to conduct a meta-analysis a random effects meta-analysis will be used given the likely presence of some clinical heterogeneity across studies. Continuous data will be expressed as the mean difference (MD) or standardized mean difference (SMD) and their respective confidence intervals (CI) will be calculated.

For dichotomous outcomes (serious and non-serious adverse events) and for outcomes of observational studies relative risk ratios (RR) along with a CI will be calculated using random effects meta-analysis.

For time to even outcome (survival, re-hospitalization) hazard ratios will be pooled if presented.

Statistical heterogeneity of the study results will be examined using Cochran Q test and quantified with I^2 values and the between study variance I^2. Qualitative assessment of heterogeneity will be assessed by comparing the characteristics of included studies. Assessment of small study bias will be assessed by calculating an Egger's test score and illustrated with a funnel plot. If small study bias is present defined by a positive Egger's test, a metatrim analysis will be conducted.

If the included studies need network meta-analysis to be pooled this will be performed, as described in chapter 16.6.3 of the Cochrane Handbook.

The confidence in estimates of the effects of interventions will be assessed using the Grading of Recommendation, Assessment, Development and Evaluation system (GRADE).

The paper will be reported according to the Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA) guidelines.

Analysis of subgroups or subsets

If possible, we will carry out the following subgroup and stratified analyses to explore heterogeneity of the studies. Location of cardiac arrest (in versus out-of-hospital).

1. Mode of delivery of intervention (supervised vs non-supervised).
2. Provision of intervention (individual vs group based).
3. Content of rehabilitation, single component (for example: exercise-based/education-based/psychological based) vs comprehensive.
4. Received an implantable cardioverter defibrillator vs did not receive an implantable cardioverter defibrillator.
5. Random sequence generation (low/some concerns/high); random sequence concealment (low/some concerns/high).
6. Overall risk of bias (low/some concerns/high).
7. Length of intervention (single session vs 1-6-weeks vs over 6-weeks) 8. Duration of trial follow-up (1-12 weeks vs 13-24 weeks vs over 24 weeks).
9. Setting of trials (single vs multicentre).
10. Continent of publication.
11. Self-reported cognitive ability vs self-reported cognitive and physical ability.

12. Clinician reported cognitive ability vs observer reported vs self-reported.

Meta-regression will be carried out to investigate the effect of continuous variables including age, sex distribution and all sub-group analyses listed above.

Contact details for further information

Vicky Joshi
victoria.louise.joshi@rsyd.dk

Organisational affiliation of the review

Danish Knowledge Centre for Rehabilitation and Palliative Care
http://www.rehpa.dk/

Review team members and their organisational affiliations

Mrs Vicky Joshi. Danish Knowledge Centre for Rehabilitation and Palliative Care
Dr Jan Christensen. Danish Knowledge Centre for Rehabilitation and Palliative Care
Mr Esben Lejsgaard. Danish Knowledge Centre for Rehabilitation and Palliative Care
Professor Ann-Dorthe Zwisler. Danish Knowledge Centre for Rehabilitation and Palliative Care
Professor Rod Taylor. Institute of Health Research, University of Exeter Medical School; Danish Knowledge Centre for Rehabilitation and Palliative Care
Professor Jørgen Feldbæk Nielsen. Aarhus University, Hammel Neurocenter Denmark
Dr Lars Tang. Danish Knowledge Centre for Rehabilitation and Palliative Care

Type and method of review

Intervention, Meta-analysis, Systematic review

Anticipated or actual start date

01 November 2018

Anticipated completion date

31 July 2021

Funding sources/sponsors

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Conflicts of interest

Language

English

Country

Denmark

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Heart Arrest; Humans; Medicine; Survivors

Date of registration in PROSPERO
11 October 2018

Date of first submission
19 September 2018

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
11 October 2018
07 May 2021
12 May 2021
15 May 2021

Supplementary data Table 1. Search Strategy

MEDLINE	
POPULATION	INTERVENTION
heart arrest [MeSH Terms] out-of-hospital cardiac arrest [MeSH Terms] heart arrest [Title/Abstract] heart arrests [Title/Abstract] cardiac arrest [Title/Abstract] cardiac arrests [Title/Abstract] cardiopulmonary arrest [Title/Abstract]	rehabilitation [MeSH Terms] physical medicine [MeSH Terms] rehabilitation nursing [MeSH Terms] exercise [MeSH Terms] social support [MeSH Terms] psychological adaptation [MeSH Terms] cognitive behavior therapy [MeSH Terms] health education [MeSH Terms] aftercare [MeSH Terms] rehabilitation, vocational [MeSH Terms] rehabilitation [Title/Abstract] vocational [Title/Abstract] aftercare [Title/Abstract] telerehabilitation [Title/Abstract] physical medicine [Title/Abstract] exercise [Title/Abstract] exercises [Title/Abstract] physical activity [Title/Abstract] social support [Title/Abstract] psychological adaptation [Title/Abstract]) coping behavior [Title/Abstract]) coping skills [Title/Abstract]) adaptive behavior [Title/Abstract]) cognitive behavior therapy [Title/Abstract] cognitive behavioral therapy [Title/Abstract] cognitive behavior therapies [Title/Abstract] cognitive behavioral therapies [Title/Abstract] cognitive psychotherapy [Title/Abstract]
	cognitive psychotherapies [Title/Abstract] acceptance and commitment therapy [Title/Abstract] mindfulness [Title/Abstract] health education [Title/Abstract])
AMED 1985 to date	
POPULATION	INTERVENTION
(MH “Heart arrest” explode)	(MH "Rehabilitation+") (MH "Physical Medicine") (MH “Rehabilitation nursing”) (MH Exercise+) (MH Support, Psychosocial+)

	(MH Adaptation, Psychological+) (MH Cognitive therapy+) (MH Health education+) (MH After Care)
TI OR AB	TI OR AB
Heart arrests Cardiac arrest Cardiac arrests Cardiopulmonary arrest	Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise Exercises Physical activity Social support psychosocial psychological adaptation coping behavior coping skills adaptive behavio* cognitive behavio#r therap* cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education
CINAHL	
POPULATION	INTERVENTION
(MH "Heart arrest" explode)	(MH "Rehabilitation+") (MH "Physical Medicine") (MH "Rehabilitation nursing") (MH Exercise+) (MH Support, Psychosocial+) (MH Adaptation, Psychological+) (MH Cognitive therapy+) (MH Health education+) (MH After Care)
TI OR AB	TI OR AB
Heart arrests Cardiac arrest Cardiac arrests Cardiopulmonary arrest	Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise

	Exercises Physical activity Social support psychosocial psychological adaptation coping behavior coping skills adaptive behavio* cognitive behavio#r therap* cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education
Embase 1974 to present	
heart arrest Exp out-of-hospital cardiac arrest Exp	Rehabilitation (Exp all) Physical medicine Rehabilitation nursing Exercise Social support Coping behavior Cognitive behavioral therapy Health education
Ti OR Ab Heart arrests Cardiac arrest Cardiac arrests Cardiopulmonary arrest	Ti or Ab Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise Exercises Physical activity Social support psychosocial psychological adaptation coping behavior coping skills adaptive behavio* cognitive behavio#r therap* cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education

PsychINFO 1806 to present	
All fields: Heart arrest Heart arrests Cardiac arrest Cardiac arrests Cardiopulmonary arrest	Subject headings: Rehabilitation Exercise Social support Cognitive therapy Health education Ti or Ab Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise Exercises Physical activity Social support psychosocial psychological adaptation coping behavior coping skills adaptive behavio* cognitive behavio#r therap* cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education
Web of Science	
Heart arrest Heart arrests Cardiac arrest Cardiac arrests Cardiopulmonary arrest <u>Search string</u>: (TS=Topic) TS=(rehabilitation) OR TS=(vocational) OR TS=(aftercare) OR TS=(telerehabilitation) OR TS=("physical medicine") OR TS=(exercise) OR TS=(exercises) OR TS=("physical activity") OR TS=("social support") OR TS=("psychological adaptation") OR TS=("coping behavio*") OR TS=("coping skills") OR TS=("adaptive behavio*") OR TS=("cognitive behavio*	Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise Exercises Physical activity Social support psychosocial psychological adaptation coping behavior coping skills adaptive behavio* cognitive behavio#r therap*

therap*") OR TS=("cognitive psychotherap*") OR TS=("acceptance and commitment therapy") OR TS=(mindfulness) OR TS=("health education") AND TS=("heart arrest") OR TS=("cardiac arrest") OR TS=("heart arrests") OR TS=("cardiac arrests") OR TS=("cardiopulmonary arrest") OR TS=("cardiopulmonary arrests")	cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education
The Cochrane library (SRs and CENTRAL)	
As for Medline but using CENTRAL's search builder syntax.	
International Standard Randomised Controlled Trial Number (ISRCTN)	
Cardiac arrest	
World Health organisation International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov	
(Condition) Cardiac arrest	OR (Other terms) Rehabilitation Vocational Aftercare Telerehabiliation Physical medicine Exercise Physical activity Social support psychosocial psychological adaptation coping behavior cognitive behavio#r therap* cognitive behavio#ral therap* cognitive behavioral therap* cognitive psychotherap* acceptance and commitment therapy mindfulness health education

Sample search matrix:

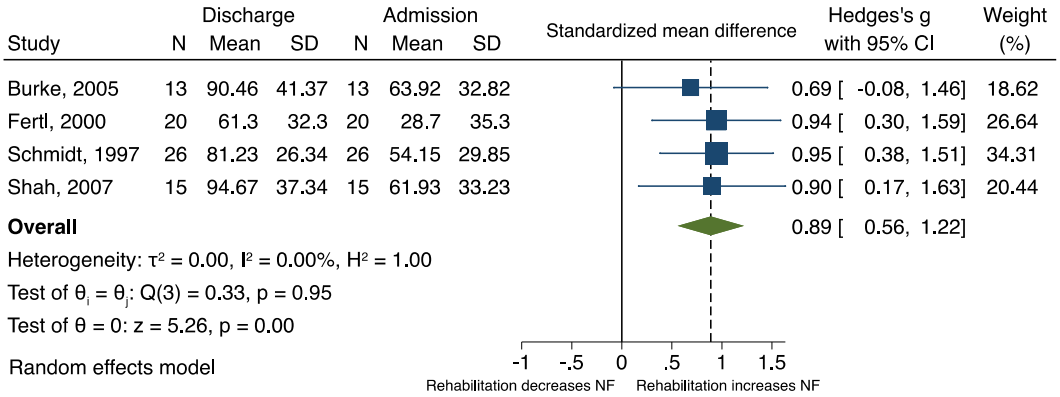
MEDLINE Search matrix:

Search ((rehabilitation[MeSH Terms]) OR physical medicine[MeSH Terms]) OR rehabilitation nursing[MeSH Terms]) OR exercise[MeSH Terms]) OR social support[MeSH Terms]) OR psychological adaptation[MeSH Terms]) OR cognitive behavior therapy[MeSH Terms]) OR health education[MeSH Terms]) OR aftercare[MeSH Terms]) OR rehabilitation, vocational[MeSH Terms]) OR rehabilitation[Title/Abstract]) OR vocational[Title/Abstract]) OR aftercare[Title/Abstract]) OR telerehabilitation[Title/Abstract]) OR physical medicine[Title/Abstract]) OR exercise[Title/Abstract]) OR exercises[Title/Abstract]) OR physical activity[Title/Abstract]) OR social support[Title/Abstract]) OR psychological adaptation[Title/Abstract]) OR coping behaviour[Title/Abstract]) OR coping skills[Title/Abstract]) OR adaptive behavior[Title/Abstract]) OR cognitive behavior therapy[Title/Abstract]) OR cognitive behavioral therapy[Title/Abstract]) OR cognitive behavior therapies[Title/Abstract]) OR cognitive behavioral therapies[Title/Abstract]) OR cognitive psychotherapy[Title/Abstract]) OR cognitive psychotherapies[Title/Abstract]) OR ((acceptance[Title/Abstract] AND commitment therapy[Title/Abstract]))) OR mindfulness[Title/Abstract]) OR health education[Title/Abstract])) AND (((((((heart arrest[MeSH Terms]) OR out of hospital cardiac arrest[MeSH Terms]) OR heart arrest[Title/Abstract]) OR heart arrests[Title/Abstract]) OR cardiac arrest[Title/Abstract]) OR cardiac arrests[Title/Abstract]) OR cardiopulmonary arrest[Title/Abstract])

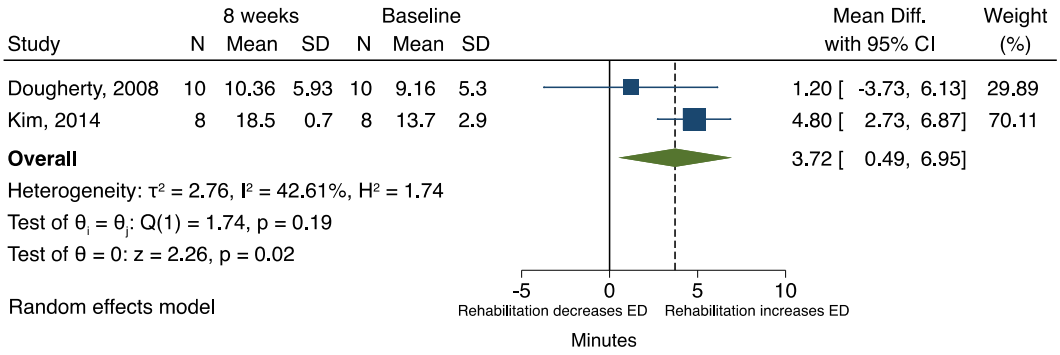
Supplementary data Table 2. Studies excluded at full text stage with reasons

Excluded study	**Reason for exclusion**
Ada, 2018	Conference abstract
Arabia, 2011	Mixed population of people who have suffered a major cardiac event
Baston, 2017	Conference abstract
Berg, 2020	Mixed population of ICDs implanted for primary and secondary prevention and authors did not have separate data on number of cardiac arrest survivors.
Bermejo, 2015	Conference abstract
Boyce, 2017	Outcome data only at baseline
Chanu, 2016	Not survivor of cardiac arrest population
Helmark, 2016	Conference abstract
Choi, 2017	No survivor of cardiac arrest population
Dougherty, 1997	Not an intervention study
Dougherty, 2015	Mixed population of ICDs implanted for primary and secondary prevention and authors did not have separate data on number of cardiac arrest survivors.
Exposito, 2012	Conference abstract
Goldman, 2013	Conference abstract
Harbinson, 2017	Not survivor of cardiac arrest population
Irvine, 2011	Not survivor of cardiac arrest population
Kim, 2017	Not effect study
Ko, 2020	Not survivor of cardiac arrest population
Konh, 2000	Not survivor of cardiac arrest population
Markus, 2017	Not rehabilitation intervention
Mochizuki 2014	Conference abstract
Moroni, 2006	Not survivor of cardiac arrest population
Moulaert, 2016	Economic evaluation
Moulaert, 2011	Study rationale
Moulaert, 2007	Study protocol
Munjal, 2018	Conference abstract
Sears, 2004	Systematic review
Stock, 2019	Not survivor of cardiac arrest population
Takahashi, 2015	Intervention in intensive care unit

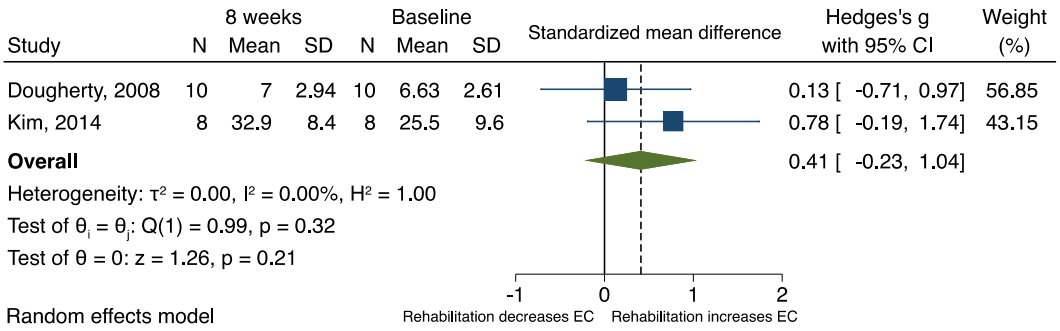
Supplementary data Fig. 1. Forest plot for effect of inpatient rehabilitation for CA-survivors with acquired brain injury on neurological function (NF) between admission and discharge, sensitivity analysis with Howell (2013) removed due to heterogeneity in study population and presence of statistical heterogeneity.



Supplementary data Fig. 2. Forest plot for effect of exercise-based rehabilitation for CA-survivors on exercise duration (ED) (minutes) between baseline and 8 weeks follow-up.



Supplementary data Fig. 3. Forest plot for effect of exercise-based rehabilitation for CA-survivors on exercise capacity (EC) between baseline and 8 weeks follow-up.



Supplementary data Table 3. Summary of findings: HRQoL

Rehabilitation for improving health related quality of life (HRQoL) in survivors of cardiac arrest					
Randomised controlled trials					
Outcome	Standard care	Rehabilitation	Number of participants (studies)	Quality of evidence[a] (GRADE)	Comments
HRQoL Physical component score difference between baseline and 12 months follow-up (0-100 points, higher scores better)	12.8	mean **4.75** points greater compared to standard care	108(2)	++oo Low[b]	
HRQoL Mental component score difference between baseline and 12 months follow-up (0-100, higher scores better)	7.57	mean **3.26** points greater compared to standard care	108(2)	++oo Low[b]	
Prospective observational studies					
HRQoL Physical component score difference between at 6 months follow-up (0-100, higher scores better)	-	mean **20.32** point increase	82(2)	+ooo Very low[c,d]	No comparison arm included in either trial
HRQoL Mental component score at 6 months follow-up (0-100, higher scores better)	-	mean **16.76** point increase	82(2)	+ooo Very low[c]	No comparison arm included in either trial
[a]GRADE Working Group grades of evidence **High quality**: Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality**: We are very uncertain about the estimate.					
Explanations [b]High risk of bias in one of the two studies ('some concerns' with criteria: deviations from intended outcomes and selection of the reported results, 'high risk of bias' with criteria: measurement of the outcome), some indirectness of evidence in one study (intervention aimed at people with new ICD implanted) and due to the serious imprecision in both studies (small number of participants). [c]High risk of bias in one study out of two studies, both studies were observational. [d]Considerable heterogeneity (I^2=90.17%) (point estimates and confidence intervals vary considerably).					

Key: CI: Confidence interval; HRQoL: Health related quality of life; SMD: Standardized mean difference

Supplementary data Table 4. Summary of findings: neurological function

Effect of inpatient rehabilitation on neurological function for survivors of cardiac arrest with acquired brain injury					
All observational studies					
Outcome follow-up	Standard care	Rehabilitation	Number of participants (studies)	Certainty of evidence (GRADE[a])	Comments
Improvement in function between admission and discharge (Functional independence measure and Barthel index)	-	SMD **0.71** effect size (CI 0.45-0.96)	187(5)	+ooo Very Low[d]	No comparison arm included in any included trial
[a]GRADE Working Group grades of evidence **High quality**: Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality**: We are very uncertain about the estimate					
[d]High risk of bias in all studies (multiple domains) and all were observational studies.					

Key: CI: Confidence interval; SMD: Standardized mean difference

Supplementary data 2: Table 1. Characteristics of studies investigating rehabilitation interventions for survivors of cardiac arrest

Study	Title	Population	Rehabilitation intervention	Outcomes		Summary of results
Author, year, country **Study design** **Setting**		**a. Participants** **b. Number of included participants (N)** **c. Age (mean)** **d. Gender (male, %)** **e. Ethnicity (% Caucasian)**	**a. Description** **b. Duration (time period and/or number of sessions)**	**Outcomes of interest**	**Follow-up period**	
Burke, 2005, USA Retrospective chart review Freestanding rehabilitation hospital	Rehabilitation outcomes of cardiac and non-cardiac anoxic brain injury: a single institution experience	a. Acquired brain injury due to cardiac arrest. b. n=13 c. 52.5 d. 54 e. 61	a. Comprehensive, multi-disciplinary inpatient rehabilitation services. b. Admission period mean 69.8 days (SD 59.4)	FIM subscales activities of daily living, mobility, cognition and total	Admission, discharge	Total FIM improved from admission mean 63.92 days (SD 32.82) to mean discharge 90.46 days (SD 41.37).
Cowan, 2001, USA Randomized controlled trial Outpatient clinic	Psychosocial nursing therapy following sudden cardiac arrest: impact on two-year survival.	a. Out-of-hospital cardiac arrest survivors b. n=66 (intervention) n=67 (control) c. NS d. 73 e. 90	a. Three components: 1) physiologic relaxation, 2) Cognitive behavioral therapy and 3) Health education focusing on cardiac risk factors. Delivered by experienced nurses. Control received only the health education component. b. 4 weeks, mean 11 sessions (30 minutes each)	All-cause mortality; Risk of cardiovascular death; Non-Fatal cardiac effects	2 years	Reduction in risk of all-cause mortality for the intervention group was 62%, but this was not statistically significant, (p=0.13). Risk of cardiovascular death was significantly reduced in the intervention group by 86% compared to conventional treatment at two-years follow-up (hazards ratio =0.14; p=0.03; one death in the intervention group due to stroke, six out of seven deaths in control group due cardiac arrest. Confidence intervals for these results were not available).
Dougherty, 2004, 2005, USA Randomized controlled trial Telephone	Short-term efficacy of a telephone intervention by expert nurses after an ICD; Long-Term Outcomes of a Telephone Intervention After an ICD	a. Cardiac arrest survivors with first time ICD implantation for secondary prevention of cardiac arrest b. n=38 (intervention), n=27 (control) c. 63.5 d. 74 e. 91	a. 1) Booklet mailed to study participants on strategies to manage recovery, 2) structured information provided by experienced cardiovascular nurses to improve self-efficacy to deal with illness demands, and to reduce anxiety, through identification of illness related problems and behavioral strategies to manage them including role playing, problem-solving, goal-setting and collaborating on the learning assignment for the coming week. Usual care participants received treatment as usual from their health care providers and standardized hospital-based education about the ICD in the form of a booklet, videotape, or both.	SF-12 Physical + Mental component sub-scale (separate results for other outcomes reported in the paper were not available for CA-survivors)	Baseline, 1, 3, 6, 12 months	Rehabilitation interventions showed no statistical effectiveness on either SF-12 physical or mental subscales at any follow-up point compared to standard care.

			b. First 8 weeks after hospital discharge and ICD implantation (15-20 minute calls, number of calls NS).			
Dougherty, 2008, USA A single group pre-post test design Outpatient group exercise	Aerobic exercise improves fitness and heart rate variability after an ICD	a. Cardiac arrest survivors with first time ICD implantation for secondary prevention of cardiac arrest b. n=10 c. 54.8 d. 90 e. NS	a. Supervised aerobic exercise plus home walking b. 3 days per week for total of 8 weeks (24 sessions) + 1 hour of home walking twice a week.	SF-12 Physical + Mental component sub-scale; State Trait Anxiety Inventory; Center for Epidemiological Studies–Depression Scale; Total exercise time (minutes); Oxygen pulse (VO2/HR); Metabolic equivalent of task; RT3 accelerometer	Baseline, 8 weeks, 6 months	Quality of life (Short Form–12) showed a non-significant improvement in physical and mental sub-scale scores and non-significant reduction in anxiety and depression. Exercise duration, oxygen uptake at anaerobic threshold, and metabolic equivalents were improved after 8 weeks of exercise. There were no lethal cardiac arrhythmias experienced during exercise testing and no participants required cardioversion. There were no sustained ventricular arrhythmias during supervised exercise or home walking sessions in any of the study subjects. SF-12 physical health were sustained at 6 months as well as an increase in daily activity as measured by RT3 accelerometer.
Dougherty, 2019, USA Randomized controlled trial Telephone	Patient plus partner trial: A randomized controlled trial of 2 interventions to improve outcomes after an initial ICD	a. Cardiac arrest survivors with first time ICD implantation for secondary prevention of cardiac arrest b. n=66 c. 62.3 d. 72 e. 94	a. Intervention consisted of 4 elements: 1) Information booklet with strategies for health recovery after ICD implant. 2) Nurse telephone support to improve self-efficacy and problem solve. Components of this support were as per the intervention in Dougherty, 2004, 2005. 3) Pager access to a study nurse 4) an informational video provided by the device company. b. 10 telephone calls over 12 weeks	SF-12 Physical + Mental component sub-scale; State Trait Anxiety Inventory; Patient health questionnaire-9	Baseline, 3, 6, 12 months	All outcomes improved between baseline and 12 months follow-up. No effect sizes available.
Fertl, 2000, Austria Retrospective chart review Inpatient neurological rehabilitation	Neurological rehabilitation of severely disabled cardiac arrest survivors. Part I. Course of post-acute inpatient treatment	a. Out-of-hospital cardiac arrest survivors who suffered anoxic brain injury and required prolonged intensive care treatment b. n=20 c. 47.6 d. 85 e. NS	a. Daily multidisciplinary neurological rehabilitation. Speech therapists and psychologist were available for those needing their service. Admission period mean 84 days (SD 57) (minimum 15 sessions per week of b. physical and occupational therapy)	Barthel Index	Admission + discharge	Mean improvement in Barthel index 3.4 (SD 4.4)

Howell, 2013, Germany Retrospective cohort study Inpatient neuro rehabilitation center	Rehabilitation outcome of anoxic-ischaemic encephalopathy survivors with prolonged disorders of consciousness	a. Cardiac arrest survivors, direct transfer from intensive care unit, all in coma, vegetative state or minimally conscious state b. n=113 c. 55 d. 74 e. NS	a. Daily neurorehabilitation b. Mean 84 days (SD 50)	Glasgow outcome scale; FIM; Coma remission scale	Admission + discharge	Total FIM improved from mean (SD) 18 (0) to 25 (19) points between admission and discharge. 6.2% of patient achieved a good functional outcome defined as Glasgow Outcome Scale 4-5. Coma remission scale improved from mean (SD) change of 9 (5) to 13 (7) points (scale 0-24, higher score indicates better recovery).
Kim, 2014, South Korea Retrospective review of medical records Outpatient hospital-based	Cardiac rehabilitation after acute MI resuscitated from cardiac arrest	a. Cardiac arrest survivors who received successful percutaneous coronary intervention for acute MI b. n= 8 c. 46.8 d. 88 e. NS	a. Cardiac rehabilitation including aerobic exercise, advice on secondary risk factors, diet and lifestyle, advice on medication by a cardiologist. Exercise was continued at home at 60% intensity of the heart rate reserve. b. 6 weeks (3x50-minute per week exercise programs for 6 weeks)	Cardiovascular-related complications during exercise monitoring; Peak oxygen consumption (VO2peak (mL/kg/min)); Exercise duration (minutes)	Baseline + 8 weeks	Significant improvement in exercise capacity. No fatal cardiac complications, such as abnormal ECG, cardiac arrest, death or myocardial infarction observed.
Kim, 2016, USA Prospective, pre-post single group experimental design Telephone	An intervention for cardiac arrest survivors with chronic fatigue: A feasibility study with preliminary outcomes	a. Cardiac arrest survivors at least 3 months post cardiac arrest with chronic fatigue b. n=8 c. 53.2 d. 56 e. 100	a. Energy Conservation and Problem Solving Therapy delivered by an occupational therapist. b. Up to 4 weeks (45 minute sessions twice a week)	Modified Fatigue Impact Scale; Fatigue Severity Scale; Patient Reported Outcomes Measurement Information System-Fatigue scale	Pre-test, post-test (range 3-5 weeks)	Significant decreases on the Modified Fatigue Impact Scale total ($p<0.001$), subscales physical ($p=0.001$) and cognitive ($p = 0.006$) fatigue were observed with small to moderate effect sizes of $r=0.23–0.25$. Change effect sizes were small for the Fatigue Severity Scale ($r=0.11$), Patient Reported Outcomes Measurement Information System-Fatigue scale ($r=0.19$).
Mion, 2019, UK Prospective cohort study In-patient and outpatient clinic	Care After Resuscitation: Implementation of the United Kingdom's First Dedicated Multidisciplinary Follow-Up Program for Survivors of Out-of-Hospital Cardiac Arrest	a. Cardiac arrest survivors with good neurological recovery, Cerebral Performance Scale Category 1-2 n=19 b. 61 c. 84 d. NS e.	a. Inpatient information provided via leaflets, bespoke video and direction to a social media website for cardiac arrest survivors and caregivers; telephone and clinic follow-up with ICU nurse, cardiologist and psychiatrist. If psychological issues were identified, patients and caregivers were offered further interventions. b. In-hospital + clinic follow-up at: 8-weeks, 6-months and 12-months post-hospital discharge.	SF-36 physical and mental domain scores	Baseline, 6 months	Significant improvement in all domains of Short-form 36 (except general health) at 6 months.
Moulaert, 2015, The Netherlands	Early neurologically-focused follow-up after cardiac arrest improves quality of	a. Survivors of cardiac arrest at least two weeks after event, living at home b. n=97 (Intervention) n=98 (Control)	a. Intervention for survivors of cardiac arrest and their caregivers provided by specialist nurses including 1. Screening for cognitive and emotional problems. 2. Provision of support and information on cardiac arrest	SF-36 domain scores; EuroQol Visual Analogue Scale; Cognitive log	Baseline, 3 + 12 months	At 12 months there were significant differences in estimated means in favour of the intervention group on three domains of quality of life on the SF-36: Role Emotional

Multicenter randomised controlled trial At clinic or at home	life at one year: A randomised controlled trial	c. 60 (Intervention) 69 (Control) d. 83 (Intervention) 84 (Control) e. NS	and possible neurological consequences. 3. Promotion of self-management strategies. 4. Referral to specialized care if indicated. Control group received standard care with potential for referral to cardiac rehabilitation. b. 1-6 individual sessions	Adult Memory and Information processing battery task A; Verbal fluency; Trail making Test A; Trail making Test B; Paragraph recall direct; Paragraph recall delayed; Cognitive Failures Questionnaire; Hospital Anxiety and Depression Scale (anxiety and depression sub-scales and total); Impact of Event Scale		(p=0.006), Mental Health (p=0.003) and General Health (p=0.010). No significant effectiveness on cognitive tests compared to standard care at any follow-up point. The intervention group scored significantly better on overall emotional state (anxiety and depression) and anxiety at one year.
Schmidt, 1997, USA Retrospective chart review In-patient rehabilitation unit	Anoxic encephalopathy: Outcome after inpatient rehabilitation	a. Patients admitted to a rehabilitation unit with cerebral anoxia (15 due to cardiac arrest and 11 for other causes) b. n=26 c. 58 d. 66 e. NS	a. In-patient rehabilitation unit b. Admission period mean 59.5 days (SD 41.4)	FIM	Admission + discharge	Total FIM improved from admission mean 54.15 (SD 29.85) to discharge mean 81.23 (SD 26.34).
Shah, 2007, USA Retrospective chart review Freestanding rehabilitation hospital	A comparison of functional outcomes in hypoxia and traumatic brain injury: A pilot study	a. Survivors of cardiac arrest who suffered anoxic brain injury b. n=15 c. 50.8 d. 60 e. 87	a. In-patient rehabilitation b. Mean 61.2 days (SD 68.4)	FIM subscales activities of daily living, mobility, cognition and total	Admission + discharge	Total FIM improved from admission mean 61.93 (SD 33.23) to discharge mean 94.67 (SD 37.34)
Tazopoulou, 2016, France Observational single cohort study Residential care	Rehabilitation following cerebral anoxia: An assessment of 27 patients	a. Adults with cerebral anoxia in residential care (11 due to cardiac arrest, 9 due to other cause) b. n=20 c. 46 d. 70 e. NS	a. Psychotherapy, support group, physical activities and cultural and/or artistic activities. Participants could choose to be in all or some of the activities. b. 2-months	Glasgow outcome score extended; Bermont Vost Alexithymia questionnaire; Patient Competency Rating scale (agnosia); Quality of Life After Brain Injury questionnaire; Barrow Neurological Institute screen of higher cerebral functions; Hospital Anxiety and Depression scale	Baseline, 2 + 4 months	Quality-of-life was significantly improved between baseline and intervention end at two months. No change found in neurological function or anxiety and depression.

ICD: Implantable Cardioverter-Defibrillator; FIM: Functional Independence Measure; NS: Not stated; SF: Short form health survey