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Resistance training for rehabilitation after burn injury: A systematic literature review and meta-analysis

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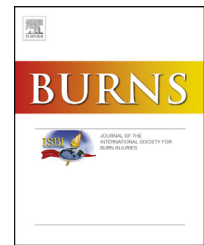
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Review

Resistance training for rehabilitation after burn injury: A systematic literature review & meta-analysis

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ABSTRACT

Background/aim: Resistance training is beneficial for rehabilitation in many clinical conditions, though this has not been systematically reviewed in burns. The objective was to determine the effectiveness of resistance training on muscle strength, lean mass, function, quality of life and pain, in children and adults after burn injury.

Methods: Medline & EMBASE, PubMed, CINAHL and CENTRAL were searched from inception to October 2016. Studies were identified that implemented resistance training in rehabilitation. Data were combined and included in meta-analyses for muscle strength and lean mass. Otherwise, narrative analysis was completed. The quality of evidence for each outcome was summarised and rated using the GRADE framework.

Results: Eleven studies matched our inclusion criteria. Primary analysis did not demonstrate significant improvements for increasing muscle strength (SMD 0.74, 95% CI -0.02 to 1.50, $p=0.06$). Sensitivity analysis to correct an apparent anomaly in published data suggested a positive effect (SMD 0.37, 95% CI 0.08-0.65, $p=0.01$). Psychological quality of life demonstrated benefit from training (MD=25.3, 95% CI 3.94-49.7). All studies were rated as having high risk of bias. The quality of the evidence was rated as low or very low.

Conclusion: Further research with robust methodology is recommended to assess the potential benefit suggested in this review.

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1. Introduction

People recovering from a burn injury will experience a range of challenges throughout their recovery. It has been reported that physical dysfunction and quality of life continue to be adversely affected up to three years after the initial burn injury [1-3]. Survivors are also challenged by long term reductions of muscle mass and strength [4-8], which can limit their ability to perform activities of daily living and participate in physical activity. Whilst a traumatic injury such as a burn

will instigate this catabolic processes, bed rest and inactivity have been shown to amplify catabolism of skeletal muscle [9]. In these circumstances, it would appear that early and intensive rehabilitation likely matters to an individual's physiological profile and functional recovery.

The aim of rehabilitation is ultimately the return of a person's physical capability and independence. In burns, modes of rehabilitation vary widely between facilities, as no evidence based consensus on best practice rehabilitation has been established. The American College of Sports Medicine recommend resistance training (RT) as a mode of exercise to

promote several health benefits, including improvements in the muscle mass and strength of healthy adults [10]. Similar recommendations have also been made for children and adolescents [11]. Resistance training, where muscles are required to contract against an opposing load, has been shown to be a beneficial form of rehabilitation in clinical populations prone to muscle wasting, providing stimuli to increase protein synthesis and muscle mass. This has been demonstrated in conditions such as HIV, cancer, rheumatoid arthritis, chronic renal impairment and bed rest [12-14]. In trauma populations, RT guidelines have been developed in spinal cord injury with modifications specific to the nature of that injury and recommendations for exercise have been published in burn injury [15].

Evidence relating to the efficacy of RT as a mode of exercise after burn injury to improve a patient's outcomes has not been systematically reviewed. Neither has it been established as a routine practice for recovery and rehabilitation after a burn injury. This review aimed to evaluate the effectiveness of RT in children and adults rehabilitating from burn injury. Specifically, we were interested in the effect of RT on muscle strength, lean body mass, physical function, quality of life and pain. The safety profile of RT in this population was also examined.

2. Methods

The protocol for this review was registered in the PROSPERO International prospective register of systematic reviews (registration number CRD42015024527).

2.1. Inclusion criteria

2.1.1. Types of studies

Randomised and non-randomized controlled trials were included to ensure a thorough evaluation of the effects of the intervention. We included studies where RT was compared to usual rehabilitation care or any rehabilitation activity that did not include RT. Studies where there was no comparison to a burned patient group were excluded. We included only studies available in English that had been published in full.

2.1.2. Types of participants

Studies of children and adults who experience a burn injury were included in this review. No limits have been placed on the extent or agent of the burn injury, the setting in which the RT occurred or the time after injury in which training commenced. Participants in studies investigating the effect of a pharmacological agent in conjunction with RT were excluded, unless the study design enabled us to estimate the unique effect of RT.

2.1.3. Types of interventions

Only studies which performed RT to recognised principles of the American College of Sports Medicine were included [10]. The parameters of RT for inclusion were: a minimum of two RT sessions per week, training at an intensity of at least 40% of a one-repetition maximum for at least two sets of eight repetitions per individual exercise. A minimum of two weeks of RT were required for inclusion as improvements in muscle

mass have been noted to occur with two weeks of RT [16]. Studies that include RT as a standalone treatment as well as those that use RT as part of a multimodal treatment regimen were considered. We included trials that compared RT with no treatment or another active treatment other than RT.

2.1.4. Outcome measures of interest

The outcomes of interest were: muscle strength, lean body mass, physical function, quality of life and pain. The occurrence of any adverse events from the intervention was also assessed.

2.2. Search strategy

A sensitive search strategy was developed to identify publications relevant to this review. To identify relevant articles the following databases were searched from inception to October 2016: Medline, EMBASE, PubMed, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL). In addition to the electronic searches, reference lists of all included studies and review articles relevant to the topic were checked. The references of potential papers retrieved were examined to identify any additional papers not captured through the initial search strategy. Abstracts from burns conferences (International Society for Burn Injury, American Burn Association and Australian and New Zealand Burn Association) were also checked to identify papers which may not have been identified through the initial search strategy. We attempted to communicate with study authors when additional information or where clarification of study procedure or data were required.

2.3. Selection of studies

Two authors (PG & TG) independently reviewed the titles generated by the literature search. Relevant abstracts were independently assessed by the same two authors. Full text reports were obtained for further assessment against our inclusion criteria. In the event of disagreement, discussion between the two authors occurred to achieve consensus. Where consensus was not reached, a third reviewer (DE) was used to independently assess the study to determine inclusion.

2.4. Data extraction and management

One author (PG) extracted all data from the included studies using a standardised extraction form. These data were checked and confirmed by two other authors independently of each other (BW & DE). Where differences in extraction existed, a plan was made to review the study and discuss to achieve consensus. The following data were extracted:

- Participant demographic details: number of participants recruited, withdrawals, loss to follow up, age and total burn surface area (TBSA).
- Intervention characteristics: time from injury to commencement of training, location of training, mode of training, volume of training, intensity of training and control group treatments.

- Outcome assessments: muscle strength, lean body mass, function, quality of life, pain and adverse events.
- Information pertaining to the assessment of risk of bias.

Where multiple longitudinal assessments were performed in a study, data provided at the end of the intervention period were used for quantitative analysis. A narrative description was undertaken of data from other time points.

Two studies investigated the use of RT in combination with a pharmacological agent: Oxandralone and growth hormone [17,18]. Only data from groups who did not receive a pharmacological agent as a co-intervention to RT were used in this review.

2.5. Assessment of risk of bias

Included studies were assessed using a risk of bias tool adapted from the Cochrane Handbook for Systematic Reviews of Interventions [19]. The selection of items and operational criteria appropriate to this clinical area for each item were agreed upon by the study team *a priori*. Non-randomised comparison studies were assessed on the same criteria as

RCT's. The tool assessed the following categories as being at high, low or unclear risk of bias: sequence generation, allocation concealment, blinding (participants, therapists and outcome assessor), incomplete outcome data, selective outcome reporting and other biases.

For individual items, where insufficient information was provided by study authors, risk of bias was determined to be "unclear". Where one or more items were deemed as high risk, the study was given an overall rating of "high risk". These assessments were undertaken by the authors as per the data extraction processes. To assess publication bias, visual inspection of funnel plots was planned but due to insufficient data, was not undertaken.

Where studies utilised self-report assessment, the participant was deemed to be the assessor. In this circumstance, low risk of bias can only be given for blinding of outcome assessment where the participant is adequately blinded to their group allocation. This was relevant to outcomes assessed by patient reported surveys for quality of life and function.

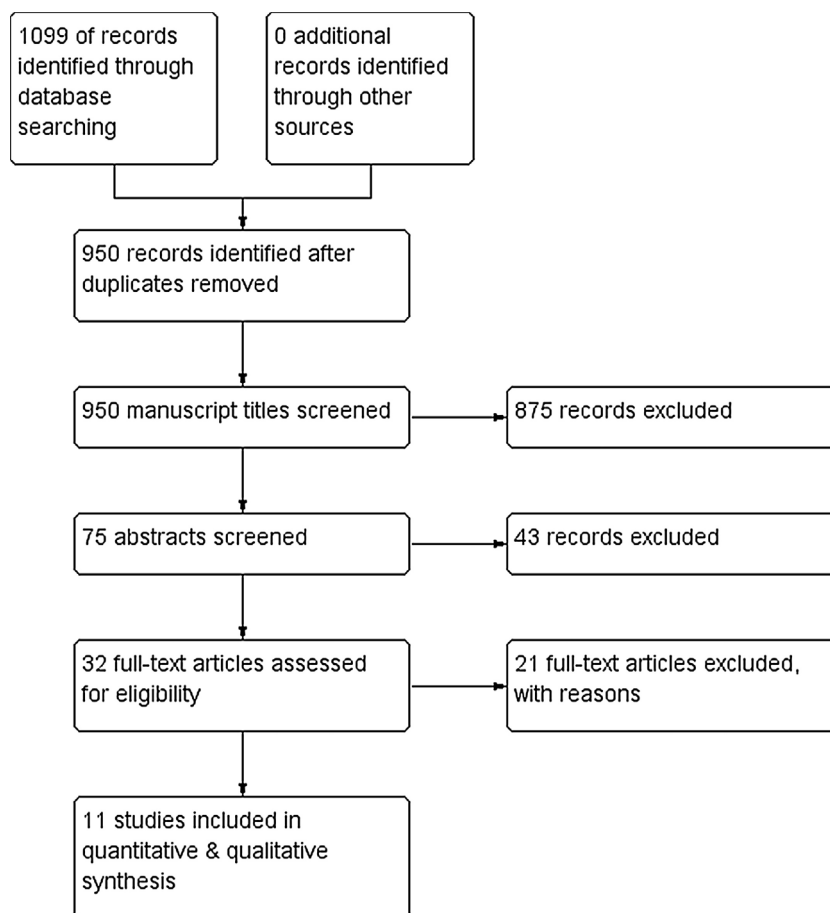


Fig. 1 – Flow of studies through review process.

Table 1 – Characteristics of included studies.

Author	Country	Study design	Sample size	Age (mean±SD) years	TBSA (mean±SD) %
Al-Mousawi et al. [22]	USA	RCT 12 weeks supervised training vs. no supervised training	Exercise=11 Control=10	Exercise=12.2±3.2 Control=13.7±3.6	Exercise=61±13 Control=56±15
Cucuzzo et al. [23]	USA	RCT 12 weeks supervised training vs. no supervised training	Exercise=11 Control=10	Exercise=11.9±1.2 Control=9.2±1.4	Exercise=62±15.2 Control=57.1±13.3
Ebid et al. [7]	Egypt	RCT 12 weeks supervised training vs. no supervised training	Exercise=20 Control=20	Exercise=24.6±5.3 Control=27.3±8.6	Exercise=46.5±3.1 Control=44.5±6.5
Ebid et al. [21]	Egypt	RCT 12 weeks supervised training vs. no supervised training	Exercise=18 Control=19	Exercise=13.4±1.2 Control=13.6±1.1	Exercise=42.1±3.1 Control=42.4±3.1
Hardee et al. [28]	USA	RCT 12 weeks supervised training vs. no supervised training	Exercise=24 Control=23 Withdrawals=4 (2 from both groups)	Exercise=13±4.9 Control=13±4.8	Exercise=59±9.8 Control=60±14.4
Mowafy et al. [24]	Egypt	Comparison trial 12 weeks supervised training vs. no supervised training	Exercise=15 Control=15	Unknown	Unknown
Paratz et al. [25]	Australia	Non-randomised trial 6 weeks supervised training vs. no supervised training	Exercise=16 Control=14 Withdrawals=4 (2 from both groups)	Exercise=30.4±10.1 Control=42.4±14.6	Exercise=47±13.6 Control=29.9±8.9
Przkora et al. [18]	USA	RCT 12 weeks supervised training vs. no supervised training. Testing Oxandrolone or Placebo ±Exercise	Exercise (OXEX)=14 Exercise (PLEX)=17 Control (OX)=9 Control (PL)=11	OXEX=12.1±2.9 PLEX=10.9±3.7 OX=11.8±3.3 PL=11.8±3.3	OXEX=52.1±12.7 PLEX=55.6±14.8 OX=54.7±11.7 PL=53.4±10.3
Suman et al. [27]	USA	RCT 12 weeks supervised training vs. no supervised training	Exercise=19 Control=16	Exercise=10.5±4.0 Control=11±4.8	Exercise=59.4±14.4 Control=58±17.7
Suman et al. [17]	USA	RCT 12 weeks supervised training vs. no supervised training. Testing use of Growth Hormone or Saline placebo ±Exercise.	Exercise (GHGX)=10 Exercise (SALEX)=13 Control (GH)=10 Control (SAL)=11 Withdrawals=25	GHGX=11±2.5 SALEX=10.5±2.5 GH=11.5±5.1 SAL=10.8±2.3	GHGX=60.3±6 SALEX=58.5±10.1 GH=53.4±10.3 SAL=59.4±14.4
Suman and Herndon [26]	USA	RCT 12 weeks supervised training vs. no supervised training	Exercise=11 Control=9	Exercise=11.8±4.9 Control=13.4±5.4	Exercise=61±6.6 Control=56±6

Table 2 – Exercise prescription characteristics of included studies.

Al-Mousawi et al. [22]

Interventions	<p>Hospital Based Exercise Group:</p> <p>Time to begin intervention: 6 months after burn Location: Hospital/Rehab Centre Mode: Isotonic Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM Volume: Week 1: familiarisation, Week 2-6: 4-10 repetitions, Week 7-12: 8-12 repetitions Rest: Not documented Frequency: 3× per week Duration: 12 weeks Additional: Aerobic training 30min 3× per week</p> <p>Standard of Care Group:</p> <p>Home based programme as instructed by the Physiotherapy and Occupational Therapy staff intended to be performed for 1 hour, twice daily. No supervised exercise therapy was undertaken</p>
Outcomes	Muscle strength: Isokinetic peak torque (Nm) at 150°/s for concentric knee extension
Notes	<p>Lean mass: DXA scanning of whole body (kg)</p> <p>Two participants in each group were unable to undergo strength testing</p> <p>One participant in intervention group had 5% loss in lean body mass after intervention</p>

Cucuzzo et al. [23]

Interventions	<p>In-House Exercise Programme Study Group:</p> <p>Time to begin intervention: 6 months after burn Location: Hospital Wellness Centre Mode: Isotonic, isometric & isokinetic Intensity: Phase 1: 50% 3RM, Phase 2: 70-85% 3RM Volume: Phase 1: 4-10 repetitions, Phase 2: 8-15 repetitions Volume increased 10-20% each week Rest: Not documented Frequency: 3× per week Duration: 12 weeks Additional: Aerobic exercise 20min 3× per week</p> <p>Home Group:</p> <p>No prescribed or supervised exercise training Patients were referred to local outpatient facility for ongoing therapy. The number of appointments attended was not standardised across centres. Did not train with weights but were permitted to continue daily activities</p>
Outcomes	Muscle strength: 3 repetition maximum for knee extension, knee flexion, elbow flexion, elbow extension, and forearm (anatomical movement not clarified) strength. Function: 6min walk test to assess distance walked.
Notes	Strength training was stated to focus on overloading primarily “key” muscle groups “namely knee extensor and elbow flexors”

Ebid et al. [7]

Interventions	<p>Isokinetic Group:</p> <p>Time to begin intervention: 6 months after burn Location: Clinic Mode: Isokinetic @ 150°/s Intensity: 60% average peak torque Session 1-5: 1-5 sets, Sessions 6-24: 6 sets, Sessions 25-36: 10 sets Volume: 10 repetitions Rest: Not documented Frequency: 3× per week Duration: 12 weeks Additional: Aerobic training and stretches</p> <p>No Exercise Group:</p> <p>Performed a prescribed home exercise programme including: range of motion exercises, stretching, splinting, massage, functional activities, ambulation and activities of daily living No supervised isokinetic exercise was performed</p>
Outcomes	Muscle strength: Isokinetic muscle peak torque at 150°/s for knee extensors and knee flexors Function: Gait speed assessment in metres per minute

Ebid et al. [21]

Interventions	<p>Isokinetic Group:</p> <p>Time to begin intervention: at hospital discharge Location: Clinic Mode: Isokinetic @ 150°/s</p>
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Intensity: 50% average peak torque
 Session 1-5: 1-5 sets, Sessions 6-24: 6 sets, Sessions 25-36: 10 sets
 Volume: 10 repetitions
 Rest: Not documented
 Frequency: 3× per week
 Duration: 12 weeks
 Additional exercise: Stretching & walking

Control Group:

Home based stretching and range of motion programme. Also completed an unquantified walking programme 3 times per week

Outcomes Muscle strength: Isokinetic muscle peak torque at 150°/s for knee extensor muscle group
 Lean Mass: Circumferential measures of quadriceps size

Hardee et al. [28]

Interventions

RET (intervention) Group:

Time to begin intervention: discharge from acute hospital
 Location: In hospital rehabilitation
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: 4-10 reps, weeks 7-12: 8-12 repetitions
 Rest: -
 Frequency: 3× per week
 Duration: 12 weeks
 Additional: Aerobic training 20-40min @ 70-85% VO₂ peak

SOC (control) Group:

Prescribed a home based programme of stretching & mobility
 No supervised exercise training

Outcomes Strength: Isokinetic peak torque 150 deg/sec for knee extensors
 Lean body mass (kg): DXA scanning for the whole body, trunk, legs and arms

Notes Muscle strength was only assessed after the intervention "because of medical limitations such as impaired mobility and incomplete wound closure at the time of discharge"

Mowafy et al. [24]

Interventions

Intervention Group:

Unknown time from burn to commence intervention
 Location: Facility
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: weeks 2-6: 4-10 reps, weeks 7-12: 8-12 repetitions
 Rest: Unknown
 Frequency: 3× per week
 Duration: 12 weeks
 Additional: Aerobic training 30min @ 70-75% VO₂ peak

Control Group:

Prescribed a home based programme of splinting, stretching, ROM exercises, strength (non-progressive) exercises, scar management

No supervised exercise training

Outcomes Lean body mass (kg/M²): calculation of fat mass subtracted from total body mass

Paratz et al. [25]

Interventions

Exercise Group:

Time to begin intervention: after final grafting procedure
 Mode: Isotonic
 Intensity: Week 1: 60% 3RM
 Volume: Increased 5-10% weekly
 Rest: Not documented
 Frequency: 3× per week
 Duration: 6 weeks supervised. After completion patients were encouraged to continue exercise but unsupervised
 Additional: Stretching programme. Aerobic exercise @ 80% HRpeak 3× per week
 Strength exercises included hand strengthening using mechanical device, foam or putty

Self-Management Group:

Prescribed a home based stretching programme
 No supervised exercise training undertaken

Outcomes Muscle strength: 3 repetition maximum & grip strength dynamometry
 Function: Quick-DASH & LEFS surveys (patient reported)

Notes Quality of life: Burn Specific Health Scale- Abbreviated (patient reported)
 Patients were reviewed monthly in outpatient clinics and reported exercise participation to therapists

(continued on next page)

Przkora et al. [18]

Interventions

Intervention Group (PLEX Group):

Time to begin intervention: 6 months after burn
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: Week 1: 3 × 4-10 reps, week 2-6: 3 × 4-10 reps, week 7-12: 3 × 8-12 reps
 Rest: ~1min
 Frequency: 3 × per week
 Duration: 12 weeks
 Additional:
 Aerobic training 5 × per week 20-40min @ 70-85% VO₂ peak.
 1 hour Physiotherapy daily – ROM and stretches

Control Group (PL Group):

Home based exercise programme including stretches, positioning and ROM
 No formal exercise training

Outcomes

Muscle strength: Isokinetic knee extension strength (Nm) at 150°/s
 Lean mass: DXA scanning of whole body and trunk (kg)
 Fitness: VO₂

Notes

Only data from non-pharmacologically treated participants were included in this review

Suman et al. [27]

Interventions

Supervised Exercise Group (REx):

Time to begin intervention: 6 months after burn
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: Weeks 2-6: 4-10 reps, weeks 7-12: 8-12 repetitions
 Rest: Not documented
 Frequency: 3 × per week
 Duration: 12 weeks
 Additional: Aerobic training 20-40min @ 70-85% VO₂ peak

Non-exercising Group (R):

Home based Physiotherapy and Occupational therapy programme was provided

Outcomes

Muscle strength: Isometric knee extension
 Muscle strength: Isokinetic knee extension 90°/s, average power & total work
 Lean mass: DXA scanning of whole body, trunk, leg and arm
 Fitness: VO₂

Suman et al. [17]

Interventions

Intervention group (SALEx group):

Time to begin intervention: 6 months after burn
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: Weeks 2-6: 4-10 reps, weeks 7-12: 8-12 repetitions
 Rest: 1min
 Frequency: 3 × per week
 Duration: 12 weeks
 Additional: Aerobic training 20-40min @ 70-85% VO₂ peak

Control Group (SAL group):

Home based Physiotherapy and Occupational therapy programme was provided for non-exercise groups

Outcomes

Muscle strength: Isokinetic knee extension strength at 150°/s
 Lean mass: DXA scanning for whole body, trunk, leg and arm
 Fitness: VO₂

Notes

Only data from non-pharmacologically treated participants were included in this review

Suman and Herndon [26]

Interventions

Exercise Group:

Time to begin intervention: 6 months after burn
 Mode: Isotonic
 Intensity: Week 1: 50-60% 3RM, Week 2-6: 70-75% 3RM, Week 7-12: 80-85% 3RM
 Volume: Weeks 2-6: 4-10 reps, weeks 7-12: 8-12 repetitions
 Rest: Not documented
 Frequency: 3 × per week
 Duration: 12 weeks
 Additional: Aerobic training 20-40min @ 70-85% VO₂ peak

No Exercise Group:

Nil formal training. 2h of therapy PT & OT daily

Outcomes	Muscle strength: Isokinetic knee extension at 150°/s. Detraining assessed at 12 weeks after training
period	Lean mass: DXA scanning of whole body (kg)
Notes	Growth hormone given to 3 control group children as part of another study

2.6. Data synthesis

Results from clinically homogeneous trials were combined using a random effects meta-analysis with Review Manager (RevMan) v5.3 where adequate data existed to support this. Estimates of effect were calculated and are presented for each outcome as mean differences (MD) and 95% CIs where measurement tools were identical, or, standardised mean differences (SMD) and 95% CIs where tools were different. Where only standard error was provided, this was converted to standard deviation (SD) using an in-built calculator within RevMan. Data were summarized in forest plots. Where inadequate data was available for meta-analysis, results were presented as a narrative synthesis with mean difference and 95% confidence intervals calculated from the study data using RevMan.

The overall quality of evidence for each outcome measure was summarised and rated using the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) framework and approach [20]. Strength of the evidence for each outcome was considered against the following factors: design limitations (downgrade if >25% of the participants were from studies with a high risk of bias), inconsistency (downgrade once if heterogeneity was statistically significant and $I^2 \geq 50\%$ or when reported treatment effects were in opposite directions), imprecision (downgrade once if, for continuous data, the number of participants was below 400), indirectness (downgrade once for direct evidence if >50% of participants were outside of the target group) and publication bias (downgrade once for direct evidence of publication bias). Single studies with fewer than 400 participants were considered both inconsistent and imprecise. These ratings were completed by one author (PG), then independently checked and confirmed by a second co-author (BW).

2.7. Assessment of heterogeneity

Statistical significance of heterogeneity was assessed using the Chi² test and deemed significant where the p-value <0.05. The amount of heterogeneity was estimated using the I² test. Where heterogeneity was deemed to exist ($I^2 \geq 50\%$), we explored pre-planned, age based sub group analyses for each of the outcome measures. Due to lack of variation in study's populations, we were unable to perform other planned sub group analyses. These included burn injury factors (TBSA $\geq 15\%$ or <15% and burn agent), intervention characteristics (intensity of prescription $\geq 70\%$ of 1 repetition max or <70%) and duration of intervention (≥ 6 weeks or <6 weeks).

2.8. Sensitivity analysis

A *post-hoc* sensitivity analysis was carried out for the muscle strength outcome. An imputed SD was used for two studies

Ebid et al. [7,21] as we believed the SDs provided in the studies were miscalculated. Contact with the primary author was attempted to request further clarification, but a reply was not forthcoming.

3. Results

3.1. Characteristics of included studies

The flow of studies through this review can be viewed in Fig. 1. We identified 11 studies (n=325) that complied with the selection criteria and were included in this review [7,17,18, 21-28] (Table 1).

Nine studies [17,18,21-24,26-28] included only paediatric burn patients, whilst two studies [7,25] were from adult populations. All studies chose to include only patients with major burn injuries. The range of mean TBSA values across all included studies was 29.9-62% TBSA. Resistance training was commenced at various time points ranging from final skin grafting and healing, to 6 months after the initial burn injury (see Table 2).

Resistance training was undertaken using free weights and cable weights for all studies except two studies by Ebid et al. [7,22] where training was undertaken with an isokinetic dynamometer. The intensity of training progressed from 60% of repetition maximum (RM) up to 85% RM in training protocols using free and cable weights. In studies using the isokinetic dynamometer, the initial intensity was set at 50-60% of average torque. Training occurred three times per week for the duration of 6 weeks in Paratz et al. [25] and 12 weeks in all other studies (see Table 2).

We excluded 24 other studies for not meeting our inclusion criteria. Reasons for exclusion were: comparisons made to non-burned participants [29-31]; investigated outcomes not appropriate to this review [32-35]; review articles [15,36-38]; not assessing RT as an intervention [39-42]; inadequate amount of RT performed [43]; control group participating in RT [44-48]; no English translation available [49]; unable to acquire study manuscript [50]; and results which had been previously reported in other individual trials [51].

3.2. Risk of bias in included studies

The results of our risk of bias assessment are displayed in detail in Table 3 and Fig. 2.

3.2.1. Allocation (selection bias)

Only two studies [7,21] described their process for allocation and concealment adequately to be assessed as low risk of bias, whilst one study [25] was rated as having a high risk. Concealment of allocation was also rated low risk for two studies [7,21] and high risk for one [25].

Table 3 – Risk of bias summary of included studies.

Al-Mousawi et al. [22]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No comment of sequence generation details
Allocation concealment (selection bias)	Unclear	No detail provided of concealment
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group
Blinding of outcome assessment (detection bias)	Unclear	No blinding of therapist to allocation & treatment
Incomplete outcome data (attrition bias)	Low	No detail provided by authors
Selective reporting (reporting bias)	Low	No drop out
Other bias	High	Nil
		No baseline comparison for primary outcome
		Randomisation occurs months prior to commencement of intervention
		No between-group comparison of baseline for primary outcome was provided
Cucuzzo et al. [23]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No comment on sequence generation process
Allocation concealment (selection bias)	Unclear	No detail of concealment
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group
Blinding of outcome assessment (detection bias)	Unclear	No blinding of therapist to allocation & treatment
Incomplete outcome data (attrition bias)	Low	No detail provided by authors
Selective reporting (reporting bias)	Low	No drop out
Other bias	Low	Within and between group outcomes discussed
Ebid et al. [7]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Low	Random sequence generator in Excel computer program
Allocation concealment (selection bias)	Low	Password protected allocation
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group
Blinding of outcome assessment (detection bias)	Unclear	No blinding of therapist to allocation & treatment
Incomplete outcome data (attrition bias)	Low	Likely that same therapist performed all assessments & treatments
Selective reporting (reporting bias)	Low	No drop out reported
Other bias	Low	Nil
Ebid et al. [21]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Low	Allocation randomised through use of opaque envelopes prepared individually
Allocation concealment (selection bias)	Low	Registration clerk performed allocation procedures
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group
Blinding of outcome assessment (detection bias)	Low	No blinding of therapist to allocation & treatment
Incomplete outcome data (attrition bias)	Low	Stated that assessors were blinded to treatment allocation
Selective reporting (reporting bias)	Low	4/37 participants drop out (~11%)
Other bias	Low	Nil
Hardee et al. [28]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail of sequence generation
Allocation concealment (selection bias)	Unclear	No detail of concealment
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group
Blinding of outcome assessment (detection bias)	Unclear	No blinding of therapist to allocation & treatment
Incomplete outcome data (attrition bias)	Low	No detail on blinding of allocation provided
Selective reporting (reporting bias)	Low	No drop out recorded
Other bias	High	Nil
		No between group comparison of baseline muscle strength for primary outcome was provided

Table 3 (continued)

Mowafy et al. [24]		
Bias	Rating	Support for judgement
Mowafy et al. [24]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail of sequence generation
Allocation concealment (selection bias)	Unclear	No detail of concealment
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group No blinding of therapist to allocation & treatment
Blinding of outcome assessment (detection bias)	Unclear	No detail on blinding of allocation provided
Incomplete outcome data (attrition bias)	High	No information provided of drop-out rate
Selective reporting (reporting bias)	High	No between group analyses
Other bias	High	No baseline assessment or comparison provided for burns severity or patient demographics No between group comparison of baseline for primary outcome was provided
Paratz et al. [25]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	High	Allocation not randomised
Allocation concealment (selection bias)	High	City dwelling patients allocated to intervention group and rural patient to control group
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group No blinding of therapist to allocation & treatment
Blinding of outcome assessment (detection bias)	High	Participants not blind to allocation, therefore where self-assessment is required (Quick-DASH, LEFS, BSHS-A), blinding not possible
Incomplete outcome data (attrition bias)	Low	4/30 (~13%) removed or withdrawn
Selective reporting (reporting bias)	Low	Nil
Other bias	Low	
Przkora et al. [18]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail provided about randomisation
Allocation concealment (selection bias)	Unclear	No information provided
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group No blinding of therapist to treatment or allocation described
Blinding of outcome assessment (detection bias)	Unclear	No information provided
Incomplete outcome data (attrition bias)	Low	No dropout reported
Selective reporting (reporting bias)	Low	
Other bias	High	Randomisation occurs months prior to commencement of intervention No between-group comparison of baseline for primary outcome was provided
Suman et al. [27]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail provided on methods for allocation
Allocation concealment (selection bias)	Unclear	No detail provided
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group No blinding of therapist to treatment or allocation described
Blinding of outcome assessment (detection bias)	Unclear	No detail provided
Incomplete outcome data (attrition bias)	Low	Nil drop out
Selective reporting (reporting bias)	Low	
Other bias	High	Randomisation occurs months prior to commencement of intervention No between group comparison of baseline for primary outcome was provided
Suman et al. [17]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail provided on methods for allocation
Allocation concealment (selection bias)	Unclear	No detail provided
	High	

(continued on next page)

Table 3 (continued)

Suman et al. [17]		
Bias	Rating	Support for judgement
Blinding of participants and personnel (performance bias)		Exercise supervised and supported only for intervention group No blinding of therapist to treatment or allocation described
Blinding of outcome assessment (detection bias)	Unclear	No detail provided
Incomplete outcome data (attrition bias)	High	25/69=36% drop out No intention to treat analysis performed
Selective reporting (reporting bias)	Low	No estimate provided on variability of between group differences
Other bias	High	Randomisation occurs months prior to commencement of intervention No between-group comparison of baseline for primary outcome was provided
Suman and Herndon [26]		
Bias	Rating	Support for judgement
Random sequence generation (selection bias)	Unclear	No detail provided on allocation process
Allocation concealment (selection bias)	Unclear	No detail provided by authors
Blinding of participants and personnel (performance bias)	High	Exercise supervised and supported only for intervention group No blinding of therapist to treatment or allocation described
Blinding of outcome assessment (detection bias)	Unclear	No detail provided by authors
Incomplete outcome data (attrition bias)	Low	Nil drop out
Selective reporting (reporting bias)	Low	
Other bias	High	Growth hormone given to some children as part of another study Randomisation occurs 6 months prior to commencement of intervention No between group comparison of baseline for primary outcome was provided

3.2.2. Blinding (performance bias and detection bias)

No studies were assessed to have adequately blinded participants or assessors throughout the research process. Blinding of outcome assessment was rated low risk for one study [21] and high risk for one [25]. The high risk rating given to the study by Paratz et al. [25] was due to their utilisation of self-report surveys for primary outcome measures. Their high risk of bias for participant blinding meant that blinding of outcome assessment must also be high risk.

3.2.3. Incomplete outcome data (attrition bias)

One study was deemed at high risk of bias for participant attrition where of the 100 subjects initially enrolled and randomised, 69 remained after death, exclusion or withdrawal. However, of these final 69, data from only 44 patients were included in analysis due to lack of compliance with the intervention [17]. One study was rated as unclear in their participant attrition as patient compliance was not reported [24].

3.2.4. Selective reporting (reporting bias)

One study [24] was judged to be at high risk of bias for selective outcome reporting for not providing any between group results. All other studies were deemed low risk.

3.2.5. Participants analysed in group to which allocated

Suman et al. [17] was rated as being at high risk of bias for this category. It was evident that intention to treat analysis was not undertaken where data was only analysed for 44 of the 69 participants who were not excluded or withdrawn from the study. All other studies were deemed to be low risk.

3.2.6. Other potential sources of bias

Seven studies were rated high risk for some other bias. In one study, a small number of patients received pharmacological agents as part of another trial [26]. One study did not provide any patient data at baseline [24], whilst one other did not provide muscle strength data at initial assessment. There was a group of studies which did not provide baseline comparison of groups at the time of recruitment into the study as randomisation and initial patient assessment occurred months apart [17,18,22,26,27]. The lack of variability in sample size for outcomes precluded conclusions for publication bias.

3.3. Effects of interventions

3.3.1. Muscle strength

Results of knee extension strength were combined and assessed in a meta-analysis as this was the muscle group most consistently assessed and treated (n=295). Modes of strength assessment were isokinetic dynamometry or 3-repetition maximum. No statistically significant effect was seen (SMD 0.74, 95% CI -0.02 to 1.50, p=0.06) and significant heterogeneity existed ($I^2=88%$, $p<0.001$). Subsequently, sub group analysis was undertaken in which adult and paediatric populations were analysed separately.

In children (n=229), there was no statistically significant effect of RT on knee extension strength (SMD 0.57, 95% CI -0.32 to 1.46, p=0.21) and significant heterogeneity remained ($I^2=88%$, $p<0.001$). Two studies (n=66) were performed with adult burns patients [7,25]. A significant effect on muscle strength was demonstrated in favour of RT in this subgroup

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Al-Mousawi 2010	?	?	-	?	+	+	-
Cucuzzo 2001	?	?	-	?	+	+	+
Ebid 2012	+	+	-	?	+	+	+
Ebid 2014	+	+	-	+	+	+	+
Hardee 2014	?	?	-	?	+	+	-
Mowafy 2016	?	?	-	?	-	-	-
Paratz 2012	-	-	-	-	+	+	+
Przkora 2007	?	?	-	?	+	+	-
Suman 2001	?	?	-	?	+	+	-
Suman 2003	?	?	-	?	-	+	-
Suman 2007	?	?	-	?	+	+	-

Fig. 2 – Risk of bias summary: authors judgement for each risk of bias domain.

(SMD 1.42, 95% CI 0.87–1.97, $p < 0.001$) with no evident heterogeneity ($I^2 = 0\%$, $p = 0.84$) (Fig. 3).

Post-hoc sensitivity analysis was undertaken with SDs imputed for the studies by [7,21]. The imputed SD was the median of all other SD values in the analysis. The effect of RT on muscle strength for the whole group was significant in favour of RT (SMD 0.37, 95% CI 0.08–0.65, $p = 0.01$) and heterogeneity was assessed as non-significant ($I^2 = 32\%$, $p = 0.15$). For children, the effect was statistically significant (SMD=0.27, 95% CI 0.01–0.53, $p = 0.04$), yet not significant in adults (SMD=0.89, 95% CI –0.19 to 1.97, $p = 0.11$) (Fig. 4).

3.3.2. Other measures of muscle strength

Knee flexion strength was assessed by two studies [7,23]. When combined, a small effect was seen in favour of the training groups (SMD 0.65, 95% CI 0.14–1.17) (Fig. 5).

The results of individual muscle groups which were unable to be combined are displayed in Table 4. Significant between group differences were shown in latissimus dorsi pull-down strength both immediately after the training period and at 6 weeks after training cessation, no significant differences were seen for any of the other muscle groups tested.

3.3.3. Lean mass

Seven studies (n=205) assessed the effect of resistance training on whole body lean mass [17,18,22,26–28]. Six studies used a dual-energy X-ray absorptiometry (DXA) scan, whilst one [24] calculated lean mass using a formula of “subtracting body fat weight from body weight”. All assessments of lean mass were completed in paediatric populations. The results for studies performing a DXA scan to assess lean mass were combined. The overall effect was non-significant (MD 1.87kg, 95% CI –2.55 to 6.30, $p = 0.41$) with no observable heterogeneity ($I^2 = 0\%$, $p = 1.00$) (Fig. 6). Mowafy et al. [24] reported a significant effect of training using their calculation of lean mass (MD 0.86kg 95% CI 0.11–1.61).

3.3.4. Physical function

Patient function was assessed using a combination of self-reported surveys and physical assessment procedures. Data were not sufficient to perform meta-analysis for either mode. Table 5 shows calculated mean difference and 95% CI for function assessments. In the study by Paratz et al. [25], patient reported surveys were used to assess lower and upper limb function. The Lower Extremity Functional Scale (LEFS) [52], where a high score equates to improved function was used to assess the lower limb. The Quick-Disability of Arm, Shoulder and Hand (Quick-DASH) survey [53], where a lower score means improved function was used to assess the upper limb. Physical assessments of function included shuttle walk distance [25] and the six minute walk test [23] for adults and gait speed was assessed in children [7]. Despite the reports of significant group differences in upper limb function, shuttle walk distance and six-minute walk test, the only significant between-group difference calculated by our group was for gait speed (MD=10.9m/min, 95% CI 7.97, 13.8).

3.3.5. Quality of life

Quality of life was assessed by Paratz et al. [25] using the Burn Specific Health Scale-Abbreviated (BSHS-A). Results were taken from each of the four quality of life domains as well as the overall score. Mean difference and 95% CI’s are displayed in Table 6. A significant effect was noted for the psychological domain in favour of the training group, 6 weeks after cessation of training (MD=25.3, 95% CI 3.94–49.7).

3.3.6. Pain

No studies included in this review investigated pain as an outcome variable.

3.3.7. Adverse events

No studies directly investigated whether RT produced adverse events in patient groups. However, it was noted in one study [22] that one RT participant demonstrated a decrease in lean mass after the intervention period.

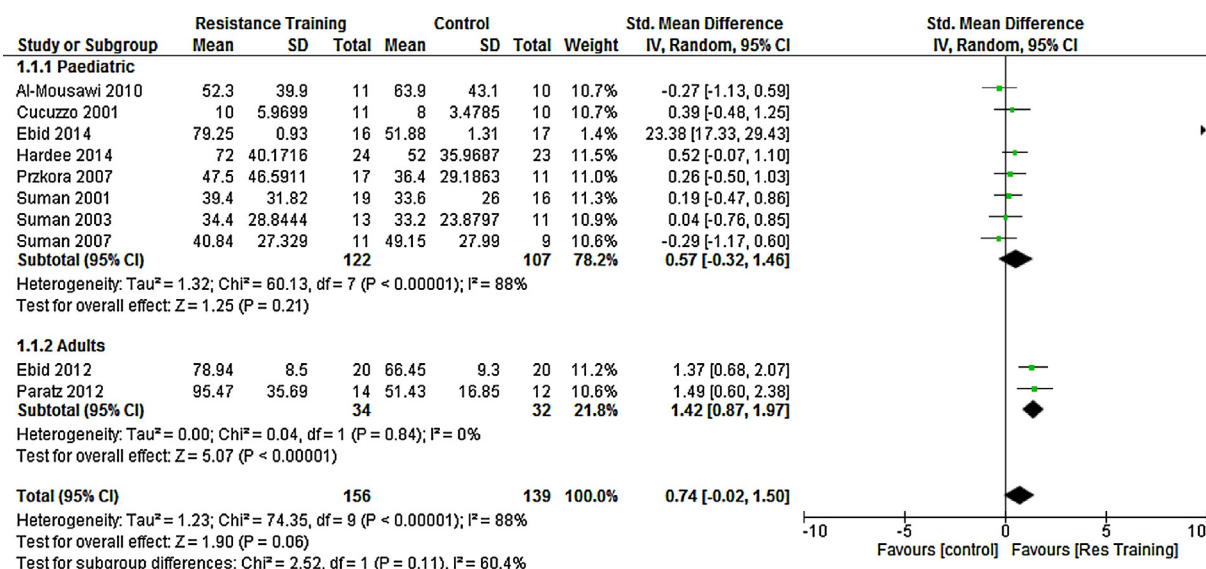


Fig. 3 – Forest plot of results for knee extensor strength.

3.4. Quality of the evidence

Judgements of the quality of evidence using GRADE can be found in Table 7. All outcomes were rated as having “low” to “very low” quality evidence. The quality of evidence was downgraded on the basis of design limitations, inconsistency and imprecision.

4. Discussion

4.1. Summary of main results

This review was undertaken to investigate the effects of resistance training when performed in patients with a burn injury. We assessed both changes in muscle physiology as well

as changes in quality of life in participants undertaking resistance training.

Initial meta-analysis of knee extensor strength data demonstrated no effect of strength training on knee extensor strength. Sub-group analysis demonstrated a significant effect of training on knee extensor strength in adult burns patients. No evidence on an effect on knee extensor strength was noted in the paediatric population. Half of the studies in adults with burn injury commenced rehabilitation prior to six months after injury, whilst in paediatric studies, rehabilitation was consistently commenced at six months after the burn injury. One hypothesis may be that in the six months between injury and commencement of formal rehabilitation, children recover a portion of their muscle strength through daily activity and play, mitigating some of the effectiveness of late rehabilitation. However, physical activity levels after burns were not

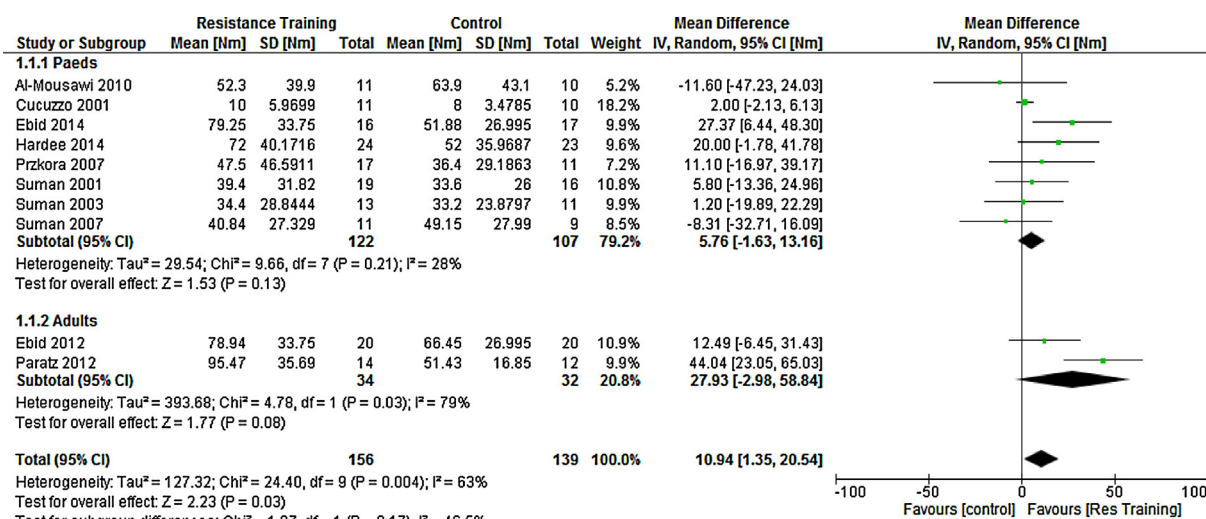


Fig. 4 – Forest plot of results for knee extensor strength, with imputed SD values for Ebid et al. [7,21].

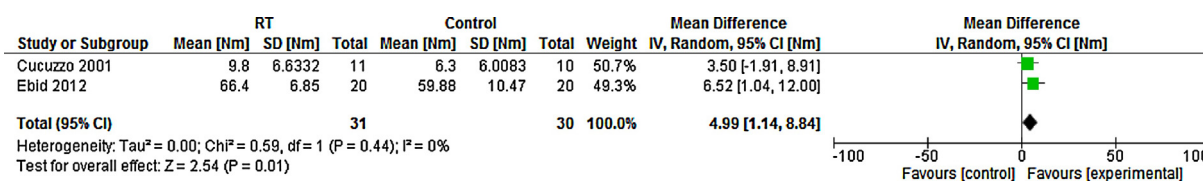


Fig. 5 – Forest plot of results for hamstring muscle strength.

quantified and time to commencing rehabilitation after injury may be a factor to consider in future research.

Results for the muscle strength meta-analysis may be confounded by the inclusion of data which may not be credible [7,21]. When imputed SDs were used, a significant effect on muscle strength for the whole group of studies was demonstrated, in favour of training after burn injury, though the statistical significance of effects for the subgroups of adults and children were changed. That the results of the overall analysis and the subgroup analyses are not robust to changes in the SDs of 2 studies from one research group indicates that they should be treated with caution.

We used back transformation to provide an estimate of the clinical change of knee extensor muscle strength for all studies. Using original data, the estimated change was 22.4 Nm (95% CI -14.7, 28.7) in intervention conditions and 19.9 Nm (95% CI -13.1, 25.5) in control conditions. It is not clear how this value translates into functional change, however, unit conversion [54] suggests that this estimate of effect would be equivalent to only 2.29 (-1.49 to 2.93)kgm and 2.04 (-1.33 to 2.60)kgm of force respectively. Determining the minimal clinically important difference of such measurements would assist clinicians in deciding on the clinical value of interventions explored in research.

Hamstring strength was assessed in one adult and one paediatric study where, when combined, the overall effect was in favour of training after a burn injury. One paper assessed latissimus dorsi muscle strength in adults and our calculations of a mean difference demonstrated significant improvement in participants undertaking training. Several individual muscle groups that were assessed but unable to be included in meta-analysis showed no additional benefit of RT.

We also found no evidence of a significant benefit from RT on lean mass in paediatric burns patients. No adult studies assessed lean mass, therefore we are unable to comment on the effect and further research should be considered in adults.

The results of studies investigating the effect of RT on physical function were synthesized narratively. Self-report of functional ability demonstrated no difference in lower limb function between training and control groups, whilst upper limb function was reported to be significantly improved in the training group [25]. However, this was not supported when mean difference and 95% CI's were calculated by our group using the available data. In children, gait speed was determined to be significantly greater in the RT group [7]. However, with our concerns about the credibility of the SD reported in this study, interpretation of this finding should be undertaken with caution. Walking distance in adults and children were reported as being significantly greater after intervention for the training groups [23], however, our calculations of between group differences do not support this view.

One study assessed quality of life as an outcome measure [25]. In this study, the exercise group was seen to have greater quality of life scores for the psychological domain of the BSHS-A six weeks after the training intervention had ceased. The authors also described the same result for the General domain of the BSHS-A, however, our calculated MD and 95% CI does not support this difference in the General domain of quality of life.

Pain and safety were not utilised as outcome measures in any of the included studies. The failure to report adverse events represents an important omission from the literature and future research should address this as a priority.

Table 4 – Calculated mean difference & 95% CI of strength assessment results not included in meta-analysis.

Author	Muscle group	Mean difference	95% CI
Cucuzzo et al. [23]	Biceps	1.10	-2.37 to 4.57
	Triceps	1.50	-1.60 to 4.60
	Forearm	1.50	-2.24 to 5.24
Paratz et al. [25]	Latissimus dorsi	20.94	11.8-30.08 ^b
	Latissimus dorsi 6 weeks ^a	26.7	15.18-38.22 ^b
	Grip (L)	-2.63	-11.37 to 6.11
	Grip (L) 6 weeks ^a	0.03	-10.32 to 10.38
	Grip (R)	-3.26	-12.52 to 6.00
	Grip (R) 6 weeks ^a	-0.97	-11.32 to 9.38

3 RM: three repetition maximum test; GSD: grip strength dynamometry, best of three attempts.

^a Assessment at 6 weeks after cessation of the training period.

^b Significant mean difference between intervention and control groups.

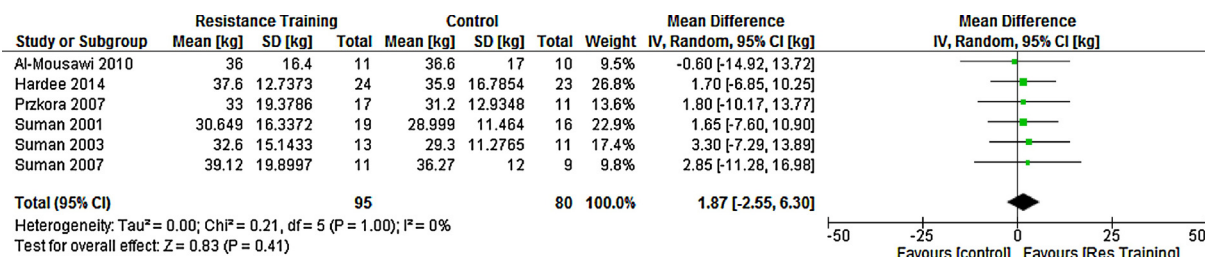


Fig. 6 – Forest plot of results for lean mass.

4.2. Quality of the evidence

Using the GRADE approach, the overall quality of evidence for all outcomes assessed in this review was “low” to “very low”. This was due, in part, to limitations in the size and design of included studies and all studies were rated as high risk of bias overall.

Bias was regularly introduced due to allocation procedures. In some studies, consent and randomisation occurred on the day of admission to acute care, often six months prior to starting the training intervention. This made the judgement of baseline compatibility difficult as the primary outcome measures could not be recorded at the time of randomisation. In addition, participants randomised to control and experimental conditions likely interacted with the research team for a significant period prior to commencement of treatment and it is possible that this may introduce substantial bias to the estimate of the treatment effect.

The current literature has poor quality reporting of allocation and concealment procedures. Just two out of eleven studies attained a low risk of bias rating. Unclear ratings were given to the remaining nine studies, as the study procedures were not described in sufficient detail. Lack of reporting clarity is an issue which has been highlighted and reported to occur in

therapeutic intervention studies previously [55,56] and these factors are known to be associated with exaggerated effect sizes [57,58].

The reporting practices in the majority of included studies made estimation of the size of any treatment effect difficult. Bland and Altman [59] have discussed how the use of within group analysis can be misleading when used to infer differences between groups. We found this to be a significant issue for this review, as many study outcomes were reported using only within group analyses and between group differences inferred from disparate within group effects. This often occurred when treatment groups did not appear to be comparable at baseline assessment. Unfortunately, the studies in question did not perform group comparisons at baseline, or attempt to adjust baseline values to allow appropriate comparison of between group results. This may have led to over interpretation of treatment effects when summarising an individual study’s results and goes some way to explaining why a collection of generally positively reported trials yield largely negative results when entered into meta-analyses. Additionally, we assume that all interventions were delivered effectively in all studies. However, this is not consistently clear in the reports. The use of checklists such as the TIDieR framework [60] or CONSORT [55] would be recommended in order to improve the clarity and depth of reporting in future trials.

Small sample sizes were a consistent feature of all studies in this review. Subsequently, most comparisons have only small numbers contributing to the estimate of the treatment

Table 5 – Calculated mean difference & 95% CI for function assessment– self report & physical assessment.

Self-report assessment of function			
Author	Measure	MD	95% CI
Paratz et al. [25]	LEFS	6.09	-6.73 to 18.9
	LEFS 6 week ^a	9.20	-6.00 to 24.4
	Quick-DASH	-7.12 ^b	-23.0 to 8.76
	Quick-DASH 6 week ^a	-8.45 ^b	-23.2 to 6.35
Physical assessment of function			
Author	Measure	MD	95% CI
Paratz et al. [25]	Shuttle walk test (m)	233.3	-21.9 to 488.6
	Shuttle walk test 6 week ^a	242.5	-4.88 to 489.9
Ebid et al. [7]	Gait speed (m/min)	10.9	7.97-13.8*
Cucuzzo et al. [23]	6-min walk test (m)	68.0	-87.4 to 223.4

* Significant between group difference (p < 0.05).
^a assessment at 6 weeks after cessation of the training period.
^b Negative value signifies less disability ie. improved function.

Table 6 – Calculated mean difference & 95% CI for quality of life assessment.

Author	BSHS-A domain	MD	95% CI
Paratz et al. [25]	Total	17.8	-20.2 to 55.8
	Total 6 week ^a	33.6	-12.6 to 80.2
	Physical	4.94	-3.76 to 13.6
	Physical 6 week ^a	8.68	-0.36 to 17.7
	Psychological	11.2	-5.83 to 28.2
	Psychological 6 week ^a	25.3	3.94-46.7*
	General	3.01	-3.53 to 9.55
	General 6 week ^a	5.03	-4.18 to 14.24
Social	Social	5.47	-3.95 to 14.9
	Social 6 week ^a	9.65	-0.13 to 19.4

* Significant between group difference (p < 0.05).
^a assessment at 6 weeks after cessation of the training period.

Table 7 – GRADE judgements for comparisons.

Comparison	Result	Design limitations	Inconsistency	Indirectness	Imprecision	Publication bias	GRADE judgement
Muscle strength							
Knee extension	SMD 0.74Nm, 95% CI -0.02 to 1.50	Down one (>25% high risk bias)	Down one (I ² =88%, p<0.001)	None	Down one (n=295)	None	Very low
Knee flexion	SMD 0.65, 95% CI 0.14-1.17	Down one (>25% high risk bias)	None	None	Down one (n=61)	None	Low
Latissimus dorsi	MD 20.94, 95% CI 11.8-30.08	Down two (>25% high risk of bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Biceps	MD=1.10kg, 95% CI -2.37 to 4.57	Down one (>25% high risk bias)	Down one (single study)	None	Down one (n=21)	None	Very low
Triceps	MD=1.5kg, 95% CI -1.60 to 4.60	Down one (>25% high risk bias)	Down one (single study)	None	Down one (n=21)	None	Very low
Forearm	MD=1.5kg, 95% CI -2.24 to 5.24	Down one (>25% high risk bias)	Down one (single study)	None	Down one (n=21)	None	Very low
Grip left	MD= -2.63kg, 95% CI -11.37 to 6.11	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Grip right	MD= -3.26kg, 95% CI -12.52 to 6.00	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Lean mass							
Whole body (DXA scan)	MD=1.87kg, 95% CI -2.55 to 6.30	Down one (>25% high risk of bias)	None	None	Down one (n=175)	None	Low
Whole body formula	MD=0.86kg 95% CI 0.11-1.61	Down one (>25% high risk of bias)	Down one (single study)	None	Down one (n=30)	None	Very low
Physical function							
LEFS	MD=6.09, 95% CI -6.73 to 18.9	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Quick-DASH	MD= -7.12, 95% CI -23.0 to 8.76	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Shuttle walk	MD=233.3, 95% CI -21.9 to 488.6	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
Gait speed	MD=10.9, 95% CI 7.97-13.8	Down one (>25% high risk of bias)	Down one (single study)	None	Down one (n=40)	None	Very low
6-min walk test	MD=68.0, 95% CI -87.4 to 223.4	Down one (>25% high risk of bias)	Down one (single study)	None	Down one (n=21)	None	Very low

(continued on next page)

Table 7 (continued)

Comparison	Result	Design limitations	Inconsistency	Indirectness	Imprecision	Publication bias	GRADE judgement
Quality of life BSHS-A total	MD=17.8, 95% CI -20.2 to 55.8	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
BSHS-A physical	MD=4.94, 95% CI -3.76 to 13.6	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
BSHS-A psychological	MD=11.2, 95% CI -5.83 to 28.2	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
BSHS-A general	MD=3.01, 95% CI -3.53 to 9.55	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low
BSHS-A social	MD=5.47, 95% CI -3.95 to 14.9	Down two (>25% high risk bias. Contributing study not randomised)	Down one (single study)	None	Down one (n=26)	None	Very low

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.

effect contributing to the imprecision of evidence in this review. It is known that, though often underpowered to detect effects, published small studies often report more favourable effects of an intervention, though with less precision than larger studies [61]. In this case, some of the positive effects reported in this review might be influenced by small study bias and the associated issue of publication bias. Though we found no formal evidence of publication bias, the relatively small number of studies and lack of larger studies means that this assessment lacks sensitivity.

4.3. Strengths & limitations

We included only studies which were published or available in English which may introduce bias into this review. However, after our thorough search of the literature, we identified only one study which was excluded for this reason as no translation was available.

The use of a multi-modal exercise programme in the included studies has made it difficult to elicit whether RT is the sole cause of benefit in rehabilitation. To determine the mode of exercise most advantageous for burn patient recovery, future work may consider choosing just one mode of exercise training to assess.

4.4. Agreements and disagreements with other studies or reviews

Our conclusions from this review for muscle strength and lean body mass differ with the conclusions from previous qualitative reviews from this body of literature. Nedelec et al. [15] selected studies pertaining to burns rehabilitation from the literature and extracted individual study data. After a narrative review of results, they concluded that significant improvements in muscle strength and lean body mass are achieved after exercise training (including RT). However, risk of bias assessments and meta-analysis of results were not undertaken in this review. Additionally, their conclusion was based largely on the within group changes reported by each study. Despite the shortage of supportive data analysis, practice guidelines were recommended by the authors that exercise training should begin after discharge from acute care and last 6-12 weeks in duration. Whilst their interpretation of results may differ to our meta-analysis, the authors acknowledge that it would be beneficial to further investigate the prescription parameters of exercise training in burn rehabilitation. The authors recommend manipulating training variables in patients with a burn injury, including the time to commencement, duration and location of undertaking an exercise

training programme. In support of this recommendation, Disseldorp et al. [36] have concluded in their own review that due to the similarities of training protocols in published studies, our knowledge of the effectiveness of different training variables in burns exercise rehabilitation is not complete. They too suggest that future research should investigate a variety of training variables in rehabilitating burn injury.

Progressive RT was recommended for outpatient burn rehabilitation by Porter et al. [37]. Their non-systematic review of the literature concluded that RT improved the physiological function of burns patients, including muscle strength and was a useful strategy to improve lean body mass. This review also did not perform risk of bias assessments or meta-analysis of results. Therefore, their conclusions are likely to also be based largely upon within group analyses performed in the individual studies. The authors have suggested that more effort should be made to identify the specific regimens of RT that would be most effective in optimising patient outcome.

4.5. Future research recommendations

It is necessary that rehabilitation specialists understand the unique effect of exercise in individuals with burn injury. The outcomes of this review would suggest that the literature is lacking variation in the prescription of exercise training in this patient cohort. In order to more completely understand the effects of training in burn injury, future research should focus on currently unknown prescription variables, such as testing exercise training during the acute and sub-acute injury phase, as well as in minor and moderate sized burns. The length of a training intervention should be investigated to gain an understanding of what the minimum effective training period could be to improve outcomes in individuals with a burn injury.

In addition to ongoing assessment of the effect of exercise on physiological outcomes of muscle strength and body composition, research in adults and children should look to include patient centred outcomes such as quality of life and physical function, including return to recreation and work. The safety of patients undertaking exercise should also be systematically investigated.

It is necessary to move toward studies which are adequately powered, where allocation is transparently randomised and concealed, and where blinded assessment can be truly undertaken to improve the quality of research outcomes. This review has identified the need for attention to reporting standards in order to improve the quality and clarity of research. Future trials should adhere to CONSORT guidance, including that related to the reporting of the development and evaluation of complex interventions [62]. This will help to eliminate ambiguity of methodology and results, ensuring clear interpretation of important outcomes.

5. Conclusions

This review has determined that low quality evidence suggests some positive effects of RT on muscle strength and psychological quality of life in adults with burns. Post-hoc sensitivity analysis suggests a positive effect of RT on muscle strength in

all patients recovering from burn injury. Analyses did not suggest an effect for RT on lean body mass in children. However, consideration needs to be taken of the low quality of evidence currently available for these outcomes in the burn injury rehabilitation literature.

The quality of evidence available for this review suggests that that additional well designed and robust longitudinal research is required to understand the effect of RT after burn injury in order to implement it successfully in rehabilitation. We noted a general lack of studies measuring outcomes which may be more meaningful to the patient group, such as pain, quality of life and return to work, sport and hobbies. Future research would benefit from this type of assessment in addition to those which investigate muscular physiology.

Conflicts of interest

The authors wish to confirm that there are no known conflicts of interest.

Authors contribution

PG: Lead researcher, study selection, data entry, data analysis, lead writing of review.

TG: Appraisal of review, study selection, methodological advice.

BW: Appraisal of review, independent assessor, expert methodological advice.

DE: Appraisal of review, independent assessor, expert subject advice.

FW: Appraisal of review, expert subject advice

NEO: Appraisal of review, expert methodological advice, statistical advice.

Differences between protocol and review

The review was compliant with the protocol registration published on PROSPERO. No differences were noted between the two.

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