National Institute for Health and Care Excellence

FINAL

Rehabilitation after traumatic injury

C.1 Specific programmes and packages in amputation for people with complex rehabilitation needs after traumatic injury

NICE guideline NG211

Evidence review underpinning recommendations 1.14.1 to 1.14.24 in the NICE guideline

January 2022

FINAL

These evidence reviews were developed by the National Guideline Alliance which is part of the Royal College of Obstetricians and Gynaecologists

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Contents

Summary of review questions covered in this report

This evidence report contains information on 2 reviews

C.1a For adults with complex rehabilitation needs after traumatic injury that that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

Specific programmes and packages in amputation for people with complex rehabilitation needs after traumatic injury

Review question

This evidence report contains information on 2 reviews relating to specific rehabilitation programmes and packages for limb reconstruction, limb loss or amputation:

C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

Introduction

The threat of limb loss due to a traumatic injury is a life changing event for individuals and is a very rare event affecting the paediatric population. Limb threatening injuries can be treated with either a limb reconstruction plan, or amputation. Either course of action brings long term issues. Limb reconstruction can be a long prospect with multipole surgeries, and psychological peaks and troughs as it is fraught with potential complications, which may eventually lead to an inability to salvage the limb. In the long term after limb salvage the outcome is unlikely to be a limb that functions at the same level as pre-injury. Amputation may occur as a time-critical, immediate necessity due to an unsalvageable limb, or may be considered at a much later stage post injury due to functional, sensory, or cosmetic reasons following complex limb reconstruction efforts. This can often include multiple theatre admissions with repeat fasting and prolonged procedures resulting in psychological trauma, especially in the paediatric population. Long term outcomes for those that suffer limb loss can be affected by a significant number of factors including: pre-injury abilities; pre-operative management and counselling; level of amputation and operative techniques; pain; post-operative rehabilitation; access to specialist facilities, equipment, and advice; and psychological support, in general, and for children and young people, in particular, these factors also include skeletal maturity; mechanism of injury; parental compliance; pre-injury abilities; and specialist play teams. Decisions around the details of the interventions and information given in the acute stages of care can have lifelong implications for the success of an individual's rehabilitation, independent living, return to education and/or work, social relationships, and quality of life. The need to garner specialist advice and support from those experienced in amputee and prosthetic rehabilitation, as soon as an amputation is considered, is crucial in ensuring that decision around acute interventions are made with the correct balance of consideration for their impact on long term rehabilitation outcomes. This approach also ensures that transition between acute and rehabilitation services are as seamless as possible. Given the lifelong implications of limb loss and its effect on return to pre-injury abilities and social integration, it is important to explore the evidence for provision of effective multidisciplinary interventions for patients

throughout all stages of their care, before or after amputation has been considered or has occurred.

The objectives of these reviews were to examine what specific rehabilitation programmes and packages are effective and acceptable for people with complex rehabilitation needs after traumatic injury that involves limb reconstruction, limb loss or amputation.

Summary of the protocol

Please see Table 1 and Table 2 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review in the adult and children and young people populations, respectively.

Table 1: Summary of the adult protocol (PICO table)

Population	Adults (aged 18 years and above) with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation and requires admission to hospital
Intervention	Standard care consisting of at least 2 of 4 of physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management, in addition to at least one of the followings <u>Limb reconstruction interventions:</u> • Splinting to maintain range of movement • Hydrotherapy • Anti-gravity treadmill training • Psychological therapies for adjustment and engagement (Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness) • Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Vocational support/ rehabilitation and workplace interventions (ergonomics) <u>Amputation interventions:</u> • Prostheses • Early/non-definitive walking aids [pneumatic post-amputation mobility aid (PPAM), femurette/ femuret, amputee mobility aid (AMA)] • Early scar/stump/residual limb swelling and oedema management (within 4 weeks of amputation) • Psychological therapies for adjustment and engagement (Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness, Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Vocational support/ rehabilitation and workplace interventions (ergonomics)
Comparison	Standard care (as defined above) Studies that employ the same intervention program as listed under 'interventions' but vary it in terms of any of the following: • Frequency

	• Intensity • Timing
Outcome	Critical: • Overall quality of life (EURO-QoL 5D 3L, SF-36, SF-12, SF-6D) • Changes in mobility (any measure) • Pain (VAS) • Patient acceptability (any direct measure) Important: • Hospital readmission • Return to work or education • Changes in mood (Depression measures – HADS, PHQ-9, BDI, DAS) • Changes in activity of daily living (Barthel ADL index, Katz, PSMS, OARS, PAT, EADL-Test)

ADL: activities of daily living; BDI: Beck's Depression Inventory; DASS: Depression Anxiety Stress Scales; EADL-Test: Erlangen Activities of Daily Living test; EURO-QoL 5D 3L: an instrument for measuring quality of life 3 levels of severity for 5 dimensions; HADS: Hospital Anxiety and Depression Scale; OARS: Older Americans Resources and Services; PAT: Performance ADL Test; PHQ-9: Patient health questionnaire; PSMS: Physical Self-Maintenance Scale; SF-6D: short-form six-dimension to assess the cost-effectiveness of health care interventions; SF-12: a short-form survey with 12 questionnaires selected from SF-36 to create 2 scales to assess mental and physical functioning and overall health-related quality of life; SF-36: Short form health survey-36; VAS: visual analog scale

Table 2: Summary of the children and young people protocol (PICO table)

Population	Children and young people (aged below 18 years) with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation and requires admission to hospital
Intervention	Standard care consisting of at least 2 of 4 (physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management) in addition to at least one of the following <u>Limb reconstruction interventions:</u> • Splinting to maintain range of movement • Hydrotherapy • Anti-gravity treadmill training • Psychological therapies for adjustment and engagement (Family therapy,Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Educational support/ rehabilitation and school-based interventions (ergonomics) • Play therapy/specialist play therapy • Theraband (stretchy elastic that provides resistance that is widely used by OTs and PTs) <u>Amputation interventions:</u> • Prostheses • Early/non-definitive walking aids (pneumatic post-amputation mobility aid, femurette/ femuret, amputee mobility aid) • Early scar/stump/residual limb swelling and oedema management (within 4 weeks of amputation)

	• Psychological therapies for adjustment and engagement (Family therapy, Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness, Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Educational support/ rehabilitation and school-based interventions (ergonomics) • Play therapy/specialist play therapy • Theraband (stretchy elastic that provides resistance that is widely used by OTs and PTs)
Comparison	Standard care (as defined above) Studies that employ the same intervention program as listed under 'interventions' but vary it in terms of any of the following: • Frequency • Intensity • Timing
Outcomes	Critical • Overall quality of life (CHQ-CF80, CHQ-PF-50, Peds-QL, EQ-5D-Y, SF-36, SF-12, SF-6D) • Changes in mobility (WeeFIM, any measure) • Pain [VAS, any measure] • Patient acceptability (any direct measure; if not reported, but patient satisfaction is, this will be reported instead) Important • Hospital readmission • Return to education or work • Changes in mood (Any measure, PEDS-QL, Depression measures – HADS, PHQ-9, BDI, DAS) • Changes in activity of daily living (Barthel ADL index, COPM, EADL-Test, Katz, OARS, PAT, PSMS)

ADL index: Activities of Daily Living; BDI: Beck's Depression Inventory; CHQ-CF80: a self-report measure of child health questionnaires; CHQ-PF-50: a measure of child health questionnaires for parents; COPM: Canadian Occupational Performance Measure; DASS: Depression Anxiety Stress Scales; EADL-Test: Erlangen Activities of Daily Living test; EQ-5D-Y: an child-friendly EQ-5D version for measuring quality of life; HADS: Hospital Anxiety and Depression Scale; Katz: a tool to assess independence in activities of daily living; OARS: Older Americans Resources and Services; OTs: occupational therapists; PAT: Performance ADL Test; Peds-QL: Pediatric Quality of Life Inventory ;PHQ-9: Patient health questionnaire; PSMS: Physical Self-Maintenance Scale; PT: physical therapists; SF-6D: short-form six-dimension to assess the cost-effectiveness of health care interventions; SF-12: a short-form survey with 12 questionnaires selected from SF-36 to create 2 scales to assess mental and physical functioning and overall health-related quality of life; SF-36: Short form health survey-36; TARN: Trauma Audit and Research Network; VAS: visual analog scale; WeeFIM: standardized measure of functional independence for use in children

For further details see the review protocols in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and in the methods chapter (Supplement 1).

Declarations of interest were recorded according to NICE's 2018 conflicts of interest policy.

Clinical evidence: Adults

Included studies

Six studies were identified for this review, all randomised controlled trials (RCTs) (Anjum 2016, Chan 2007, Cunha 2017, Finn 2017, Ol 2018, and Topuz 2012). Among them, 1 was a three-armed RCT (Chan 2007).

The included studies are summarised in Table 2.

One study compared proprioceptive neuromuscular facilitation and traditional prosthetic strength training (Anjum 2016). Another study compared complex decongestive physiotherapy (CDP) and conventional bandaging (CB) (Topuz 2012). Four other studies looked at different kinds of psychological therapy: 1 study compared mirror therapy and covered-mirror therapy (Finn 2017); 1 three-armed study compared mirror therapy versus mental-visualisation therapy versus covered-mirror therapy (Chan 2007); 1 study compared mirror therapy and tactile treatment (Ol 2018) and the last study compared gait-oriented mental practice and non-motor mental practice (Cunha 2017).

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review are presented in Table .

Table 2: Summary of included studies

Study	Population	Intervention[a]	Comparison[a]	Outcomes
Anjum 2016 RCT Pakistan	N=63; Included subjects with unilateral transtibial amputation, no contracture, first time or old prosthetic user and one-third stump length • Side of amputation – Right/Left: 26/37 • Percentage of subjects without any co-morbidity: 27%	Proprioceptive neuromuscular facilitation (PNF) group (n=31): 30 minutes session each, included PNF principle (e.g. manual contact, verbal command, etc) in addition to TPST	Traditional prosthetic strength training (TPST) group (n=32) : 30 minutes session each	• Critical ○ Mobility (at 4 weeks) • Important ○ None
Chan 2007 RCT (3-armed trial) Unclear, Probably USA*	N=22 (18 analysed); Included subjects with phantom limb pain (PLP) after leg or foot amputation • Similar VAS at baseline among the group (p=0.62)	• Mirror therapy (n=6) • Mental-visualisation group (n=6)	• Covered-mirror therapy (n=6)	• Critical ○ Pain (at 4 weeks) • Important ○ None

Study	Population	Intervention[a]	Comparison[a]	Outcomes
Cunha 2017 RCT Brazil	N=16; Included male subjects with transtibial amputee with MIQ-RS score ≥4 • Age in years [Mean (SD)]: ○ Intervention = 33.2 (2.69); ○ Control = 35.4 (3.2) • Average time since amputation in years [Mean (SD)]: ○ Intervention = 15.5 (2.1) ○ Control = 24.4 (2.92) • Average ○ Intervention = 22.7 (1.76) ○ Control = 22 (2.91)	Gait-oriented mental practice (MP) (n=10)	Non-motor mental practice (MP) (n=5)	• Critical ○ Mobility (at 4 weeks). • Important ○ None
Finn 2017 RCT USA	N=15; Included active male military members, beneficiaries or retirees with unilateral upper limb amputees who complaint of PLP • Average age in years: 28.73 • Side of injury (Right/Left): 10/5 • Site of injury: ○ Trans-humeral = 6 ○ Trans-radial = 7 ○ Wrist disarticulation = 2	Mirror therapy (n=9)	Covered-mirror therapy (n=6)	• Critical ○ Pain (at 4 weeks) • Important ○ None
Ol 2018 RCT Cambodia	N=30; Included subjects who had PLP after unilateral trans-tibial amputation after landmine trauma • Age in years [Mean (SD)]: ○ Intervention = 57.5 (6.0); ○ Control = 52.0 (7.0) • Years since surgical amputation [Mean (SD)]:	Mirror therapy (n=15)	Tactile treatment (n=15)	• Critical ○ Pain (at 1 week) • Important ○ None

Study	Population	Intervention[a]	Comparison[a]	Outcomes
	○ Intervention = 23.1 (4.7) ○ Control = 23.2 (4.4) • Level of injury, number of subjects: ○ Proximal 1/3 ▪ Intervention = 5 ▪ Control = 5 ○ Mid-shaft ▪ Intervention = 6 ▪ Control = 4 ○ Distal 1/3 ▪ Intervention = 4 ▪ Control = 6			
Topuz 2012 RCT Turkey	N= 17 (11 analysed); Included subjects with unilateral trans-tibial amputees who were able to use prosthesis • Age in years [Mean (SD)]: ○ Intervention = 66.2 (3.96); ○ Control = 67.67 (2.42) • Transition to permanent prostheses in days [Mean (SD)]: ○ Intervention = 33 (2.92) ○ Control = 126 (33.73)	Complex decongestive physiotherapy (CDP) (n=5)	Conventional bandaging (CB) (n=6)	• Critical ○ Mobility (at 4 weeks) • Important ○ None

CB: conventional bandaging; CDP: complex decongestive physiotherapy; MIQ-RS: Movement Imagery Questionnaire- Revised second version; MP: mental practice; N: total number of subjects: n: number of subjects in each group; PLP: phantom limb pain; PNF: proprioceptive neuromuscular facilitation; RCT: randomised controlled trial; SD: standard deviation; TPST: traditional prosthetic strength training; VAS: visual analogue scale
**The study did not mention the country where it was conducted. All the authors are affiliated with organisations based in USA.*
[a] *For full details about the intervention/comparison, please see the evidence tables in Appendix D*

See the full evidence tables in appendix D.

Results and quality assessment of clinical outcomes included in the evidence review

Summary of the evidence

A meta-analysis of 2 RCTs comparing mirror therapy to covered-mirror therapy was performed (see below). No other meta-analyses were performed as the interventions or outcomes were either not sufficiently similar to allow them to be combined or they were not reported by more than 1 study.

Of the pre-defined outcomes, evidence was found for mobility and pain. There was no evidence for the following outcomes: overall quality of life, patient acceptability, hospital readmission, return to work or education, changes in mood, or changes in activity of daily living. Moreover, all the evidence was for people with amputations due to traumatic injury. There was no evidence for people with limb reconstruction.

Proprioceptive neuromuscular facilitation

One RCT compared proprioceptive neuromuscular facilitation to traditional prosthetic strength training (Anjum 2016). The locomotor capability index, manual muscle strength knee flexors and manual muscle strength knee extensors were statistically significantly worse in the proprioceptive neuromuscular facilitation group than the traditional prosthetic strength training group at 4 weeks follow-up, however, these differences were not clinically important. There was no statistically significant or clinically important difference in manual muscle strength hip extensors. The evidence was of very low quality.

Complex decongestive physiotherapy

One RCT compared complex decongestive physiotherapy to conventional bandaging (Topuz 2012). The Circumferential measurement at medial tibial platol and distal residual limb at 4 weeks post-intervention did not differ statistically significantly or clinically importantly between the complex decongestive physiotherapy and the conventional bandaging groups. The evidence was of very low quality.

Mirror therapy

Two RCTs compared mirror therapy with covered-mirror therapy (Chan 2007, Finn 2017). Meta-analysis showed that the number of people reporting a decrease in pain were statistically significantly and clinically importantly higher in the mirror therapy group compared to the covered-mirror therapy at 4 weeks post-randomisation (Chan 2007, Finn 2017; for the forest plot, see Appendix E). There was no statistically significant or clinically important difference between mirror therapy and covered-mirror therapy in the number of people reporting worsening pain 4 weeks post-randomisation (Chan, 2007), but the VAS pain scores were statistically significantly and clinically importantly better at 4 weeks post-intervention in the mirror therapy group compared to the covered-mirror therapy group (Finn 2017). The evidence was of very low quality.

One RCT compared mental-visualisation therapy with covered-mirror therapy (Chan 2007). There was no statistically significant or clinically important difference in the number of people who reported a decrease or worsening of pain in the mental-visualisation therapy group compared to the covered-mirror therapy group at 4 weeks follow-up. The evidence was of very low quality.

One RCT compared mirror therapy with tactile treatment (Ol 2008). There was no statistically significant or clinically important difference in phantom or residual limb pain in the mirror therapy group compared to the tactile treatment group at 1 week post-intervention. The evidence was of very low quality.

Gait-oriented mental practice

One RCT compared gait-oriented mental practice to non-motor mental practice (Cunha 2017). The first and second peak of vertical ground reaction force, the first and second peak of anterior-posterior ground reaction force, and the medio-lateral

ground reaction force were all statistically significantly better and clinically importantly better in the gait-oriented mental practice group compared to the non-motor mental practice group at 4 weeks post-intervention. The evidence was of very low quality.

The quality of the evidence was assessed using GRADE. See the clinical evidence profiles in appendix F.

Clinical evidence: Children and young people

Included studies

A systematic review of the clinical literature was conducted but no studies were identified which were applicable to this review question.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

No studies were identified which were applicable to this review question (and so there are no evidence tables in Appendix D). No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix E).

Results and quality assessment of clinical outcomes included in the evidence review

Summary of the evidence

No studies were identified which were applicable to this review question.

Economic evidence: Adults and children and young people

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to these review questions. See the study selection flow chart in appendix G.

Excluded studies

No studies were identified which were applicable to this review question.

Summary of studies included in the economic evidence review

No economic evidence was identified which was applicable to these review questions.

Economic model

No economic modelling was undertaken for these reviews because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most.

When selecting the critical and important outcomes, the committee agreed that the outcomes needed to be sufficiently generalisable to adequately capture patient-important outcomes for the whole adult and child and young people populations, respectively, which they recognised are quite large and very heterogeneous.

For both adults and children and young people, they therefore prioritised overall quality of life and changes in mobility as critical outcomes because the committee considered that one of the main aims of people with limb loss, amputation or limb reconstruction due to traumatic injury would be to achieve similar quality of life and mobility as before the injury. Pain was also selected as a critical outcome because pain plays a pivotal role in patients' compliance with rehabilitation programmes and critically affects quality of life and the ability to undertake activities of daily living. Patient acceptability was also included as a critical outcome as how acceptable a patient finds the rehabilitation intervention is likely to have a large impact in their compliance

Hospital readmission was considered as an important outcome. The committee also selected return to education or work as well as changes in activity of daily living as important outcomes as these outcomes measure the level of functional independence of the patient after traumatic injury. Changes in mood was also considered to be important because depression and post-traumatic stress disorders are common in people with traumatic injury and this outcome reflects their psychological wellbeing.

The only outcomes reported in the included studies were changes in mobility and pain and that was only for adults who had had a limb amputated.

The quality of the evidence

For adults, 6 randomised controlled trials were included as evidence for amputation interventions. The overall quality of the evidence was assessed using GRADE and was very low for all the results, even in the case of the meta-analysis of mirror therapy. The main reasons for downgrading the evidence were risk of bias in the studies (e.g., commonly due to lack of information about the patient allocation process, missing data and concerns about selective reporting), indirectness where it was unclear if the amputation was due to trauma or not, and imprecision of the effect size. Moreover, the included studies did not cover all the target interventions and populations (no evidence was found for people with limb reconstruction due to trauma), and most results were based on single studies with small sample sizes. Taken together, this meant that the available results were uncertain and very limited and the committee were therefore unable to use them to make recommendations. Instead they made recommendations based on their experience and expertise.

For children and young people, no evidence was identified which was applicable to this review question.

Benefits and harms

When considering the evidence the committee agreed that it was of very low quality and very limited - only reporting on 2 of the target outcomes (mobility and pain) in adults with amputation due to traumatic injury with no evidence found for people with limb reconstruction after traumatic injury. The committee therefore did not use the evidence to make recommendations, which were instead all based on the experience and expertise of the committee, and most of the recommendations relate to all people, including children and young people. The committee agreed that the needs of rehabilitation programmes are different for patients with limb amputation and limb reconstruction because in the former group they lose a limb whereas in the latter group they retain the limb, but with reduced function, and therefore recommendations were made for both these groups.

The committee agreed that when decisions about rehabilitation treatment pathways are being made, each person, and their families if the person agree, need to be informed about the downstream impact for the person's rehabilitation and outcomes of different treatment options for traumatic limb loss, i.e., amputation or limb reconstruction, in order to make the right choice for them in terms of delivering the person's most important rehabilitation goals. For some people who have had a complex limb-threatening injury this may be amputation even when limb reconstruction is an option.

The committee recognised that a pre-amputation consultation is best practice but not always possible if it is a limb threatening injury that requires urgent surgical intervention. The pre-amputation consultation gives the person the opportunity to discuss their concerns, the level of amputation, their recovery and rehabilitation pathway with members of the MDT who specialise in this area. This includes the prosthetic service who will deliver the person's on-going rehabilitation and care.

The committee also agreed that members of a specialist team (for example, a limb reconstruction team or prosthetic team) alongside the trauma rehabilitation team should discuss the implications of the following as soon as possible with the person, and their family members or carers, as appropriate: rehabilitation pathways, pain management, recovery timescales, long-term expectations and impact on daily life, and that alongside these discussions trauma-informed psychological support should be offered before limb reconstruction or limb amputation. This is because amputation and limb reconstruction can be life changing and traumatic and the committee agreed that having such discussions alongside trauma-informed psychological support will help prepare the person and help them to cope with ongoing and upcoming challenges of their injury, both physical and psychological.

Limb reconstruction may result in joint stiffness and muscle shortening, which can affect range of movement and therefore the ability to regain functional independence. Starting rehabilitation early can ease this, prevent complications and shorten time to recovery. The committee discussed that range of movement may be rehabilitated and preserved by engaging in exercise, hand therapy, mobility and positioning, and by using splinting, pain management and swelling and oedema management to enhance the person's ability to engage in range of movement interventions by ensuring they are sufficiently pain-free and comfortable. The committee therefore agreed that rehabilitation should be started as early as possible in order to avoid early rapid irreversible loss of range of movement by ensuring that range of movement exercises for affected and other joints are done to optimise recovery and avoid contractures. They also agreed that people with limb reconstruction should continue to have access to psychological and emotional support because adjusting to life after limb reconstruction due to traumatic injury can be very difficult.

Prosthetics can play an important part in rehabilitation after amputation or limb loss, and the committee therefore agreed that people who have experienced limb loss or amputation should be referred to prosthetic and amputee rehabilitation services as soon as possible in order to optimise their rehabilitation and functional outcomes.

Based on their experience and expertise, the committee agreed that rehabilitation should begin as soon as possible and ideally the day after surgery has taken place to ensure optimal patient outcomes as any delay in starting rehabilitation may lead to complications or worsen pain, quality of life and functional impairment, which can all lengthen the recovery time and compromise the person's outcomes. This approach is also in line with external guidance from the British Association of Chartered Physiotherapists in Amputee Rehabilitation (specifically Clinical guidelines for the pre and post-operative physiotherapy management of adults with lower limb amputations and Evidence based clinical guidelines for the physiotherapy management of adults with lower limb prostheses).

Adequate pain relief plays a vital part in rehabilitation and inadequate pain control can severely compromise a person's ability to participate in rehabilitation as well as their quality of life. The committee therefore agreed that analgesia needs to be proactively agreed and managed with the person, including which kinds of analgesia to use, and that this may require specialist input at times if adequate pain relief cannot be achieved for certain kinds of pain, such as, phantom limb pain, neurogenic pain, psychogenic pain, myogenic pain and complex regional pain. There was very low quality evidence that mirror therapy was associated with clinically importantly reduced pain compared to covered-mirror therapy. Although the committee agreed that this evidence was based on very low numbers of people with amputations and of very low quality, they noted that it was consistent with their experience that mirror therapy can be an effective intervention for phantom limb pain in people who have had an amputation or limb loss after trauma. Mirror therapy is a type of grade motor imagery intervention which is inexpensive, non-invasive and without any obvious side effects. The committee therefore agreed that grade motor imagery and mirror therapy should be considered as potentially useful rehabilitation interventions for this population.

The committee recognised that residual limb oedema needs to be managed proactively because it may otherwise disrupt optimal rehabilitation and agreed that elevation and compression therapy help reduce swelling and improve shaping in preparation for prosthetics fitting. Moreover, the committee discussed that for people with below-knee amputation, management of residual limb oedema also includes using a residual limb board to keep the residual limb elevated when using a wheelchair. In addition to helping reduce swelling and oedema, this will also help support the residual limb. However, this is not always done in their experience, and they therefore agreed a recommendation to that effect. The committee recognised that the use of walking aids, such as crutches or a frame with the limb in a dependent position, may contribute to residual limb swelling and therefore delay prosthetic fitting and rehabilitation, and they therefore agreed that this residual limb swelling should be avoided by proactive residual limb oedema management.

In order for people who have had an amputation to maintain and improve range of movement, particularly in hip flexors, hip abductors and knee flexors, the committee agreed that rehabilitation should be started which includes exercise, mobility including walking aids, and positioning, and that rehabilitation should not be delayed by waiting for prosthetics to be fitted, as the maintenance and improvement of range of movement will help prevent complications and optimise functional outcomes. The committee discussed that the muscles they emphasised (that is, the hip flexors, the hip abductors and knee flexors) were all related to leg function and therefore only

applicable to leg or lower limb amputations or loss, but they agreed that they were the muscles that needed emphasising because the optimisation of their function is central to the successful the rehabilitation of people with leg or lower limb loss or amputation. They noted that the recommendation is still applicable to people with loss or amputations of other limbs (than the leg), because it is still important for them to maintain and improve their range of movement to achieve optimal function, and exercise, mobility and positioning are also appropriate means to do so for them. The committee also recognised that providing appropriately fitted and adjusted wheelchairs as early as possible will significantly contribute to the person's rehabilitation by promoting independence and mobility and thereby increasing their ability to engage in activities of daily living.

In addition, the committee also agreed that most people with amputation are likely to require psychological support throughout their rehabilitation and recovery and that they therefore should continue to have access to psychological support with the option of input from a specialist practitioner psychologist, as adjusting to life after amputation due to traumatic injury can be very psychologically challenging. This support should include helping enable the person to adjust to their altered body image, manage pain and cope with the possibility that they may need further procedures. The committee agreed that this support does not need to be provided by a practitioner psychologist, but can be provided by any member of the specialist multidisciplinary team because the most important aspect of the delivery is that the person who delivers it has a specialist understanding of the issues that a person who has experienced limb reconstruction, limb loss or amputation may face. The committee therefore specified that the psychological and emotional support should include, that is, listening carefully and validating feelings, supporting reflection and reasoning around realistic goals and care, supporting planning and ensuring that there is feedback on success.

The person's needs and circumstances will continue to change and evolve over time and the committee therefore agreed that in order to optimise physical, psychological and other functional rehabilitation outcomes they should be offered a goal-orientated continual programme of multi-disciplinary rehabilitation that includes exercise and mobility, psychological and emotional support, referral and signposting to support groups, pin-site review and frame adjustment (for limb reconstruction) and prosthetics team review if relevant. Their rehabilitation plan should be reviewed at key points in their pathways, such as at discharge or if readmitted due to complications, to ensure it is fully reflective of the person's changing goals and needs, which in turn will help to ensure their full engagement in their rehabilitation.

Finally, the committee agreed that there are additional issues to take into account for children and young people because they are in a state of growth and development both physically and psychologically. These issues include the need to proactively assess and manage the impact of growth on the residual limb and prosthetic fitting to ensure that function is not compromised by the use of a prosthetic that is too small. They also include the need to consider the long term psychological impact of changing body image resulting from the limb reconstruction, loss or amputation, which the committee agreed is also an issue that is applicable to adults. Moreover, it is also important to actively monitor and accommodate any new and emerging emotional difficulties which may develop as the child or young person grow, for example, at key transition points such as moving to a new school. This is because some of these psychological and emotional issues may not emerge until later in the child or young person's life, and may emerge in connection with key transition points in their life, that are already potentially associated with psychological and emotional challenges, such as moving to a new school. Nevertheless, the committee agreed that they are still rehabilitation needs arising from the traumatic injury and should

therefore be proactively monitored and taken into account when their rehabilitation is planned or undertaken. The committee also agreed based on their experience that for children play and play therapy may be a useful way to offer psychological and emotional support.

Despite the limited evidence for these review questions, the committee decided not to make a research recommendation in this area. The committee discussed that, in their clinical experience, no intervention discussed had evidence of either significant harms or significant benefits. They therefore decided to prioritise other research areas where new evidence might allow new recommendations to be made or existing recommendations to be strengthened.

Cost effectiveness and resource use

No economic studies assessing the cost effectiveness of rehabilitation programmes and packages in people with a traumatic injury that results in limb reconstruction, limb loss or amputation were identified.

The committee explained that additional consultation time may be required to discuss with the child or young person and their family the potential treatment options. Understanding patients' and their families' preferences should improve the quality of care received and reduce uncertainty and anxiety patients and their families may have about treatment options, in particular, concerning limb amputation. Although this is currently done across services and the impact on the resources is likely to be negligible, if any.

The committee discussed the resource impact associated with a pre-amputation consultation that involves a specialist multidisciplinary team with expertise in prosthetic prescription and rehabilitation i.e. additional clinician time to attend such multidisciplinary team consultations. However, the committee noted that this is standard practice in most centres and is essential in ensuring the success of treatment in people undergoing amputation. These recommendations are therefore not expected to result in a resource impact.

The committee explained that offering trauma-informed psychological support before limb reconstruction or limb amputation may result in resource implications. However, amputation leads to high levels of anxiety, depression and emotional stress in the individual. If left unaddressed, such symptoms may require expensive care further down the line. Such symptoms are also associated with persistent poor long-term quality of life and may result in a substantial loss in quality-adjusted life years (QALYs). For the same reasons, the committee justified the provision of trauma-focused psychological support following limb loss or amputation. The committee explained that most services have access to a psychologist and this would not result in additional resources to services. The committee explained that the psychological impact is likely to be more pronounced in children and young people due to the changing body image and the benefits of such psychological support would far outweigh intervention costs. Also, such support is already widely available across the health service.

The committee explained that the rehabilitation package following limb reconstruction comprises of therapies that are widely used across rehabilitation centres and would not incur additional resources to the health service. Similarly, the recommendations about the timing of rehabilitation and specific rehabilitation therapies following limb loss or amputation reflect standard practice and would not incur additional resources. Moreover, the committee explained that given the clinical need such care is essential in ensuring the success of rehabilitation.

The recommendations about pain management, and residual limb oedema and shaping reflect standard practice and would not incur additional resources to the services. Similarly, mirror therapy is widely available and is a low-cost intervention. Graded motor imagery is less commonly used and should be delivered by staff with appropriate skills, potentially resulting in extra training costs where it is currently unavailable. However, it can reduce pain and lead to substantial improvements in quality of life in people who have undergone amputations, and it is expected to represent value for money.

Therapy interventions to prevent loss of range of motion and improve range of motion specifically, muscle groups prone to loss of length (hip flexors hip abductors, knee flexors that may inhibit functional and prosthetic outcomes long term) are widely available and are low-cost interventions. Given the clinical need, their use was judged to be essential for the success of rehabilitation.

The initiation of rehabilitation before a prosthetic is fitted should speed up access to rehabilitation and may reduce the duration of expensive inpatient rehabilitation. Also, delays in rehabilitation may prolong recovery and result in higher utilisation of health care resources. This recommendation may potentially be cost-saving.

The committee discussed difficulties surrounding access to wheelchairs. However, the implied timing, i.e. as early as possible in the recommendation, may pressure services to provide these quicker. However, this recommendation is not expected to result in additional resources to the health service because services would have had to provide a wheelchair anyway.

It was explained that following limb reconstruction, limb loss or amputation more clinicians' time may be required to discuss with the person and their family, goals plan for discharge, etc., however, this is currently done by most services and is not expected to result in additional resources to the services.

A goal-orientated continual program of multidisciplinary rehabilitation represents standard practice. Given the clinical need, the committee was of a view that such rehabilitation programme is justified and is essential to ensure the success of rehabilitation for limb reconstruction, limb loss or amputation.

Children's rehabilitation services closely monitor the impact of growth on the residual limb and prosthetic fitting and refer early for expert assessment when there are changes. Such practice is standard across rehabilitation services and would not result in additional referrals.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.14.1 to 1.14.24 in the NICE guideline.

References

Evidence for adults

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Ol, Ha Sam, Van Heng, Yang, Danielsson, Lena, Husum, Hans, Mirror therapy for phantom limb and stump pain: a randomized controlled clinical trial in landmine amputees in Cambodia, Scandinavian journal of pain, 18, 603-610, 2018

Topuz 2012

Topuz, S., Ulger, O., Bakar, Y., Sener, G., Comparison of the effects of complex decongestive physiotherapy and conventional bandaging on edema of geriatric amputees: a pilot study, Topics in geriatric rehabilitation, 28, 275-280, 2012

Evidence for children and young people

A systematic review of the literature was conducted, but no studies were identified which were applicable to this review questions

Appendices

Appendix A – Review protocols

Review protocol for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Table 3: Review protocol for specific programmes and packages in limb reconstruction, limb loss or amputation for adults

ID	Field	Content
0.	PROSPERO registration number	CRD42019123909
1.	Review title	Specific programmes and packages in amputation for adults
2.	Review question	For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?
3.	Objective	To evaluate the effectiveness of specific rehabilitation programmes and packages including prosthetics among adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • Date: 1995 onwards as there has been significant change in practice since then • English language • Human studies The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Complex rehabilitation needs resulting from traumatic injury 'Complex rehab needs' refers to 'multiple needs, and will always involve coordinated multidisciplinary input from 2 or more allied health professional disciplines, and could also include the following: • Vocational or educational social support for the person to return to their pervious functional level, including return to work, school or college

ID	Field	Content
		• Emotional, psychological and psychosocial support • Equipment or adaptations • Ongoing recovery from injury that may change the person's rehabilitation needs (for example, restrictions of weight bearing, cast immobilisation in feature clinic) • Further surgery and readmissions to hospital Traumatic injury is defined as 'traumatic injury as injury that requires admission to hospital at the time of injury.'
6	Population	Inclusion: • Adults (aged 18 years and above) with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation and requires admission to hospital Exclusion: • Adults with complex rehabilitation needs resulting from traumatic brain injury (including anoxic brain injury, for example, drowning and strangulation) • Adults with traumatic injuries who do not have complex rehabilitation needs and/or do not require admission to hospital • Adults with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation who are admitted to the ICU
7	Intervention	Standard care consisting of at least 2 of 4 (physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management) in addition to at least one of the following <u>Limb reconstruction interventions:</u> • Splinting to maintain range of movement • Hydrotherapy • Anti-gravity treadmill training • Psychological therapies for adjustment and engagement (Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness • Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Vocational support/ rehabilitation and workplace interventions (ergonomics)

ID	Field	Content
		Amputation interventions: • Prostheses • Early/non-definitive walking aids (PPAM pneumatic post-amputation mobility aid, femurette/ femuret, AMA amputee mobility aid) • Early scar/stump/residual limb swelling and oedema management (within 4 weeks of amputation) • Psychological therapies for adjustment and engagement (Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness, Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Vocational support/ rehabilitation and workplace interventions (ergonomics) Exclusion: • Rehabilitation packages and programmes relating to traumatic brain injury, sight loss and hearing loss • Social care interventions (for example, home care or personal assistance) • Long-term care and rehabilitation packages for people with long-term care needs • Specific pain management interventions
8	Comparator/Reference standard/Confounding factors	1) Standard care consisting of at least 2 of 4 (physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management) 2) Studies that employ the same intervention program as listed under 'interventions' but vary it in terms of any of the following: ○ Frequency ○ Intensity ○ Timing
9	Types of study to be included	• Systematic review of RCTs • Randomised controlled trial If no RCT data are available for an intervention, evidence from the followings will be considered in order • Cluster-randomised trial • Systematic review of non-randomised studies • Comparative prospective cohort studies with N≥100 per treatment arm • Comparative retrospective cohort studies with N≥100 per treatment arm

ID	Field	Content
10	Other exclusion criteria	Study design: • Cross-over design • Case-controls • Cross-sectional • Case series and case reports • Audits • Language: • Non-English Publication status: • Abstract only
11	Context	Settings - Inclusion: • All inpatient, outpatient and community settings in which rehabilitation services following traumatic injury are provided Exclusion: • Accident and emergency departments • Critical care units • Prisons
12	Primary outcomes (critical outcomes)	Critical: • Overall quality of life [EURO-QoL 5D 3L, SF-36, SF-12, SF-6D] • Changes in mobility (any measure) • Pain (VAS) • Patient acceptability (any direct measure) Timeframe for the follow-up will be 6-18 months. This will be grouped into short-term (0-6 months) and long-term (more than 6 months).
13	Secondary outcomes (important outcomes)	Important: • Hospital readmission • Return to work or education • Changes in mood [Depression measures – HADS, PH-Q9, BDI, DASS] • Changes in activity of daily living (Barthel ADL index, EADL-Test, Katz, OARS, PAT, PSMS)

ID	Field	Content
		• Timeframe for the follow-up will be 6-18 months. This will be grouped into short-term (0-6 months) and long-term (more than 6 months).
14	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4.
15	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.
16	Strategy for data synthesis	NGA STAR software will be used for generating bibliographies/citations, study sifting and data extraction. 'GRADEpro' will be used to assess the quality of evidence for each outcome If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan). MIDs: See methods chapter of the guideline
17	Analysis of sub-groups	No subgroups were identified for this question, but if there is heterogeneity, we will look at the following subgroups to try to identify the source of it:. • People with pre-existing physical and/or mental health conditions (including substance misuse), physical and learning disability, or frailty • People who require safeguarding
18	Type and method of review	Intervention
19	Language	English
20	Country	England
21	Anticipated or actual start date	10/01/2019
22	Anticipated completion date	24/11/2020
23	Stage of review at time of this submission	**Review stage** / **Started** / **C** Preliminary searches / ☑ / ☑ Piloting of the study selection process / ☑ / ☑ Formal screening of search results against eligibility criteria / ☑ / ☑ Data extraction / ☐ / ☐ Risk of bias (quality) assessment / ☐ / ☐

ID	Field	Content
		Data analysis
24	Named contact	National Guideline Alliance
25	Review team members	National Guideline Alliance
26	Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.
27	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10105
29	Other registration details	
30	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019123909
31	Dissemination plans	
32	Keywords	
33	Details of existing review of same topic by same authors	
34	Current review status	
35	Additional information	
36	Details of final publication	www.nice.org.uk

ADL: activities of daily living; AMA: amputee mobility aid; BDI: Beck's Depression Inventory; DASS: Depression Anxiety Stress Scales; EADL-Test: Erlangen Activities of Daily Living test; EURO-QoL 5D 3L: an instrument for measuring quality of life 3 levels of severity for 5 dimensions; HADS: Hospital Anxiety and Depression Scale; ICU: intensive care unit; MID(s): minimally important difference(s); N: Number; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; OARS: Older Americans Resources and Services; PAT: Performance ADL Test; PHQ-9: Patient health questionnaire; PSMS: Physical Self-Maintenance Scale;

RCT(s): randomised controlled trial(s); RoB: risk of bias; SF-6D: short-form six-dimension to assess the cost-effectiveness of health care interventions; SF-12: a short-form survey with 12 questionnaires selected from; VAS: Visual analogue scale

Review protocol for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Table 4: Review protocol for specific programmes and packages in limb reconstruction, limb loss or amputation for children and young people

ID	Field	Content
0.	PROSPERO registration number	CRD42019129992
1.	Review title	Specific programmes and packages in amputation for children and young people
2.	Review question	For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?
3.	Objective	To evaluate the effectiveness of specific rehabilitation programmes and packages including prosthetics among children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction
4.	Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Searches will be restricted by: Date: 1995 onwards as there has been significant change in practice since then English language Human studies The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Complex rehabilitation needs resulting from traumatic injury 'Complex rehab needs' refers to 'multiple needs, and will always involve coordinated multidisciplinary input from 2 or

ID	Field	Content
		more allied health professional disciplines, and could also include the following: • Vocational or educational social support for the person to return to their previous functional level, including return to work, school or college • Emotional, psychological and psychosocial support • Equipment or adaptations • Ongoing recovery from injury that may change the person's rehabilitation needs (for example, restrictions of weight bearing, cast immobilisation in feature clinic) • Further surgery and readmissions to hospital Further surgery and readmissions to hospital Traumatic injury is defined as 'traumatic injury as injury that requires admission to hospital at the time of injury.'
6	Population	Inclusion: Children and young people (aged below 18 years) with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation and requires admission to hospital Exclusion: • Children and young people with complex rehabilitation needs resulting from traumatic brain injury (including anoxic brain injury, for example, drowning and strangulation) • Children and young people with traumatic injuries who do not have complex rehabilitation needs and/or do not require admission to hospital • Children and young people with complex rehabilitation needs resulting from traumatic injury that results in limb reconstruction, limb loss or amputation who are currently admitted to the PICU
7	Intervention	Standard care consisting of at least 2 of 4 (physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management) in addition to at least one of the following <u>Limb reconstruction interventions:</u> • Splinting to maintain range of movement • Hydrotherapy • Anti-gravity treadmill training • Psychological therapies for adjustment and engagement (Family therapy,Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness Visualisation or 'mentalisation' to support physical rehab,

ID	Field	Content
		Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Educational support/ rehabilitation and school-based interventions (ergonomics) • Play therapy/specialist play therapy • Theraband (stretchy elastic that provides resistance that is widely used by OTs and PTs) <u>Amputation interventions:</u> • Prostheses • Early/non-definitive walking aids (PPAM pneumatic post-amputation mobility aid, femurette/ femuret, AMA amputee mobility aid) • Early scar/stump/residual limb swelling and oedema management (within 4 weeks of amputation) • Psychological therapies for adjustment and engagement (Family therapy, Compassionate mind therapy, Acceptance and commitment therapy, Mindfulness, Visualisation or 'mentalisation' to support physical rehab, Relaxation [progressive, or breathing based, or other], Mirror therapy, Cognitive behavioural therapy) • Educational support/ rehabilitation and school-based interventions (ergonomics) • Play therapy/specialist play therapy • Theraband (stretchy elastic that provides resistance that is widely used by OTs and PTs) Exclusion: • Rehabilitation packages and programmes relating to traumatic brain injury, sight loss and hearing loss • Social care interventions (for example, home care or personal assistance) • Long-term care and rehabilitation packages for people with long-term care needs • Specific pain management interventions • Eye Movement Desensitization and reprocessing is not include as it is part of PTSD treatment for which there is a NICE guideline • Early weight-bearing is not included as it is considered as part of standard care
8	Comparator/Reference standard/Confounding factors	Standard care consisting of at least 2 of 4 (physiotherapy [range of movement exercises, exercises to maintain muscle function, mobilisation and training with mobilisation aids such as crutches or frame], occupational therapy assessment, identification and support of activities of daily living through training or aids, and acute pain management)

ID	Field	Content
		Studies that employ the same intervention program as listed under 'interventions' but vary it in terms of any of the following: • Frequency • Intensity • Timing
9	Types of study to be included	• Systematic review of RCTs • Randomised controlled trial If no RCT data are available for an intervention, evidence from the followings will be considered in order • Cluster-randomised trial • Systematic review of non-randomised studies • Comparative prospective cohort studies with N≥100 per treatment arm • Comparative retrospective cohort studies with N≥100 per treatment arm
10	Other exclusion criteria	Study design: • Cross-over design • Case-controls • Cross-sectional • Case series and case reports • Audits Language: • Non-English Publication status: • Abstract only
11	Context	Settings - Inclusion: All inpatient, outpatient and community settings in which rehabilitation services following traumatic injury are provided Exclusion: • Accident and emergency departments • Critical care units

ID	Field	Content
		• Prisons
12	Primary outcomes (critical outcomes)	Critical: • Overall quality of life (CHQ-CF80, CHQ-PF-50, PEDS-QL, EURO-QoL 5D 3L, SF-36, SF-12, SF-6D) • Changes in mobility (WeeFIM, any measure) • Pain (VAS, any measure) • Patient acceptability (any direct measure; if not reported, but patient satisfaction is, this will be reported instead) Timeframe for the follow-up will be 0-18 months. This will be grouped into short-term (0-6 months) and long-term (more than 6 months)
13	Secondary outcomes (important outcomes)	Important: • Hospital readmission • Return to education or work • Changes in mood (Any measure, PEDS-QL, Depression measures – HADS, PH-Q9, BDI, DAS) • Changes in activity of daily living (Barthel ADL index, COPM, EADL-Test, Katz, OARS, PAT, PSMS) Timeframe for the follow-up will be 0-18 months. This will be grouped into short-term (0-6 months) and long-term (more than 6 months).
14	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4.
15	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.
16	Strategy for data synthesis	NGA STAR software will be used for generating bibliographies/citations, study sifting and data extraction. If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan). 'GRADEpro' will be used to assess the quality of evidence for each outcome.
17	Analysis of sub-groups	No subgroups were specified for this question for stratification of the data, but if there is heterogeneity, we will look at the following subgroups to try to identify the source of it:. • Children and young people with pre-existing physical and/or mental health conditions (including substance misuse), physical and learning disability, or prematurity versus no preexisting conditions • Children and young people who are suspected of sustaining non-accidental injuries versus accidental injuries • Children and young people whose parents are very involved in their rehabilitation/recovery (e.g., by staying

ID	Field	Content
		overnight in hospital) versus not involved • Age (0-3 versus 4-7 versus 8-12 versus 13-17)
18	Type and method of review	Intervention
19	Language	English
20	Country	England
21	Anticipated or actual start date	25 March 2019
22	Anticipated completion date	24 November 2020
23	Stage of review at time of this submission	Preliminary searches done
24	Named contact	National Guideline Alliance
25	Review team members	National Guideline Alliance
26	Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.
27	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10105
29	Other registration details	
30	Reference/URL for	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019129992

ID	Field	Content
	published protocol	
31	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: C.1a notifying registered stakeholders of publication C.1b publicising the guideline through NICE's newsletter and alerts, issuing a press release or briefing as appropriate C.1c posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32	Keywords	
33	Details of existing review of same topic by same authors	New review
34	Current review status	
35	Additional information	
36	Details of final publication	www.nice.org.uk

Barthel ADL index: Barthel Index for Activities of Daily Living; BDI: Beck's Depression Inventory; CHQ-CF80: a self-report measure of child health questionnaires; CHQ-PF-50: a measure of child health questionnaires for parents; COPM: Canadian Occupational Performance Measure; DASS: Depression Anxiety Stress Scales; EADL-Test: Erlangen Activities of Daily Living test; EQ-5D-Y: an child-friendly EQ-5D version for measuring quality of life; HADS: Hospital Anxiety and Depression Scale; ICU: intensive care unit; Katz: a tool to assess independence in activities of daily living; N: Number; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; OARS: Older Americans Resources and Services; OTs: occupational therapists; PAT: Performance ADL Test; Peds-QL: Pediatric Quality of Life Inventory ;PHQ-9: Patient health questionnaire; PICU: Paediatric intensive care unit; PSMS: Physical Self-Maintenance Scale; PT: physical therapists; PTSD: Post-traumatic stress disorder; RCT(s): randomised controlled trial(s); RoB: risk of bias; SF-6D: short-form six-dimension to assess the cost-effectiveness of health care interventions; SF-12: a short-form survey with 12 questionnaires selected from SF-36 to create 2 scales to assess mental and physical functioning and overall health-related quality of life; SF-36: Short form health survey-36; VAS: visual analog scale; WeeFIM: standardized measure of functional independence for use in children

Appendix B – Literature search strategies

Literature search strategies for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Note the searches for this review question were re-run on 10/11/2020 but with a randomized controlled search filter added. This was in order to capture any high level evidence published since the original search was run on 01/01/2019.

Review question search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	exp AMPUTATION/
2	AMPUTATION, TRAUMATIC/
3	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
4	AMPUTEES/
5	amputee?.ti,ab.
6	(limb? adj3 (loss or losing or lost)).ti,ab.
7	AMPUTATION STUMPS/
8	LIMB SALVAGE/
9	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
10	or/1-9
11	SPLINTS/
12	exp ORTHOTIC DEVICES/
13	splint$.ti,ab.
14	orthos?s.ti,ab.
15	orthotic?.ti,ab.
16	brace?.ti,ab.
17	HYDROTHERAPY/
18	hydrotherap$.ti,ab.
19	HYPOGRAVITY/
20	hypograv$.ti,ab.
21	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
22	PROSTHESIS FITTING/
23	(prosthe$ adj5 fit$).ti,ab.
24	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
25	ARTIFICIAL LIMBS/ and TIME FACTORS/
26	exp JOINT PROSTHESIS/ and TIME FACTORS/
27	WEIGHT-BEARING/ and TIME FACTORS/
28	(prosthe$ adj3 (time or timing)).ti,ab.
29	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
30	(prosthe$ adj3 earl$).ti,ab.
31	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
32	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
33	(prosthe$ adj5 temporar$).ti,ab.
34	EARLY AMBULATION/mt [Methods]
35	(earl$ adj3 walk$ adj3 aid?).ti,ab.
36	EWA.ti,ab.
37	(mobilit$ adj3 aid?).ti,ab.
38	PPAM?.ti,ab.
39	AMA.ti,ab.
40	femuret$.ti,ab.
41	EDEMA/pc [Prevention & Control]
42	EDEMA/th [Therapy]
43	EDEMA/ and (BANDAGES/ or COMPRESSION BANDAGES/ or STOCKINGS, COMPRESSION/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICES/ or NEGATIVE-PRESSURE WOUND THERAPY/ or MASSAGE/ or BED REST/)

#	Searches
44	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
45	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
46	"ACCEPTANCE AND COMMITMENT THERAPY"/
47	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
48	MINDFULNESS/
49	Mindfulness.ti,ab.
50	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
51	mentali?ation.ti,ab.
52	RELAXATION THERAPY/
53	BREATHING EXERCISES/
54	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
55	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
56	COGNITIVE THERAPY/
57	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
58	CBT.ti,ab.
59	REHABILITATION, VOCATIONAL/
60	(EMPLOYMENT/ or EMPLOYMENT, SUPPORTED/ or WORKPLACE/) and (ADAPTATION, PHYSIOLOGICAL/ or ACCLIMATIZATION/ or exp ADAPTATION, PSYCHOLOGICAL/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF-HELP DEVICES/)
61	((vocation$ or work$ or job? or employment or employee? or profession? or occupation?) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
62	RETURN TO WORK/
63	(return$ adj3 work$).ti,ab.
64	VOCATIONAL GUIDANCE/
65	((vocation$ or work$ or job? or employment or employee? or profession? or occupation? or career?) adj5 (guid$ or counsel$)).ti,ab.
66	or/11-65
67	10 and 66
68	limit 67 to english language
69	limit 68 to yr="1995 -Current"
70	LETTER/
71	EDITORIAL/
72	NEWS/
73	exp HISTORICAL ARTICLE/
74	ANECDOTES AS TOPIC/
75	COMMENT/
76	CASE REPORT/
77	(letter or comment*).ti.
78	or/70-77
79	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
80	78 not 79
81	ANIMALS/ not HUMANS/
82	exp ANIMALS, LABORATORY/
83	exp ANIMAL EXPERIMENTATION/
84	exp MODELS, ANIMAL/
85	exp RODENTIA/
86	(rat or rats or mouse or mice).ti.
87	or/80-86
88	69 not 87

Databases: Embase; and Embase Classic

#	Searches
1	exp AMPUTATION/
2	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
3	AMPUTEE/
4	amputee?.ti,ab.
5	(limb? adj3 (loss or losing or lost)).ti,ab.
6	LIMB SALVAGE/
7	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
8	or/1-7
9	exp ORTHOSIS/
10	splint$.ti,ab.
11	orthos?s.ti,ab.
12	orthotic?.ti,ab.
13	brace?.ti,ab.
14	HYDROTHERAPY/
15	hydrotherap$.ti,ab.
16	MICROGRAVITY/

#	Searches
17	hypograv$.ti,ab.
18	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
19	PROSTHETIC FITTING/
20	(prosthe$ adj5 fit$).ti,ab.
21	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
22	exp LIMB PROSTHESIS/ and TIME FACTOR/
23	exp JOINT PROSTHESIS/ and TIME FACTOR/
24	WEIGHT BEARING/ and TIME FACTOR/
25	(prosthe$ adj3 (time or timing)).ti,ab.
26	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
27	(prosthe$ adj3 earl$).ti,ab.
28	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
29	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
30	(prosthe$ adj5 temporar$).ti,ab.
31	*MOBILIZATION/
32	(earl$ adj3 walk$ adj3 aid?).ti,ab.
33	EWA.ti,ab.
34	(mobilit$ adj3 aid?).ti,ab.
35	PPAM?.ti,ab.
36	AMA.ti,ab.
37	femuret$.ti,ab.
38	exp EDEMA/pc [Prevention]
39	exp EDEMA/th [Therapy]
40	exp EDEMA/ and (BANDAGE/ or COMPRESSION BANDAGE/ or COMPRESSION STOCKINGS/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICE/ or VACUUM ASSISTED CLOSURE/ or MASSAGE/ or BED REST/)
41	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
42	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
43	"ACCEPTANCE AND COMMITMENT THERAPY"/
44	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
45	MINDFULNESS/
46	Mindfulness.ti,ab.
47	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
48	mentali?ation.ti,ab.
49	RELAXATION TRAINING/
50	BREATHING EXERCISE/
51	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
52	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
53	COGNITIVE BEHAVIORAL THERAPY/
54	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
55	CBT.ti,ab.
56	VOCATIONAL REHABILITATION/
57	JOB ADAPTATION/
58	(exp EMPLOYMENT/ or WORKPLACE/) and (ADAPTATION/ or ACCLIMATIZATION/ or exp COPING BEHAVIOR/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF HELP DEVICE/ or ASSISTIVE TECHNOLOGY DEVICE/)
59	((vocation$ or work$ or job? or employment or employee? or profession? or occupation?) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
60	RETURN TO WORK/
61	WORK RESUMPTION/
62	(return$ adj3 work$).ti,ab.
63	VOCATIONAL GUIDANCE/
64	((vocation$ or work$ or job? or employment or employee? or profession? or occupation? or career?) adj5 (guid$ or counsel$)).ti,ab.
65	or/9-64
66	8 and 65
67	limit 66 to english language
68	limit 67 to yr="1995 -Current"
69	letter.pt. or LETTER/
70	note.pt.
71	editorial.pt.
72	CASE REPORT/ or CASE STUDY/
73	(letter or comment*).ti.
74	or/69-73
75	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
76	74 not 75
77	ANIMAL/ not HUMAN/
78	NONHUMAN/

#	Searches
79	exp ANIMAL EXPERIMENT/
80	exp EXPERIMENTAL ANIMAL/
81	ANIMAL MODEL/
82	exp RODENT/
83	(rat or rats or mouse or mice).ti.
84	or/76-83
85	68 not 84

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

#	Searches
#1	[mh AMPUTATION]
#2	[mh ^"AMPUTATION, TRAUMATIC"]
#3	(amputat* or disarticulation* or dis-articulation* or hemipelvectom*):ti,ab
#4	[mh ^AMPUTEES]
#5	amputee*:ti,ab
#6	(limb* near/3 (loss or losing or lost)):ti,ab
#7	[mh ^"AMPUTATION STUMPS"]
#8	[mh ^"LIMB SALVAGE"]
#9	(limb* near/3 (salvag* or re-construct* or reconstruct*)):ti,ab
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
#11	[mh ^SPLINTS]
#12	[mh "ORTHOTIC DEVICES"]
#13	splint*:ti,ab
#14	orthos*:ti,ab
#15	orthotic*:ti,ab
#16	brace*:ti,ab
#17	[mh ^HYDROTHERAPY]
#18	hydrotherap*:ti,ab
#19	[mh ^HYPOGRAVITY]
#20	hypograv*:ti,ab
#21	((antigravit* or ((anti or low or reduc*) near/3 gravit*)) near/5 (treadmill* or 'running machine*')):ti,ab
#22	[mh ^"PROSTHESIS FITTING"]
#23	(prosthe* near/5 fit*):ti,ab
#24	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 fit*):ti,ab
#25	[mh ^"ARTIFICIAL LIMBS"]
#26	[mh "JOINT PROSTHESIS"]
#27	[mh ^"WEIGHT-BEARING"]
#28	#25 or #26 or #27
#29	[mh ^"TIME FACTORS"]
#30	#28 and #29
#31	(prosthe* near/3 (time or timing)):ti,ab
#32	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 (time or timing)):ti,ab
#33	(prosthe* near/3 earl*):ti,ab
#34	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 earl*):ti,ab
#35	(weight* near/3 (bear* or load*) near/5 earl*):ti,ab
#36	(prosthe* near/5 temporar*):ti,ab
#37	[mh ^"EARLY AMBULATION"/mt]
#38	(earl* near/3 walk* near/3 aid*):ti,ab
#39	EWA:ti,ab
#40	(mobilit* near/3 aid*):ti,ab
#41	PPAM*:ti,ab
#42	AMA:ti,ab
#43	femuret*:ti,ab
#44	[mh ^EDEMA/pc]
#45	[mh ^EDEMA/th]
#46	[mh ^EDEMA]
#47	[mh ^BANDAGES]
#48	[mh ^"COMPRESSION BANDAGES"]
#49	[mh ^"STOCKINGS, COMPRESSION"]
#50	[mh ^"INTERMITTENT PNEUMATIC COMPRESSION DEVICES"]
#51	[mh ^"NEGATIVE-PRESSURE WOUND THERAPY"]
#52	[mh ^MASSAGE]
#53	[mh ^"BED REST"]
#54	#47 or #48 or #49 or #50 or #51 or #52 or #53
#55	#46 and #54

#	Searches
#56	((oedema* or edema* or swell*) near/7 (manag* or therap* or bandag* or stocking* or compres* or massag* or (bed* near/3 rest*) or (leg* near/3 rais*))):ti,ab
#57	(Compassion* near/3 mind* near/3 (therap* or train*)):ti,ab
#58	[mh ^"ACCEPTANCE AND COMMITMENT THERAPY"]
#59	(Accept* near/3 commit* near/3 (therap* or train*)):ti,ab
#60	[mh ^MINDFULNESS]
#61	Mindfulness:ti,ab
#62	((Visualisation or visualization) near/3 (therap* or train*)):ti,ab
#63	(mentalisation or mentalization):ti,ab
#64	[mh ^"RELAXATION THERAPY"]
#65	[mh ^"BREATHING EXERCISES"]
#66	((Relax* or progressive* or breath*) near/3 (therap* or train* or exercis*)):ti,ab
#67	(Mirror* near/3 (therap* or train* or feedback)):ti,ab
#68	[mh ^"COGNITIVE THERAPY"]
#69	(Cognit* near/3 behav* near/3 (therap* or train*)):ti,ab
#70	CBT:ti,ab
#71	[mh ^"REHABILITATION, VOCATIONAL"]
#72	[mh ^EMPLOYMENT]
#73	[mh ^"EMPLOYMENT, SUPPORTED"]
#74	[mh ^WORKPLACE]
#75	#72 or #73 or #74
#76	[mh ^"ADAPTATION, PHYSIOLOGICAL"]
#77	[mh ^ACCLIMATIZATION]
#78	[mh "ADAPTATION, PSYCHOLOGICAL"]
#79	[mh ^ERGONOMICS]
#80	[mh ^"EQUIPMENT DESIGN"]
#81	[mh ^"SELF-HELP DEVICES"]
#82	#76 or #77 or #78 or #79 or #80 or #81
#83	#75 and #82
#84	((vocation* or work* or job* or employment or employee* or profession* or occupation*) near/5 (rehab* or support* or adjust* or adapt* or chang* or reintegrat* or re-integrat* or facilitat* or intervention* or equipment or ergonomic* or "assist* tech*")):ti,ab
#85	[mh ^"RETURN TO WORK"]
#86	(return* near/3 work*):ti,ab
#87	[mh ^"VOCATIONAL GUIDANCE"]
#88	((vocation* or work* or job* or employment or employee* or profession* or occupation* or career*) near/5 (guid* or counsel*)):ti,ab
#89	#11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #83 or #84 or #85 or #86 or #87 or #88
#90	#10 and #89 with Publication Year from 1995 to 2019, in Trials
#91	#10 and #89 with Cochrane Library publication date Between Jan 1995 and Jan 2019, in Cochrane Reviews, Cochrane Protocols

Health economics search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.

#	Searches
20	ec.fs.
21	or/1-20
22	exp AMPUTATION/
23	AMPUTATION, TRAUMATIC/
24	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
25	AMPUTEES/
26	amputee?.ti,ab.
27	(limb? adj3 (loss or losing or lost)).ti,ab.
28	AMPUTATION STUMPS/
29	LIMB SALVAGE/
30	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
31	or/22-30
32	SPLINTS/
33	exp ORTHOTIC DEVICES/
34	splint$.ti,ab.
35	orthos?s.ti,ab.
36	orthotic?.ti,ab.
37	brace?.ti,ab.
38	HYDROTHERAPY/
39	hydrotherap$.ti,ab.
40	HYPOGRAVITY/
41	hypograv$.ti,ab.
42	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
43	PROSTHESIS FITTING/
44	(prosthe$ adj5 fit$).ti,ab.
45	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
46	ARTIFICIAL LIMBS/ and TIME FACTORS/
47	exp JOINT PROSTHESIS/ and TIME FACTORS/
48	WEIGHT-BEARING/ and TIME FACTORS/
49	(prosthe$ adj3 (time or timing)).ti,ab.
50	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
51	(prosthe$ adj3 earl$).ti,ab.
52	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
53	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
54	(prosthe$ adj5 temporar$).ti,ab.
55	EARLY AMBULATION/mt [Methods]
56	(earl$ adj3 walk$ adj3 aid?).ti,ab.
57	EWA.ti,ab.
58	(mobilit$ adj3 aid?).ti,ab.
59	PPAM?.ti,ab.
60	AMA.ti,ab.
61	femuret$.ti,ab.
62	EDEMA/pc [Prevention & Control]
63	EDEMA/th [Therapy]
64	EDEMA/ and (BANDAGES/ or COMPRESSION BANDAGES/ or STOCKINGS, COMPRESSION/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICES/ or NEGATIVE-PRESSURE WOUND THERAPY/ or MASSAGE/ or BED REST/)
65	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
66	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
67	"ACCEPTANCE AND COMMITMENT THERAPY"/
68	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
69	MINDFULNESS/
70	Mindfulness.ti,ab.
71	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
72	mentali?ation.ti,ab.
73	RELAXATION THERAPY/
74	BREATHING EXERCISES/
75	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
76	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
77	COGNITIVE THERAPY/
78	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
79	CBT.ti,ab.
80	REHABILITATION, VOCATIONAL/
81	(EMPLOYMENT/ or EMPLOYMENT, SUPPORTED/ or WORKPLACE/) and (ADAPTATION, PHYSIOLOGICAL/ or ACCLIMATIZATION/ or exp ADAPTATION, PSYCHOLOGICAL/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF-HELP DEVICES/)
82	((vocation$ or work$ or job? or employment or employee? or profession? or occupation?) adj5 (rehab$ or support$ or

#	Searches
	adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
83	RETURN TO WORK/
84	(return$ adj3 work$).ti,ab.
85	VOCATIONAL GUIDANCE/
86	((vocation$ or work$ or job? or employment or employee? or profession? or occupation? or career?) adj5 (guid$ or counsel$)).ti,ab.
87	or/32-86
88	31 and 87
89	limit 88 to english language
90	limit 89 to yr="1995 -Current"
91	LETTER/
92	EDITORIAL/
93	NEWS/
94	exp HISTORICAL ARTICLE/
95	ANECDOTES AS TOPIC/
96	COMMENT/
97	CASE REPORT/
98	(letter or comment*).ti.
99	or/91-98
100	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
101	99 not 100
102	ANIMALS/ not HUMANS/
103	exp ANIMALS, LABORATORY/
104	exp ANIMAL EXPERIMENTATION/
105	exp MODELS, ANIMAL/
106	exp RODENTIA/
107	(rat or rats or mouse or mice).ti.
108	or/101-107
109	90 not 108
110	21 and 109

Databases: Embase; and Embase Classic

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp AMPUTATION/
19	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
20	AMPUTEE/
21	amputee?.ti,ab.
22	(limb? adj3 (loss or losing or lost)).ti,ab.
23	LIMB SALVAGE/
24	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
25	or/18-24
26	exp ORTHOSIS/
27	splint$.ti,ab.
28	orthos?s.ti,ab.
29	orthotic?.ti,ab.
30	brace?.ti,ab.
31	HYDROTHERAPY/
32	hydrotherap$.ti,ab.
33	MICROGRAVITY/
34	hypograv$.ti,ab.
35	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.

#	Searches
36	PROSTHETIC FITTING/
37	(prosthe$ adj5 fit$).ti,ab.
38	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
39	exp LIMB PROSTHESIS/ and TIME FACTOR/
40	exp JOINT PROSTHESIS/ and TIME FACTOR/
41	WEIGHT BEARING/ and TIME FACTOR/
42	(prosthe$ adj3 (time or timing)).ti,ab.
43	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
44	(prosthe$ adj3 earl$).ti,ab.
45	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
46	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
47	(prosthe$ adj5 temporar$).ti,ab.
48	*MOBILIZATION/
49	(earl$ adj3 walk$ adj3 aid?).ti,ab.
50	EWA.ti,ab.
51	(mobilit$ adj3 aid?).ti,ab.
52	PPAM?.ti,ab.
53	AMA.ti,ab.
54	femuret$.ti,ab.
55	exp EDEMA/pc [Prevention]
56	exp EDEMA/th [Therapy]
57	exp EDEMA/ and (BANDAGE/ or COMPRESSION BANDAGE/ or COMPRESSION STOCKINGS/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICE/ or VACUUM ASSISTED CLOSURE/ or MASSAGE/ or BED REST/)
58	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
59	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
60	"ACCEPTANCE AND COMMITMENT THERAPY"/
61	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
62	MINDFULNESS/
63	Mindfulness.ti,ab.
64	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
65	mentali?ation.ti,ab.
66	RELAXATION TRAINING/
67	BREATHING EXERCISE/
68	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
69	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
70	COGNITIVE BEHAVIORAL THERAPY/
71	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
72	CBT.ti,ab.
73	VOCATIONAL REHABILITATION/
74	JOB ADAPTATION/
75	(exp EMPLOYMENT/ or WORKPLACE/) and (ADAPTATION/ or ACCLIMATIZATION/ or exp COPING BEHAVIOR/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF HELP DEVICE/ or ASSISTIVE TECHNOLOGY DEVICE/)
76	((vocation$ or work$ or job? or employment or employee? or profession? or occupation?) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
77	RETURN TO WORK/
78	WORK RESUMPTION/
79	(return$ adj3 work$).ti,ab.
80	VOCATIONAL GUIDANCE/
81	((vocation$ or work$ or job? or employment or employee? or profession? or occupation? or career?) adj5 (guid$ or counsel$)).ti,ab.
82	or/26-81
83	25 and 82
84	limit 83 to english language
85	limit 84 to yr="1995 -Current"
86	letter.pt. or LETTER/
87	note.pt.
88	editorial.pt.
89	CASE REPORT/ or CASE STUDY/
90	(letter or comment*).ti.
91	or/86-90
92	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
93	91 not 92
94	ANIMAL/ not HUMAN/
95	NONHUMAN/
96	exp ANIMAL EXPERIMENT/
97	exp EXPERIMENTAL ANIMAL/

#	Searches
98	ANIMAL MODEL/
99	exp RODENT/
100	(rat or rats or mouse or mice).ti.
101	or/93-100
102	85 not 101
103	17 and 102

Database: Cochrane Central Register of Controlled Trials

#	Searches
#1	MeSH descriptor: [Economics] this term only
#2	MeSH descriptor: [Value of Life] this term only
#3	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#4	MeSH descriptor: [Economics, Hospital] explode all trees
#5	MeSH descriptor: [Economics, Medical] explode all trees
#6	MeSH descriptor: [Resource Allocation] explode all trees
#7	MeSH descriptor: [Economics, Nursing] this term only
#8	MeSH descriptor: [Economics, Pharmaceutical] this term only
#9	MeSH descriptor: [Fees and Charges] explode all trees
#10	MeSH descriptor: [Budgets] explode all trees
#11	budget*:ti,ab
#12	cost*:ti,ab
#13	(economic* or pharmaco?economic*):ti,ab
#14	(price* or pricing*):ti,ab
#15	(financ* or fee or fees or expenditure* or saving*):ti,ab
#16	(value near/2 (money or monetary)):ti,ab
#17	resourc* allocat*:ti,ab
#18	(fund or funds or funding* or funded):ti,ab
#19	(ration or rations or rationing* or rationed) .ti,ab.
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	[mh AMPUTATION]
#22	[mh ^"AMPUTATION, TRAUMATIC"]
#23	(amputat* or disarticulation* or dis-articulation* or hemipelvectom*):ti,ab
#24	[mh ^AMPUTEES]
#25	amputee*:ti,ab
#26	(limb* near/3 (loss or losing or lost)):ti,ab
#27	[mh ^"AMPUTATION STUMPS"]
#28	[mh ^"LIMB SALVAGE"]
#29	(limb* near/3 (salvag* or re-construct* or reconstruct*)):ti,ab
#30	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29
#31	[mh ^SPLINTS]
#32	[mh "ORTHOTIC DEVICES"]
#33	splint*:ti,ab
#34	orthos*:ti,ab
#35	orthotic*:ti,ab
#36	brace*:ti,ab
#37	[mh ^HYDROTHERAPY]
#38	hydrotherap*:ti,ab
#39	[mh ^HYPOGRAVITY]
#40	hypograv*:ti,ab
#41	((antigravit* or ((anti or low or reduc*) near/3 gravit*)) near/5 (treadmill* or 'running machine*')):ti,ab
#42	[mh ^"PROSTHESIS FITTING"]
#43	(prosthe* near/5 fit*):ti,ab
#44	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 fit*):ti,ab
#45	[mh ^"ARTIFICIAL LIMBS"]
#46	[mh "JOINT PROSTHESIS"]
#47	[mh ^"WEIGHT-BEARING"]
#48	#45 or #46 or #47
#49	[mh ^"TIME FACTORS"]
#50	#48 and #49
#51	(prosthe* near/3 (time or timing)):ti,ab
#52	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 (time or timing)):ti,ab
#53	(prosthe* near/3 earl*):ti,ab
#54	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 earl*):ti,ab
#55	(weight* near/3 (bear* or load*) near/5 earl*):ti,ab
#56	(prosthe* near/5 temporar*):ti,ab
#57	[mh ^"EARLY AMBULATION"/mt]

#	Searches
#58	(earl* near/3 walk* near/3 aid*):ti,ab
#59	EWA:ti,ab
#60	(mobilit* near/3 aid*):ti,ab
#61	PPAM*:ti,ab
#62	AMA:ti,ab
#63	femuret*:ti,ab
#64	[mh ^EDEMA/pc]
#65	[mh ^EDEMA/th]
#66	[mh ^EDEMA]
#67	[mh ^BANDAGES]
#68	[mh ^"COMPRESSION BANDAGES"]
#69	[mh ^"STOCKINGS, COMPRESSION"]
#70	[mh ^"INTERMITTENT PNEUMATIC COMPRESSION DEVICES"]
#71	[mh ^"NEGATIVE-PRESSURE WOUND THERAPY"]
#72	[mh ^MASSAGE]
#73	[mh ^"BED REST"]
#74	#67 or #68 or #69 or #70 or #71 or #72 or #73
#75	#66 and #74
#76	((oedema* or edema* or swell*) near/7 (manag* or therap* or bandag* or stocking* or compres* or massag* or (bed* near/3 rest*) or (leg* near/3 rais*))):ti,ab
#77	(Compassion* near/3 mind* near/3 (therap* or train*)):ti,ab
#78	[mh ^"ACCEPTANCE AND COMMITMENT THERAPY"]
#79	(Accept* near/3 commit* near/3 (therap* or train*)):ti,ab
#80	[mh ^MINDFULNESS]
#81	Mindfulness:ti,ab
#82	((Visualisation or visualization) near/3 (therap* or train*)):ti,ab
#83	(mentalisation or mentalization):ti,ab
#84	[mh ^"RELAXATION THERAPY"]
#85	[mh ^"BREATHING EXERCISES"]
#86	((Relax* or progressive* or breath*) near/3 (therap* or train* or exercis*)):ti,ab
#87	(Mirror* near/3 (therap* or train* or feedback)):ti,ab
#88	[mh ^"COGNITIVE THERAPY"]
#89	(Cognit* near/3 behav* near/3 (therap* or train*)):ti,ab
#90	CBT:ti,ab
#91	[mh ^"REHABILITATION, VOCATIONAL"]
#92	[mh ^EMPLOYMENT]
#93	[mh ^"EMPLOYMENT, SUPPORTED"]
#94	[mh ^WORKPLACE]
#95	#92 or #93 or #94
#96	[mh ^"ADAPTATION, PHYSIOLOGICAL"]
#97	[mh ^ACCLIMATIZATION]
#98	[mh "ADAPTATION, PSYCHOLOGICAL"]
#99	[mh ^ERGONOMICS]
#100	[mh ^"EQUIPMENT DESIGN"]
#101	[mh ^"SELF-HELP DEVICES"]
#102	#96 or #97 or #98 or #99 or #100 or #101
#103	#95 and #102
#104	((vocation* or work* or job* or employment or employee* or profession* or occupation*) near/5 (rehab* or support* or near/ust* or adapt* or chang* or reintegrat* or re-integrat* or facilitat* or intervention* or equipment or ergonomic* or "assist* tech*")):ti,ab
#105	[mh ^"RETURN TO WORK"]
#106	(return* near/3 work*):ti,ab
#107	[mh ^"VOCATIONAL GUIDANCE"]
#108	((vocation* or work* or job* or employment or employee* or profession* or occupation* or career*) near/5 (guid* or counsel*)):ti,ab
#109	#31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #103 or #104 or #105 or #106 or #107 or #108
#110	#30 and #109 with Publication Year from 1995 to 2019, in Trials
#111	#30 and #109 with Cochrane Library publication date Between Jan 1995 and Jan 2019, in Cochrane Reviews, Cochrane Protocols
#112	#20 and #110

Literature search strategies for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation

programmes and packages, including prosthetics, are effective and acceptable?

Note the searches for this review question were re-run on 10/11/2020 but with a randomized controlled trial search filter added. This was in order to capture any high level evidence published since the original search was run on 28/02/2019.

Review question search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 28/02/2019

#	Searches
1	ADOLESCENT/ or MINORS/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw,nw.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw,nw.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw,nw.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw,nw.
9	or/1-8
10	exp AMPUTATION/
11	AMPUTATION, TRAUMATIC/
12	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
13	AMPUTEES/
14	amputee?.ti,ab.
15	(limb? adj3 (loss or losing or lost)).ti,ab.
16	AMPUTATION STUMPS/
17	LIMB SALVAGE/
18	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
19	or/10-18
20	SPLINTS/
21	exp ORTHOTIC DEVICES/
22	splint$.ti,ab.
23	orthos?s.ti,ab.
24	orthotic?.ti,ab.
25	brace?.ti,ab.
26	HYDROTHERAPY/
27	hydrotherap$.ti,ab.
28	HYPOGRAVITY/
29	hypograv$.ti,ab.
30	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
31	PROSTHESIS FITTING/
32	(prosthe$ adj5 fit$).ti,ab.
33	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
34	ARTIFICIAL LIMBS/ and TIME FACTORS/
35	exp JOINT PROSTHESIS/ and TIME FACTORS/
36	WEIGHT-BEARING/ and TIME FACTORS/
37	(prosthe$ adj3 (time or timing)).ti,ab.
38	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
39	(prosthe$ adj3 earl$).ti,ab.
40	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
41	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
42	(prosthe$ adj5 temporar$).ti,ab.
43	EARLY AMBULATION/mt [Methods]
44	(earl$ adj3 walk$ adj3 aid?).ti,ab.
45	EWA.ti,ab.
46	(mobilit$ adj3 aid?).ti,ab.
47	PPAM?.ti,ab.
48	AMA.ti,ab.
49	femuret$.ti,ab.
50	EDEMA/pc [Prevention & Control]

#	Searches
51	EDEMA/th [Therapy]
52	EDEMA/ and (BANDAGES/ or COMPRESSION BANDAGES/ or STOCKINGS, COMPRESSION/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICES/ or NEGATIVE-PRESSURE WOUND THERAPY/ or MASSAGE/ or BED REST/)
53	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
54	FAMILY THERAPY/
55	(famil$ adj3 therap$).ti,ab.
56	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
57	"ACCEPTANCE AND COMMITMENT THERAPY"/
58	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
59	MINDFULNESS/
60	Mindfulness.ti,ab.
61	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
62	mentali?ation.ti,ab.
63	RELAXATION THERAPY/
64	BREATHING EXERCISES/
65	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
66	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
67	COGNITIVE THERAPY/
68	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
69	CBT.ti,ab.
70	(EDUCATION/ or SCHOOLS/) and (ADAPTATION, PHYSIOLOGICAL/ or ACCLIMATIZATION/ or exp ADAPTATION, PSYCHOLOGICAL/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF-HELP DEVICES/)
71	((education$ or school$) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
72	(return$ adj3 (education$ or school$)).ti,ab.
73	PLAY THERAPY/
74	(play$ adj3 therap$).ti,ab.
75	theraband?.ti,ab.
76	or/20-75
77	19 and 76
78	limit 77 to english language
79	limit 78 to yr="1995 -Current"
80	LETTER/
81	EDITORIAL/
82	NEWS/
83	exp HISTORICAL ARTICLE/
84	ANECDOTES AS TOPIC/
85	COMMENT/
86	CASE REPORT/
87	(letter or comment*).ti.
88	or/80-87
89	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
90	88 not 89
91	ANIMALS/ not HUMANS/
92	exp ANIMALS, LABORATORY/
93	exp ANIMAL EXPERIMENTATION/
94	exp MODELS, ANIMAL/
95	exp RODENTIA/
96	(rat or rats or mouse or mice).ti.
97	or/90-96
98	79 not 97
99	9 and 98

Databases: Embase; and Embase Classic

Date of last search: 28/02/2019

#	Searches
1	exp ADOLESCENT/
2	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3	exp CHILD/
4	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5	exp INFANT/
6	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7	exp PEDIATRICS/ or exp PUBERTY/
8	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9	or/1-8
10	exp AMPUTATION/

#	Searches
11	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
12	AMPUTEE/
13	amputee?.ti,ab.
14	(limb? adj3 (loss or losing or lost)).ti,ab.
15	LIMB SALVAGE/
16	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
17	or/10-16
18	exp ORTHOSIS/
19	splint$.ti,ab.
20	orthos?s.ti,ab.
21	orthotic?.ti,ab.
22	brace?.ti,ab.
23	HYDROTHERAPY/
24	hydrotherap$.ti,ab.
25	MICROGRAVITY/
26	hypograv$.ti,ab.
27	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
28	PROSTHETIC FITTING/
29	(prosthe$ adj5 fit$).ti,ab.
30	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
31	exp LIMB PROSTHESIS/ and TIME FACTOR/
32	exp JOINT PROSTHESIS/ and TIME FACTOR/
33	WEIGHT BEARING/ and TIME FACTOR/
34	(prosthe$ adj3 (time or timing)).ti,ab.
35	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
36	(prosthe$ adj3 earl$).ti,ab.
37	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
38	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
39	(prosthe$ adj5 temporar$).ti,ab.
40	*MOBILIZATION/
41	(earl$ adj3 walk$ adj3 aid?).ti,ab.
42	EWA.ti,ab.
43	(mobilit$ adj3 aid?).ti,ab.
44	PPAM?.ti,ab.
45	AMA.ti,ab.
46	femuret$.ti,ab.
47	exp EDEMA/pc [Prevention]
48	exp EDEMA/th [Therapy]
49	exp EDEMA/ and (BANDAGE/ or COMPRESSION BANDAGE/ or COMPRESSION STOCKINGS/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICE/ or VACUUM ASSISTED CLOSURE/ or MASSAGE/ or BED REST/)
50	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
51	FAMILY THERAPY/
52	(famil$ adj3 therap$).ti,ab.
53	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
54	"ACCEPTANCE AND COMMITMENT THERAPY"/
55	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
56	MINDFULNESS/
57	Mindfulness.ti,ab.
58	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
59	mentali?ation.ti,ab.
60	RELAXATION TRAINING/
61	BREATHING EXERCISE/
62	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
63	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
64	COGNITIVE BEHAVIORAL THERAPY/
65	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
66	CBT.ti,ab.
67	(EDUCATION/ or SCHOOL/ or COLLEGE/ or COMMUNITY COLLEGE/ or HIGH SCHOOL/ or KINDERGARTEN/ or MIDDLE SCHOOL/ or NURSERY SCHOOL/ or PRIMARY SCHOOL/) and (ADAPTATION/ or ACCLIMATIZATION/ or exp COPING BEHAVIOR/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF HELP DEVICE/ or ASSISTIVE TECHNOLOGY DEVICE/)
68	((education$ or school$) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
69	(return$ adj3 (education$ or school$)).ti,ab.
70	PLAY THERAPY/
71	(play$ adj3 therap$).ti,ab.
72	theraband?.ti,ab.

#	Searches
73	or/18-72
74	17 and 73
75	limit 74 to english language
76	limit 75 to yr="1995 -Current"
77	letter.pt. or LETTER/
78	note.pt.
79	editorial.pt.
80	CASE REPORT/ or CASE STUDY/
81	(letter or comment*).ti.
82	or/77-81
83	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84	82 not 83
85	ANIMAL/ not HUMAN/
86	NONHUMAN/
87	exp ANIMAL EXPERIMENT/
88	exp EXPERIMENTAL ANIMAL/
89	ANIMAL MODEL/
90	exp RODENT/
91	(rat or rats or mouse or mice).ti.
92	or/84-91
93	76 not 92
94	9 and 93

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

Date of last search 28/02/2019

#	Searches
#1	[mh ^"ADOLESCENT"]
#2	[mh ^"MINORS"]
#3	(adolescen* or teen* or youth* or young or juvenile* or minors or highschool*):ti,ab
#4	[mh "CHILD"]
#5	(child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid* or kindergar* or boy* or girl*):ti,ab
#6	[mh "INFANT"]
#7	(infan* or neonat* or newborn* or baby or babies):ti,ab
#8	[mh "PEDIATRICS"]
#9	[mh "PUBERTY"]
#10	(pediatric* or paediatric* or prepubert* or pubescen* or prepubescen*):ti,ab
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12	[mh AMPUTATION]
#13	[mh ^"AMPUTATION, TRAUMATIC"]
#14	(amputat* or disarticulation* or dis-articulation* or hemipelvectom*):ti,ab
#15	[mh ^AMPUTEES]
#16	amputee*:ti,ab
#17	(limb* near/3 (loss or losing or lost)):ti,ab
#18	[mh ^"AMPUTATION STUMPS"]
#19	[mh ^"LIMB SALVAGE"]
#20	(limb* near/3 (salvag* or re-construct* or reconstruct*)):ti,ab
#21	#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20
#22	[mh ^SPLINTS]
#23	[mh "ORTHOTIC DEVICES"]
#24	splint*:ti,ab
#25	orthos*:ti,ab
#26	orthotic*:ti,ab
#27	brace*:ti,ab
#28	[mh ^HYDROTHERAPY]
#29	hydrotherap*:ti,ab
#30	[mh ^HYPOGRAVITY]
#31	hypograv*:ti,ab
#32	((antigravit* or ((anti or low or reduc*) near/3 gravit*)) near/5 (treadmill* or 'running machine*')):ti,ab
#33	[mh ^"PROSTHESIS FITTING"]
#34	(prosthe* near/5 fit*):ti,ab
#35	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 fit*):ti,ab
#36	[mh ^"ARTIFICIAL LIMBS"]
#37	[mh "JOINT PROSTHESIS"]
#38	[mh ^"WEIGHT-BEARING"]
#39	#36 or #37 or #38

#	Searches
#40	[mh ^"TIME FACTORS"]
#41	#39 and #40
#42	(prosthe* near/3 (time or timing)):ti,ab
#43	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 (time or timing)):ti,ab
#44	(prosthe* near/3 earl*):ti,ab
#45	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 earl*):ti,ab
#46	(weight* near/3 (bear* or load*) near/5 earl*):ti,ab
#47	(prosthe* near/5 temporar*):ti,ab
#48	[mh ^"EARLY AMBULATION"/mt]
#49	(earl* near/3 walk* near/3 aid*):ti,ab
#50	EWA:ti,ab
#51	(mobilit* near/3 aid*):ti,ab
#52	PPAM*:ti,ab
#53	AMA:ti,ab
#54	femuret*:ti,ab
#55	[mh ^EDEMA/pc]
#56	[mh ^EDEMA/th]
#57	[mh ^EDEMA]
#58	[mh ^BANDAGES]
#59	[mh ^"COMPRESSION BANDAGES"]
#60	[mh ^"STOCKINGS, COMPRESSION"]
#61	[mh ^"INTERMITTENT PNEUMATIC COMPRESSION DEVICES"]
#62	[mh ^"NEGATIVE-PRESSURE WOUND THERAPY"]
#63	[mh ^MASSAGE]
#64	[mh ^"BED REST"]
#65	#58 or #59 or #60 or #61 or #62 or #63 or #64
#66	#57 and #65
#67	((oedema* or edema* or swell*) near/7 (manag* or therap* or bandag* or stocking* or compres* or massag* or (bed* near/3 rest*) or (leg* near/3 rais*))):ti,ab
#68	[mh ^"FAMILY THERAPY"]
#69	(famil* near/3 therap*):ti,ab
#70	(Compassion* near/3 mind* near/3 (therap* or train*)):ti,ab
#71	[mh ^"ACCEPTANCE AND COMMITMENT THERAPY"]
#72	(Accept* near/3 commit* near/3 (therap* or train*)):ti,ab
#73	[mh ^MINDFULNESS]
#74	Mindfulness:ti,ab
#75	(Visualization near/3 (therap* or train*)):ti,ab
#76	(Visualisation near/3 (therap* or train*)):ti,ab
#77	mentalization:ti,ab
#78	mentalisation:ti,ab
#79	[mh ^"RELAXATION THERAPY"]
#80	[mh ^"BREATHING EXERCISES"]
#81	((Relax* or progressive* or breath*) near/3 (therap* or train* or exercis*)):ti,ab
#82	(Mirror* near/3 (therap* or train* or feedback)):ti,ab
#83	[mh ^"COGNITIVE THERAPY"]
#84	(Cognit* near/3 behav* near/3 (therap* or train*)):ti,ab
#85	CBT:ti,ab
#86	[mh ^"EDUCATION"]
#87	[mh ^"SCHOOLS"]
#88	#86 or #87
#89	[mh ^"ADAPTATION, PHYSIOLOGICAL"]
#90	[mh ^ACCLIMATIZATION]
#91	[mh "ADAPTATION, PSYCHOLOGICAL"]
#92	[mh ^ERGONOMICS]
#93	[mh ^"EQUIPMENT DESIGN"]
#94	[mh ^"SELF-HELP DEVICES"]
#95	#89 or #90 or #91 or #92 or #93 or #94
#96	#88 and #95
#97	((education* or school*) near/5 (rehab* or support* or adjust* or adapt* or chang* or reintegrat* or re-integrat* or facilitat* or intervention* or equipment or ergonomic* or "assist* tech*")):ti,ab
#98	(return* near/3 (education* or school*)):ti,ab
#99	[mh ^"PLAY THERAPY"]
#100	(play* near/3 therap*):ti,ab
#101	theraband*:ti,ab
#102	#22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #96 or #97 or #98 #99 or #100 or #101
#103	#21 and #102

#	Searches
#104	#11 and #103
#105	#11 and #103 with Cochrane Library publication date Between Jan 1995 and Mar 2019, in Cochrane Reviews, Cochrane Protocols
#106	#11 and #103 with Publication Year from 1995 to 2019, in Trials

Health economics search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 28/02/2019

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	ADOLESCENT/ or MINORS/
23	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw,nw.
24	exp CHILD/
25	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw,nw.
26	exp INFANT/
27	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw,nw.
28	exp PEDIATRICS/ or exp PUBERTY/
29	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw,nw.
30	or/22-29
31	exp AMPUTATION/
32	AMPUTATION, TRAUMATIC/
33	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
34	AMPUTEES/
35	amputee?.ti,ab.
36	(limb? adj3 (loss or losing or lost)).ti,ab.
37	AMPUTATION STUMPS/
38	LIMB SALVAGE/
39	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
40	or/31-39
41	SPLINTS/
42	exp ORTHOTIC DEVICES/
43	splint$.ti,ab.
44	orthos?s.ti,ab.
45	orthotic?.ti,ab.
46	brace?.ti,ab.
47	HYDROTHERAPY/
48	hydrotherap$.ti,ab.
49	HYPOGRAVITY/
50	hypograv$.ti,ab.
51	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
52	PROSTHESIS FITTING/
53	(prosthe$ adj5 fit$).ti,ab.
54	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.

#	Searches
55	ARTIFICIAL LIMBS/ and TIME FACTORS/
56	exp JOINT PROSTHESIS/ and TIME FACTORS/
57	WEIGHT-BEARING/ and TIME FACTORS/
58	(prosthe$ adj3 (time or timing)).ti,ab.
59	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
60	(prosthe$ adj3 earl$).ti,ab.
61	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
62	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
63	(prosthe$ adj5 temporar$).ti,ab.
64	EARLY AMBULATION/mt [Methods]
65	(earl$ adj3 walk$ adj3 aid?).ti,ab.
66	EWA.ti,ab.
67	(mobilit$ adj3 aid?).ti,ab.
68	PPAM?.ti,ab.
69	AMA.ti,ab.
70	femuret$.ti,ab.
71	EDEMA/pc [Prevention & Control]
72	EDEMA/th [Therapy]
73	EDEMA/ and (BANDAGES/ or COMPRESSION BANDAGES/ or STOCKINGS, COMPRESSION/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICES/ or NEGATIVE-PRESSURE WOUND THERAPY/ or MASSAGE/ or BED REST/)
74	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
75	FAMILY THERAPY/
76	(famil$ adj3 therap$).ti,ab.
77	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
78	"ACCEPTANCE AND COMMITMENT THERAPY"/
79	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
80	MINDFULNESS/
81	Mindfulness.ti,ab.
82	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
83	mentali?ation.ti,ab.
84	RELAXATION THERAPY/
85	BREATHING EXERCISES/
86	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
87	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
88	COGNITIVE THERAPY/
89	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
90	CBT.ti,ab.
91	(EDUCATION/ or SCHOOLS/) and (ADAPTATION, PHYSIOLOGICAL/ or ACCLIMATIZATION/ or exp ADAPTATION, PSYCHOLOGICAL/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF-HELP DEVICES/)
92	((education$ or school$) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
93	(return$ adj3 (education$ or school$)).ti,ab.
94	PLAY THERAPY/
95	(play$ adj3 therap$).ti,ab.
96	theraband?.ti,ab.
97	or/41-96
98	40 and 97
99	limit 98 to english language
100	limit 99 to yr="1995 -Current"
101	LETTER/
102	EDITORIAL/
103	NEWS/
104	exp HISTORICAL ARTICLE/
105	ANECDOTES AS TOPIC/
106	COMMENT/
107	CASE REPORT/
108	(letter or comment*).ti.
109	or/101-108
110	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
111	109 not 110
112	ANIMALS/ not HUMANS/
113	exp ANIMALS, LABORATORY/
114	exp ANIMAL EXPERIMENTATION/
115	exp MODELS, ANIMAL/
116	exp RODENTIA/
117	(rat or rats or mouse or mice).ti.
118	or/111-117

#	Searches
119	100 not 118
120	30 and 119
121	21 and 120

Databases: Embase; and Embase Classic

Date of last search: 28/02/2019

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp ADOLESCENT/
19	(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
20	exp CHILD/
21	(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
22	exp INFANT/
23	(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
24	exp PEDIATRICS/ or exp PUBERTY/
25	(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
26	or/18-25
27	exp AMPUTATION/
28	(amputat$ or disarticulation? or dis-articulation? or hemipelvectom$).ti,ab.
29	AMPUTEE/
30	amputee?.ti,ab.
31	(limb? adj3 (loss or losing or lost)).ti,ab.
32	LIMB SALVAGE/
33	(limb? adj3 (salvag$ or re-construct$ or reconstruct$)).ti,ab.
34	or/27-33
35	exp ORTHOSIS/
36	splint$.ti,ab.
37	orthos?s.ti,ab.
38	orthotic?.ti,ab.
39	brace?.ti,ab.
40	HYDROTHERAPY/
41	hydrotherap$.ti,ab.
42	MICROGRAVITY/
43	hypograv$.ti,ab.
44	((antigravit$ or ((anti or low or reduc$) adj3 gravit$)) adj5 (treadmill? or running machine?)).ti,ab.
45	PROSTHETIC FITTING/
46	(prosthe$ adj5 fit$).ti,ab.
47	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 fit$).ti,ab.
48	exp LIMB PROSTHESIS/ and TIME FACTOR/
49	exp JOINT PROSTHESIS/ and TIME FACTOR/
50	WEIGHT BEARING/ and TIME FACTOR/
51	(prosthe$ adj3 (time or timing)).ti,ab.
52	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 (time or timing)).ti,ab.
53	(prosthe$ adj3 earl$).ti,ab.
54	(artificial$ adj3 (limb? or leg? or foot or feet? or arm? or hand? or extremit$ or joint? or knee? or elbow? or hip? or shoulder?) adj5 earl$).ti,ab.
55	(weight? adj3 (bear$ or load$) adj5 earl$).ti,ab.
56	(prosthe$ adj5 temporar$).ti,ab.
57	*MOBILIZATION/

#	Searches
58	(earl$ adj3 walk$ adj3 aid?).ti,ab.
59	EWA.ti,ab.
60	(mobilit$ adj3 aid?).ti,ab.
61	PPAM?.ti,ab.
62	AMA.ti,ab.
63	femuret$.ti,ab.
64	exp EDEMA/pc [Prevention]
65	exp EDEMA/th [Therapy]
66	exp EDEMA/ and (BANDAGE/ or COMPRESSION BANDAGE/ or COMPRESSION STOCKINGS/ or INTERMITTENT PNEUMATIC COMPRESSION DEVICE/ or VACUUM ASSISTED CLOSURE/ or MASSAGE/ or BED REST/)
67	((oedema? or edema? or swell$) adj7 (manag$ or therap$ or bandag$ or stocking? or compres$ or massag$ or (bed? adj3 rest$) or (leg? adj3 rais$))).ti,ab.
68	FAMILY THERAPY/
69	(famil$ adj3 therap$).ti,ab.
70	(Compassion$ adj3 mind$ adj3 (therap$ or train$)).ti,ab.
71	"ACCEPTANCE AND COMMITMENT THERAPY"/
72	(Accept$ adj3 commit$ adj3 (therap$ or train$)).ti,ab.
73	MINDFULNESS/
74	Mindfulness.ti,ab.
75	(Visuali?ation adj3 (therap$ or train$)).ti,ab.
76	mentali?ation.ti,ab.
77	RELAXATION TRAINING/
78	BREATHING EXERCISE/
79	((Relax$ or progressive$ or breath$) adj3 (therap$ or train$ or exercis$)).ti,ab.
80	(Mirror? adj3 (therap$ or train$ or feedback)).ti,ab.
81	COGNITIVE BEHAVIORAL THERAPY/
82	(Cognit$ adj3 behav$ adj3 (therap$ or train$)).ti,ab.
83	CBT.ti,ab.
84	(EDUCATION/ or SCHOOL/ or COLLEGE/ or COMMUNITY COLLEGE/ or HIGH SCHOOL/ or KINDERGARTEN/ or MIDDLE SCHOOL/ or NURSERY SCHOOL/ or PRIMARY SCHOOL/) and (ADAPTATION/ or ACCLIMATIZATION/ or exp COPING BEHAVIOR/ or ERGONOMICS/ or EQUIPMENT DESIGN/ or SELF HELP DEVICE/ or ASSISTIVE TECHNOLOGY DEVICE/)
85	((education$ or school$) adj5 (rehab$ or support$ or adjust$ or adapt$ or chang$ or reintegrat$ or re-integrat$ or facilitat$ or intervention? or equipment or ergonomic$ or assist$ tech$)).ti,ab.
86	(return$ adj3 (education$ or school$)).ti,ab.
87	PLAY THERAPY/
88	(play$ adj3 therap$).ti,ab.
89	theraband?.ti,ab.
90	or/35-89
91	34 and 90
92	limit 91 to english language
93	limit 92 to yr="1995 -Current"
94	letter.pt. or LETTER/
95	note.pt.
96	editorial.pt.
97	CASE REPORT/ or CASE STUDY/
98	(letter or comment*).ti.
99	or/94-98
100	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
101	99 not 100
102	ANIMAL/ not HUMAN/
103	NONHUMAN/
104	exp ANIMAL EXPERIMENT/
105	exp EXPERIMENTAL ANIMAL/
106	ANIMAL MODEL/
107	exp RODENT/
108	(rat or rats or mouse or mice).ti.
109	or/101-108
110	93 not 109
111	26 and 110
112	17 and 111

Database: Cochrane Central Register of Controlled Trials

Date of last search: 28/02/2019

#	Searches
#1	[mh ^"ECONOMICS"]
#2	[mh "VALUE OF LIFE"]
#3	[mh "COSTS AND COST ANALYSIS"]
#4	[mh "ECONOMICS, HOSPITAL"]

#	Searches
#5	[mh "ECONOMICS, MEDICAL"]
#6	[mh "RESOURCE ALLOCATION"]
#7	[mh ^"ECONOMICS, NURSING"]
#8	[mh "ECONOMICS, PHARMACEUTICAL"]
#9	[mh "FEES AND CHARGES"]
#10	[mh "BUDGETS"]
#11	budget*:ti,ab
#12	cost*:ti,ab
#13	(economic* or pharmaco?economic*):ti,ab
#14	(price* or pricing*):ti,ab
#15	(financ* or fee or fees or expenditure* or saving*):ti,ab
#16	(value near/2 (money or monetary)):ti,ab
#17	resourc* allocat*:ti,ab
#18	(fund or funds or funding* or funded):ti,ab
#19	(ration or rations or rationing* or rationed) .ti,ab.
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	[mh ^"ADOLESCENT"]
#22	[mh ^"MINORS"]
#23	(adolescen* or teen* or youth* or young or juvenile* or minors or highschool*):ti,ab
#24	[mh "CHILD"]
#25	(child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid* or kindergar* or boy* or girl*):ti,ab
#26	[mh "INFANT"]
#27	(infan* or neonat* or newborn* or baby or babies):ti,ab
#28	[mh "PEDIATRICS"]
#29	[mh "PUBERTY"]
#30	(pediatric* or paediatric* or prepubert* or pubescen* or prepubescen*):ti,ab
#31	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32	[mh AMPUTATION]
#33	[mh ^"AMPUTATION, TRAUMATIC"]
#34	(amputat* or disarticulation* or dis-articulation* or hemipelvectom*):ti,ab
#35	[mh ^AMPUTEES]
#36	amputee*:ti,ab
#37	(limb* near/3 (loss or losing or lost)):ti,ab
#38	[mh ^"AMPUTATION STUMPS"]
#39	[mh ^"LIMB SALVAGE"]
#40	(limb* near/3 (salvag* or re-construct* or reconstruct*)):ti,ab
#41	#32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40
#42	[mh ^SPLINTS]
#43	[mh "ORTHOTIC DEVICES"]
#44	splint*:ti,ab
#45	orthos*:ti,ab
#46	orthotic*:ti,ab
#47	brace*:ti,ab
#48	[mh ^HYDROTHERAPY]
#49	hydrotherap*:ti,ab
#50	[mh ^HYPOGRAVITY]
#51	hypograv*:ti,ab
#52	((antigravit* or ((anti or low or reduc*) near/3 gravit*)) near/5 (treadmill* or 'running machine*')):ti,ab
#53	[mh ^"PROSTHESIS FITTING"]
#54	(prosthe* near/5 fit*):ti,ab
#55	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 fit*):ti,ab
#56	[mh ^"ARTIFICIAL LIMBS"]
#57	[mh "JOINT PROSTHESIS"]
#58	[mh ^"WEIGHT-BEARING"]
#59	#56 or #57 or #58
#60	[mh ^"TIME FACTORS"]
#61	#59 and #60
#62	(prosthe* near/3 (time or timing)):ti,ab
#63	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 (time or timing)):ti,ab
#64	(prosthe* near/3 earl*):ti,ab
#65	(artificial* near/3 (limb* or leg* or foot or feet* or arm* or hand* or extremit* or joint* or knee* or elbow* or hip* or shoulder*) near/5 earl*):ti,ab
#66	(weight* near/3 (bear* or load*) near/5 earl*):ti,ab
#67	(prosthe* near/5 temporar*):ti,ab
#68	[mh ^"EARLY AMBULATION"/mt]
#69	(earl* near/3 walk* near/3 aid*):ti,ab
#70	EWA:ti,ab

#	Searches
#71	(mobilit* near/3 aid*):ti,ab
#72	PPAM*:ti,ab
#73	AMA:ti,ab
#74	femuret*:ti,ab
#75	[mh ^EDEMA/pc]
#76	[mh ^EDEMA/th]
#77	[mh ^EDEMA]
#78	[mh ^BANDAGES]
#79	[mh ^"COMPRESSION BANDAGES"]
#80	[mh ^"STOCKINGS, COMPRESSION"]
#81	[mh ^"INTERMITTENT PNEUMATIC COMPRESSION DEVICES"]
#82	[mh ^"NEGATIVE-PRESSURE WOUND THERAPY"]
#83	[mh ^MASSAGE]
#84	[mh ^"BED REST"]
#85	#78 or #79 or #80 or #81 or #82 or #83 or #84
#86	#77 and #85
#87	((oedema* or edema* or swell*) near/7 (manag* or therap* or bandag* or stocking* or compres* or massag* or (bed* near/3 rest*) or (leg* near/3 rais*))):ti,ab
#88	[mh ^"FAMILY THERAPY"]
#89	(famil* near/3 therap*):ti,ab
#90	(Compassion* near/3 mind* near/3 (therap* or train*)):ti,ab
#91	[mh ^"ACCEPTANCE AND COMMITMENT THERAPY"]
#92	(Accept* near/3 commit* near/3 (therap* or train*)):ti,ab
#93	[mh ^MINDFULNESS]
#94	Mindfulness:ti,ab
#95	(Visualization near/3 (therap* or train*)):ti,ab
#96	(Visualisation near/3 (therap* or train*)):ti,ab
#97	mentalization:ti,ab
#98	mentalisation:ti,ab
#99	[mh ^"RELAXATION THERAPY"]
#100	[mh ^"BREATHING EXERCISES"]
#101	((Relax* or progressive* or breath*) near/3 (therap* or train* or exercis*)):ti,ab
#102	(Mirror* near/3 (therap* or train* or feedback)):ti,ab
#103	[mh ^"COGNITIVE THERAPY"]
#104	(Cognit* near/3 behav* near/3 (therap* or train*)):ti,ab
#105	CBT:ti,ab
#106	[mh ^"EDUCATION"]
#107	[mh ^"SCHOOLS"]
#108	#106 or #107
#109	[mh ^"ADAPTATION, PHYSIOLOGICAL"]
#110	[mh ^ACCLIMATIZATION]
#111	[mh "ADAPTATION, PSYCHOLOGICAL"]
#112	[mh ^ERGONOMICS]
#113	[mh ^"EQUIPMENT DESIGN"]
#114	[mh ^"SELF-HELP DEVICES"]
#115	#109 or #110 or #111 or #112 or #113 or #114
#116	#108 and #115
#117	((education* or school*) near/5 (rehab* or support* or adjust* or adapt* or chang* or reintegrat* or re-integrat* or facilitat* or intervention* or equipment or ergonomic* or "assist* tech*")):ti,ab
#118	(return* near/3 (education* or school*)):ti,ab
#119	[mh ^"PLAY THERAPY"]
#120	(play* near/3 therap*):ti,ab
#121	theraband*:ti,ab
#122	#42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #86 or #87 or #88 or #89 or #90 or #91 or #92 or #93 or #94 or #95 or #96 or #97 or #98 or #99 or #100 or #101 or #102 or #103 or #104 or #105 or #116 or #117 or #118 #119 or #120 or #121
#123	#41 and #122
#124	#31 and #123
#125	#31 and #123 with Publication Year from 1995 to 2019, in Trials
#126	#20 and #125

Appendix C – Clinical evidence study selection

Clinical study selection for review questions:

C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

A combined update search was conducted for both review questions.

Figure 1: Study selection flow chart: Adults

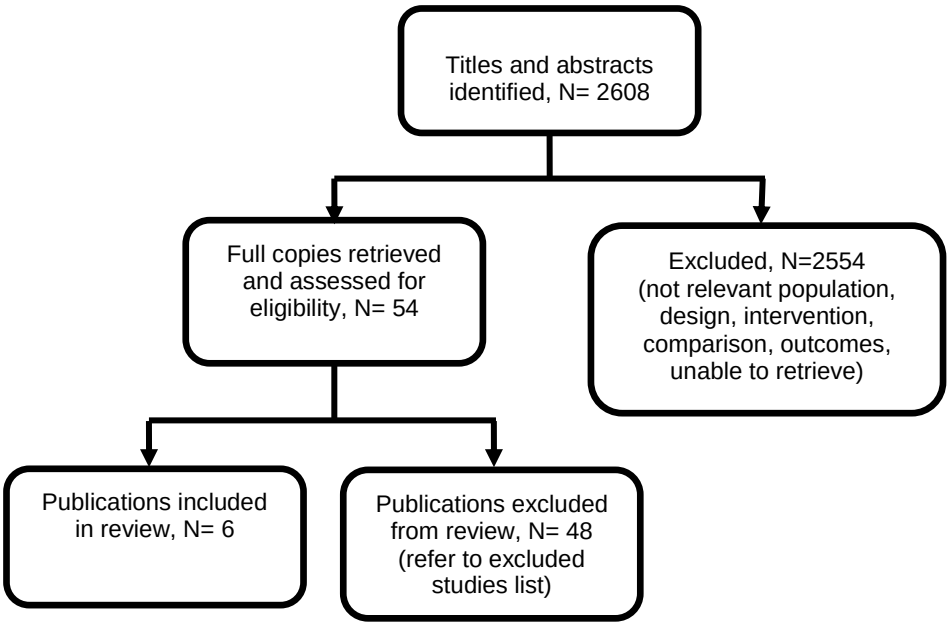
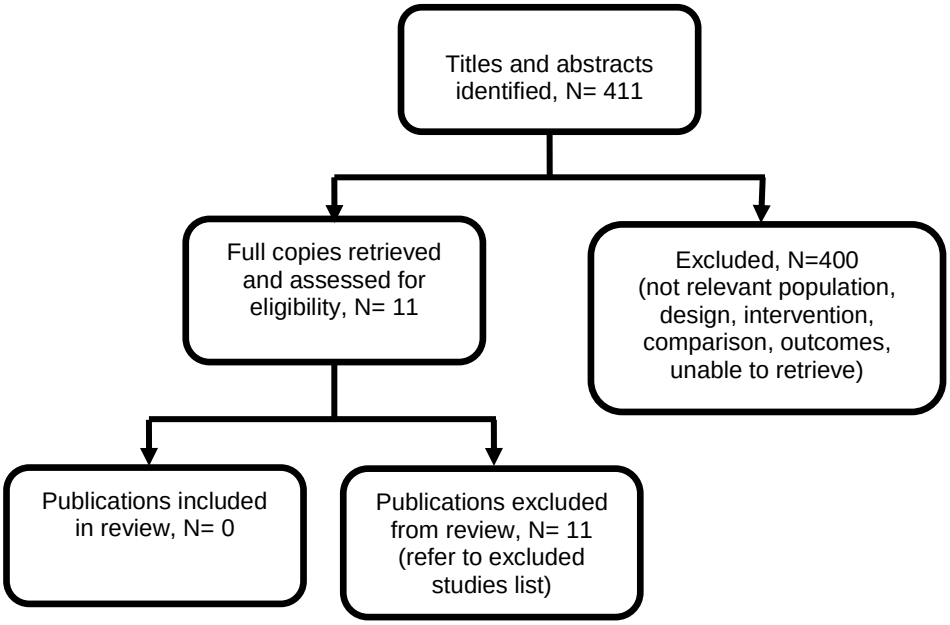


Figure 2: Study selection flow chart: Children and young people



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Table 5: Clinical evidence tables

Study details	Participants	Interventions	Outcomes and Results	Comments
Full citation Anjum, Hadeya, Amjad, Imran, Malik, Arshad Nawaz, Effectiveness of Proprioceptive Neuromuscular Facilitation Techniques as Compared to Traditional Strength Training in Gait Training Among Transtibial Amputees, Journal of the College of Physicians and Surgeons--Pakistan : JCPSP, 26, 503-6, 2016 **Ref Id** 945090 **Country/ies where the study was carried out** Pakistan **Study type** RCT	**Sample size** N=63 **Characteristics** • Right-sided amputation = 26/63 • Left-sided amputation = 37/63 • Subjects without any co-morbidity = 27% **Inclusion criteria** • "Subjects with unilateral transtibial amputation, lack of contracture, first time or old prosthetic user and one-third stump length" **Exclusion criteria** • "Subjects with wet wounds, phantom pain, neuroma, swelling, contractures or bilateral lower extremity	Proprioceptive neuromuscular facilitation (PNF) group (n=31): "30 minutes session of weight bearing, weight shifting, balance exercise, single limb loading, and stepping. The PNF principal (e.g. manual contact, verbal command, vision, and timing for emphasis, resistance, approximation, stretch, slow reversal, and rhythmic stabilization) were applied to this group." Traditional prosthetic strength training (TPT) group (n=32): "30 minutes session of weight bearing, weight shifting, balance exercise, single limb loading, stepping, and strength training through sand bag" Duration of treatment - 4 weeks	**Mean locomotor capability index** PNF : 23.93 ±4.24 Traditional : 18.18 ±7.78*, p<0.01 Manual muscle strength (MMT) knee flexors PNF: 4.96 (±.179) Traditional: 4.75 (±.439)*, p=0.013 Manual muscle strength (MMT) knee extensors PNF: 4.96 (±.179) Traditional: 4.75 (±.439)*, p=0.013 Manual muscle strength (MMT) hip extensors PNF: 4.96 (±.179) Traditional: 4.90 (±.296), p=0.322	**Limitations** **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization process** 1.1 Was the allocation sequence random? NI 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? NI 1.3 Did baseline differences between intervention groups suggest a problem with the randomization process? PY Risk-of-bias judgement: High risk • **Domain 2: Risk of**

Study details	Participants	Interventions	Outcomes and Results	Comments
Aim of the study To evaluate the effectiveness of proprioceptive neuromuscular facilitation (PNF) techniques compared to traditional prosthetic strength training among participants with transtibial amputation **Study dates** July to December 2014 **Source of funding** Not reported	amputations"			**bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y 2.7 If N/PN/NI to 2.6:

Study details	Participants	Interventions	Outcomes and Results	Comments
				Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? Y 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? NA 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NA 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NA Risk-of-bias judgement: Low risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N 4.2 Could measurement

Study details	Participants	Interventions	Outcomes and Results	Comments
				or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk • **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result being assessed likely to

Study details	Participants	Interventions	Outcomes and Results	Comments
				have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns **Overall risk of bias** High risk
Full citation Chan, Brenda L., Witt, Richard, Charrow, Alexandra P., Magee, Amanda, Howard, Robin, Pasquina, Paul F., Heilman, Kenneth M., Tsao, Jack W., Mirror therapy for phantom limb pain, The New England journal of medicine, 357, 2206-7, 2007 **Ref Id** 945341 **Country/ies where the study was carried out** Unclear, probably USA **Study type**	**Sample size** N=22 randomised and N=18 completed (6 in each of the 3 groups) **Characteristics** • Visual analogue scales at baseline were similar among the groups (p=0.62) **Inclusion criteria** • "Subjects with phantom limb pain after the amputation of a leg or foot" **Exclusion criteria** Not reported	Mirror therapy : "performed movements with the amputated limb while viewing the reflected image of the movement of their intact limb" Covered-mirror group : "performed movements with both their intact and amputated limbs when the mirror was covered by an opaque sheet" Mental-visualisation group: "closed their eyes and imagined performing movements with their amputated limb." "Under direct observation, patients performed their assigned therapy for 15 minutes daily. They also recorded the number and duration of pain episodes and the intensity of pain with the use of a 100-mm visual-analogue	**Number of subjects reporting a decrease in pain** Mirror group: 6/6 (100%) Covered-mirror group: 1/6 (17%) Mental-visualisation group: 2/6 (33%) **Number of subjects reporting worsening pain** Mirror group: 0 Covered-mirror group: 3/6 (50%) Mental-visualisation group: 4/6 (67%) **Visual-analogue scale at 4 weeks** **-** "the mirror group differed significantly from both the covered-mirror group (P =	**Limitations** **Quality assessment:** Risk of **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization process** 1.1 Was the allocation sequence random? NI 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? NI 1.3 Did baseline differences between intervention groups

Study details	Participants	Interventions	Outcomes and Results	Comments
3-armed randomised sham-controlled trial **Aim of the study** To examine the effectiveness of mirror therapy in comparison with imagery therapy among subjects with phantom limb pain after the amputation of a leg or a foot **Study dates** Not reported **Source of funding** A grant from the Military Amputee Research Program and a grant from the Defense Advanced Research Projects Agency		scale; they also recorded the number and duration of pain episodes. The primary end point was the severity of pain after 4 weeks of therapy." Duration - 4 weeks	0.04) and the mental-visualization group (P = 0.002)"	suggest a problem with the randomization process? PY Risk-of-bias judgement: High risk • **Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the

Study details	Participants	Interventions	Outcomes and Results	Comments
				outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? N - Likely attrition bias due to amount of incomplete outcome data: only 18 out of 22 randomised patients were included in analyses and the reasons for loss of patients were not described 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? N 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NI

Study details	Participants	Interventions	Outcomes and Results	Comments
				3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NI Risk-of-bias judgement: High risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N 4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk

Study details	Participants	Interventions	Outcomes and Results	Comments
				• **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result being assessed likely to have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns **Overall risk of bias** High risk
Full citation Cunha, R. G., Da-Silva, P. J., Dos Santos Couto Paz, C. C., da Silva Ferreira, A. C., Tierra-Criollo, C. J., Influence of functional task-oriented mental practice on the gait of transtibial	**Sample size** N=16 randomised, 8 in each group - After preliminary analysis using data from 5 volunteers per group, which indicated benefit in gait function for gait-oriented mental practice (MP) group. The authors considered that it was unethical to expose volunteers to	Gait-oriented mental practice group (n=10): "the MP was performed from a first person perspective, wherein the difficulty of the motor task was increased during the sessions according to the continuum of intensity reported by the	**Pre-MP** Vertical ground reaction force 1(GRF) Gait-oriented MP: 89.6 ± 7.2 Non-motor MP:89.9 ± 6.9 Vertical ground reaction force 2(GRF) Gait-oriented MP:66.4 ± 7.3	**Limitations** **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization**

Study details	Participants	Interventions	Outcomes and Results	Comments
amputees: a randomized, clinical trial, Journal of NeuroEngineering and Rehabilitation, 14, 28, 2017 **Ref Id** 945433 **Country/ies where the study was carried out** Brazil **Study type** RCT (A1-B-A2 design: "when the therapist is faced with stabilization of the patient and need to implement treatment strategies to increase the functional capacity of these individuals. Phase A1 did not include any intervention (MP or conventional physical therapy treatment), Phase B included MP intervention, and Phase A2 did not include any intervention (MP or conventional physical therapy treatment)." **Aim of the study** To evaluate the effectiveness of gait-	an intervention which did not have a significant improvement in gait function. Thus, 3 subjects from non-motor MP group were then included in the gait-oriented MP group. **Characteristics** • "none of the volunteers presented: A) a previous history of lower limb surgery; B) rheumatic, orthopedic, or neurological diseases with motor sequelae; C) vestibular and/or cerebellar disorders; D) serious hearing and/or visual impairment that had not been corrected; or E) heart disorders that might influence gait." • 16 male transtibial amputee volunteers • MIQ-RS score ≥4 Gait-oriented MP=10 Non-motor MP=5 Age Gait-oriented MP:33.2 ±2.69 years Non-motor MP:35.4 ± 3.2 years Average time since amputation Gait-oriented MP: 15.5 ± 2.1 years Non-motor MP:24.4 ± 2.92 years Average visual scores Gait-oriented MP:22.7 ± 1.76 Non-motor MP:22 ± 2.91 Average kinesthetic score	volunteers. The volunteers from this group imagined each task 10 times and, subsequently, were instructed to describe the movements of each joint (hip extension, knee extension, knee flexion, plantar flexion, etc.) imagined during the oriented-gait functional task. This group also performed gait training after the MP session in order to emphasize the movement tasks imagined." MP tasks included were - Sitting down and arising from a chair, walking with the prothesis, walking fast, jumping over obstacles, running, walking up a staircase, walking up a ramp, walking and running in a "zig-zag" manner, walking down a staircase and walking down a ramp Non-motor mental practice group (n=5): "volunteers from this group imagined a number of non-motor tasks (Table 1) a total of 10 times each, and were subsequently instructed to describe each task. All MP sessions were guided by Researcher I (physical therapist)." MP tasks included were - imagining and thinking of life goals, imagining trips, imagining and thinking about one's family relationships and	Non-motor MP:62.4 ± 2.3 Anterior-posterior ground reaction force 1 Gait-oriented MP:-19.4 ± 0.5 Non-motor MP:-22.8 ± 2.9 Anterior-posterior ground reaction force 2 Gait-oriented MP:10.5 ± 0.7 Non-motor MP:10.2 ± 0.5 Medio-lateral ground reaction force Gait-oriented MP:3.1 ± 0.4 Non-motor MP:3.2 ± 0.3 Duration of support Gait-oriented MP: 0.434 ± 0.088 Non-motor MP: 0.431 ± 0.094 **Post-MP** Vertical ground reaction force 1(GRF) Gait-oriented MP: 77.2 ± 6.2 Non-motor MP: 89.9 ± 4.2 Vertical ground reaction force 2(GRF) Gait-oriented MP:79.4 ± 3.0 Non-motor MP: 67.2 ± 3.3 Anterior-posterior ground reaction force 1 Gait-oriented MP:-11.9 ± 3.4 Non-motor MP:-24.4 ± 4.7 Anterior-posterior ground reaction force 2 Gait-oriented MP:12.8 ± 2.2 Non-motor MP:9.2 ± 1.2 Medio-lateral ground reaction force	**process** 1.1 Was the allocation sequence random? NI 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? NI 1.3 Did baseline differences between intervention groups suggest a problem with the randomization process? PY Risk-of-bias judgement: High risk • **Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that

Study details	Participants	Interventions	Outcomes and Results	Comments
oriented mental practice among transtibial amputees **Study dates** **Source of funding** National Council of Technological and Scientific Development, Research Support Foundation of Minas Gerais and Coordination for the improvement of Higher Education Personnel	Gait-oriented MP:22.3 ± 2.66 Non-motor MP:22.2± 2.58 Vertical ground reaction force 1(GRF) Gait-oriented MP: 93.8 ± 5.1 Non-motor MP:90.9 ± 3.7 Vertical ground reaction force 2(GRF) Gait-oriented MP:63.3 ± 3.3 Non-motor MP:62.5 ± 1.5 Anterior-posterior ground reaction force 1 Gait-oriented MP:-13.6 ± 0.7 Non-motor MP:-13.2 ± 0.4 Anterior-posterior ground reaction force 2 Gait-oriented MP:10.2 ± 0.4 Non-motor MP:9.9 ± 0.4 Medio-lateral ground reaction force Gait-oriented MP:3.3 ± 0.3 Non-motor MP:3.1 ± 0.2 Duration of support Gait-oriented MP: 0.420 ± 0.074 Non-motor MP: 0.421 ± 0.029 **Inclusion criteria** • Subjects with unilateral transtibial amputees • 18 to 60 years old • Amputated 1-40 years ago • Those who were able to perform motor imagination tasks, assessed by using the Motor Imagery Questionnaire-Revised,	thinking and remembering moments of happiness "Each MP session had a duration of 40 min, and was performed 3 times per week over 4 weeks. Thus, a total of 12 sessions were conducted in a quiet and controlled environment by using objects and obstacles that replicated the gait variation." Outcomes: Gait performance during 4 distinct stages (at baseline ; at 1 month before the first MP session; at 1-3 days before the first MP session and 1-3 days after the last MP session; follow-up at 1 month after the last MP session) was evaluated using "a force platform embedded into the lab floor" - "Each volunteer was instructed to walk along a 10 m linear trajectory, in his own footwear at his natural cadence. A valid step was considered a step in which the prosthetic foot is directly hitting the force platform, with the entire foot making contact on the platform (not touching the platform edges)." Outcome analysis : "The average values over 5 valid repetitions of walking were analyzed by a physical therapist (Researcher	Gait-oriented MP:2.6 ± 0.2 Non-motor MP:3.3 ± 0.2 Duration of support Gait-oriented MP: 0.640 ± 0.054 Non-motor MP: 0.431 ± 0.016 **1-month follow-up** Vertical ground reaction force 1(GRF) Gait-oriented MP: 64.9 ± 3.2 Non-motor MP:86.5 ± 3.9 Vertical ground reaction force 2(GRF) Gait-oriented MP:74.0 ± 2.8 Non-motor MP:62.3 ± 2.0 Anterior-posterior ground reaction force 1 Gait-oriented MP:-13.2 ± 0.6 Non-motor MP:-23.4 ± 2.5 Anterior-posterior ground reaction force 2 Gait-oriented MP:12.8 ± 0.6 Non-motor MP:9.9 ± 0.4 Medio-lateral ground reaction force Gait-oriented MP:2.2 ± 0.1 Non-motor MP:3.4 ± 0.2 Duration of support Gait-oriented MP: 0.647 ± 0.090 Non-motor MP: 0.442 ± 0.095	arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? N - Likely attrition bias due to amount of incomplete outcome data: 3/8 patients who were initially in the control group were

Study details	Participants	Interventions	Outcomes and Results	Comments
	Second Edition (MIQ-RS) **Exclusion criteria** Not reported	II), who had not participated in the MP sessions"		then moved to the intervention group after preliminary analysis 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? N 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NI 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NI Risk-of-bias judgement: High risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N 4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been

Study details	Participants	Interventions	Outcomes and Results	Comments
				influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk • **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result being assessed likely to have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns

Study details	Participants	Interventions	Outcomes and Results	Comments
				Overall risk of bias High risk
Full citation Finn, Sacha B., Perry, Briana N., Clasing, Jay E., Walters, Lisa S., Jarzombek, Sandra L., Curran, Sean, Rouhanian, Minoo, Keszler, Mary S., Hussey-Andersen, Lindsay K., Weeks, Sharon R., Pasquina, Paul F., Tsao, Jack W., A Randomized, Controlled Trial of Mirror Therapy for Upper Extremity Phantom Limb Pain in Male Amputees, Frontiers in neurology, 8, 267, 2017 **Ref Id** 945662 **Country/ies where the study was carried out** USA **Study type** RCT **Aim of the study** To examine the effectiveness of mirror therapy to relieve Phantom limb pain in unilateral,	**Sample size** n=15 **Characteristics** Average age = 28.73 years Right sided unilateral injury = 10/15 Left sided unilateral injury = 5/15 Cause of injury = 2 motor vehicle accident; 11 improvised explosive device; 1 Boating accident and 1 Dynamite Site of injury = 6 trans-humeral; 7 trans-radial; 2 wrist disarticulation Average time since injury (months) = 4.5 **Inclusion criteria** • Participants with active duty United States Military Service Members, beneficiaries or retirees between 18 and 70 years old • Those with unilateral upper extremity amputees • Male only included (due to limited number of female military amputee) • Those "with a minimum of three PLP (Phantom Limb Pain) episodes per week and a minimum of pain score on the Visual Analog Scale (VAS) of 30 mm (out of a	Treatment group (n=9): Each received "15 min of the assigned therapy daily for 5 days/week for 4 weeks". "Volunteer subjects assigned to the mirror therapy group were asked to place their intact hand in front of a vertically placed mirror in the mid-sagittal line and to perform a series of hand movements while viewing the reflected image of the intact hand and moving the phantom in a similar manner. The movements performed were abduction/adduction of the thumb and fifth finger, flexion/extension of the thumb, flexion/extension of the fingers, pronation/supination of the hand, flexion/extension of the hand at the wrist, and flexion/extension of the elbow (for trans-humeral amputees). Subjects were asked to start with slow movements of the intact hand so that the phantom hand could keep pace with the viewed reflected image and to gradually increase the range of motion of the intact hand movements if the phantom hand had limited range of motion." Control group (n=6): "The	**Decrease in phantom limb pain (PLP)** Mirror group: 8/9 (89%) Control group: 2/6 (20%) **Increase in PLP** Mirror group: 1/9 (11%) Control group: Not reported **Change in pain score (100 mm VAS) from baseline (mean ± SD)** Mirror group: 41.4±17.6 to 27.5±17.2 mm, p= 0.001 Control group: 35.2±25.5 to 48.5±29 mm, p=0.601 **Cohen's d (Effect size of the initial and final VAS scores for those receiving mirror therapy)** = 0.971 **Total daily time experiencing pain (mean ± SD)** Mirror group: 1022±673 to 448±565 minutes, p=0.003 Control group: 743 ±806 to 726 ± 825 minutes, p=0.49 **Cohen's d (Effect size of the initial and final time experiencing pain per day for those receiving mirror therapy)** = 0.924	**Limitations** **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization process** 1.1 Was the allocation sequence random? Y – Randomisation done by computer generated list 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? NI 1.3 Did baseline differences between intervention groups suggest a problem with the randomization process? PY Risk-of-bias judgement: High risk • **Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants

Study details	Participants	Interventions	Outcomes and Results	Comments
upper extremity male amputees **Study dates** August 2007 to December 2012 **Source of funding** Military Amputee Research Program at Walter Reed Army Medical Center (WRAMC) and the Centre for Rehabilitation Sciences	maximum of 100 mm) at the time of screening." **Exclusion criteria** • Those "with concomitant traumatic brain injury, history of vertebral disc disease or radiculopathy, uncontrolled systemic disease, significant Axis I or II diagnosis, or having participated in another PLP study within 30 days preceding intended participation in this study"	volunteer subjects assigned to the covered mirror therapy group were given a mirror to use in the same manner as the treatment group; however, it was covered with an opaque sheet to prevent viewing of the reflection of the intact limb. They then performed the same movements with both the intact and phantom limbs. The volunteer subjects assigned to mental visualization therapy group were asked to mentally visualize the phantom limb performing the aforementioned gestures without moving their intact limb and without using a mirror. Subjects assigned to the control groups were given the option of switching to mirror therapy treatment after 4 weeks (20 treatment sessions). However, because of lack of treatment efficacy or increased pain, all subjects assigned to the control groups switched after 11 treatment sessions." "All participants were using or had used gabapentin, methadone, pregabalin, and/or percocet for PLP without relief."		aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA

Study details	Participants	Interventions	Outcomes and Results	Comments
				Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? Y 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? NA 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NA 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NA Risk-of-bias judgement: Low risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N 4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome

Study details	Participants	Interventions	Outcomes and Results	Comments
				assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk • **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result being assessed likely to have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time

Study details	Participants	Interventions	Outcomes and Results	Comments
				points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns **Overall risk of bias** High risk
Full citation Ol, Ha Sam, Van Heng, Yang, Danielsson, Lena, Husum, Hans, Mirror therapy for phantom limb and stump pain: a randomized controlled clinical trial in landmine amputees in Cambodia, Scandinavian journal of pain, 18, 603-610, 2018 **Ref Id** 946583 **Country/ies where the study was carried out** Cambodia **Study type** RCT **Aim of the study** To evaluate the effectiveness of mirror therapy and tactile therapy on phantom and stump pain in patients with	**Sample size** n=30 **Characteristics** Phantom limb pain (mean±SD) Mirror group: 6.7±2.7 Tactile group: 7.8±1.9 Stump pain (mean±SD) Mirror group: 8.0±1.7 Tactile group: 8.4±1.4 Age (mean±SD) years Mirror group: 57.5±6.0 Tactile group: 52.0±7.0 Years since surgical amputation Mirror group: 23.1±4.7 Tactile group: 23.2±4.4 Level of amputation, number of patients Proximal 1/3 Mirror group: 5/15 Tactile group: 5/15 Mid-shaft Mirror group: 6/15 Tactile group: 4/15 Distal 1/3 Mirror group: 4/15 Tactile group: 6/15	"Mirror therapy: the patient sits on a chair, both lower limbs bared. A mirror measuring 30 cm x 80 cm is placed between the legs along the trans-tibial amputation stump so that the patient can see the uninjured limb in the mirror while the amputated limb is hidden behind the mirror screen. For 5 min every morning and night, the patient fully concentrates on performing slow repeated movements of the foot from a neutral position to maximum dorsal flexion while closely observing the reflected image of the uninjured limb in the mirror." "Tactile treatment: The patient lies on a bed, not watching the stump, just concentrating on feeling the tactile stimuli, while for 5 min every morning and evening a close family member carefully exposes the skin of the medial, frontal, lateral, and dorsal parts of the amputation stump to five	After first-round treatment, 1. Phantom pain, mean VAS difference Mirror therapy: 5 (3.6 to 6.4) Tactile therapy: 4.3 (2.9 to 5.7) 2. Stump pain, mean VAS difference Mirror therapy: 6.2 (4.9 to 7.5) Tactile therapy: 4.9 (3.6 to 6.3) At 3 months follow-up, 1. Change in PLP pain (VAS score) from the end of the last intervention to 3 months follow-up: 0.9±0.8 2. Change in stump pain (VAS score) from the end of the last intervention to 3 months follow-up:	**Limitations** **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization process** 1.1 Was the allocation sequence random? Y - Randomisation done by computer-generated list without stratification 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? NI 1.3 Did baseline differences between intervention groups suggest a problem with the randomization process? PN Risk-of-bias judgement: Some concerns

Study details	Participants	Interventions	Outcomes and Results	Comments
traumatic trans-tibial amputations in low-income communities **Study dates** May to August 2016 **Source of funding** Grant from Lancelot Holding AS, Norway, org.	**Inclusion criteria** • Adults who had phantom pain after trans-tibial amputations after landmine trauma • Age > 16 years • Unilateral trans-tibial amputation after landmine trauma >12 months before entering the study • Those suffering from phantom limb pain with or without stump pain **Exclusion criteria** • Participants with amputation stump anomalies requiring surgical reconstructions such as chronic infections, neuroma or major soft tissue deformities • Those with chronic alcoholism or drug abuse • Those with loss or deformities of limbs other than the present amputation • Mental and/or cognitive disorders rendering self-rating of health unreliable	different stimuli: a stone, a wooden stick, a soft brush, a soft clot and a soft feather. The same sequence of tactile stimuli is applied in all treatment sessions." Duration - 1 week • "Sample size calculation was based on the distribution of self-rated PLP. A change of VAS of 33% considered to be relevant. Given an assumed standard deviation of VAS rating of 10%, power at 80%, 5% significant level, with a semi-crossover design, 15 patients were included in each of the three treatment arms. • Compliance - "Local expert staff monitored compliance by weekly interviews in the Khmer-Khmer language at the home of each study patient. The compliance rate was estimated as the rate of actual treatment periods by required treatment periods (two times per day for 28 days)	1.0±0.9 "Response to treatment was defined as a 33% reduction in VAS-rated PLP. Non-responders to the first-round tactile treatment were crossed over for secondary mirror therapy and initial non-responders in the mirror group crossed over for secondary tactile treatment." "For the first-round non-responders to M or T, a second-round treatment of 4 weeks with the alternative treatment started within a month after ending the initial treatment. A "drop-out" was a patient who decided to leave for reasons not related to the study and its implementation. There was only one drop-out in the study. • Analyses were done at three stages. 1. at the end of first-round treatment - 2. Based on the assumption that a patient exposed to mirror or tactile therapy	• **Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y

Study details	Participants	Interventions	Outcomes and Results	Comments
			remains primed by this treatment when later exposed to alternative treatment, the responders to the second-round of treatment were re-assigned to the combined mirror and tactile group 3. Differences between baseline and end-point pain after 3 months were compared between the three sub-samples Note - For our review, we considered the first and third analyses were relevant and reported.	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? Y 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? NA 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NA 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NA Risk-of-bias judgement: Low risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N

Study details	Participants	Interventions	Outcomes and Results	Comments
				4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk • **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result

Study details	Participants	Interventions	Outcomes and Results	Comments
				being assessed likely to have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns **Overall risk of bias** High risk **Other information** • This is a three-armed study and mirror therapy plus tactile treatment arm was not recorded as combined therapy is not an intervention of interest in the protocol. • The results from round 2 treatment were not recorded as this group was also considered as combined therapy which is

Study details	Participants	Interventions	Outcomes and Results	Comments
				• not an intervention of interest in the protocol • The results at 3-months follow-up were not included in analyses as there was no report on control group's results.
Full citation Topuz, S., Ulger, O., Bakar, Y., Sener, G., Comparison of the effects of complex decongestive physiotherapy and conventional bandaging on edema of geriatric amputees: a pilot study, Topics in geriatric rehabilitation, 28, 275-280, 2012 **Ref Id** 947206 **Country/ies where the study was carried out** Turkey **Study type** RCT	**Sample size** N=17 **Characteristics** Age, years CDP: 66.2±3.96 CB: 67.67±2.42 Height, cm CDP: 168.6±6.07 CB: 170.17±4.45 Body weight, kg CDP: 78.8±5.63 CB: 72.5±6.5 Hospital stay, day CDP: 6.6±1.14 CB: 6.17±1.47 Transition to permanent protheses, days("Transition to permanent prostheses was provided when there is not any difference between the amputated and the intact limb measurements. The period between	"The study started on the fi rst postoperative day with the amputees who are appropriate for CDP (n=5) and CB (n=6)." CDP: "includes manual lymphatic drainage (MLD), skin care, application of compression using short-stretch bandages and exercise.6 The treatment consisted of 1 MLD session per day until permanent prosthetic fitting. Manual lymphatic drainage was applied by a certified lymphedema therapist. Specific MLD techniques include manual therapy of the inguinal lymph nodes, lymphatic drainage of the thigh, stimulating popliteal lymph nodes, and lymphatic drainage of the stump (cruris). A pH-balanced moisturizer is applied to	Differences of Circumferential measurement differences of the first and last session values between CDP (n=5) and CB (n=6) groups MTP (first session) CDP: 2.6±0.89 CB: 3.17±0.75 MTP (last session) CDP: 1.6±0.55 CB: 2.75±0.76* Middle stump (first session) CDP: 2.9±0.74 CB: 33.17±1.17 Middle stump (last session) CDP: 1.6±0.55 CB: 2.58±0.74* Distal stump (first session) CDP: 3.4±0.89 CB: 3.33±1.03 Distal stump (last session) CDP: 1.8±0.45	**Limitations** **Quality assessment:** Risk of bias assessed using revised Cochrane risk of bias tool (RoB 2) • **Domain 1: Risk of bias arising from the randomization process** 1.1 Was the allocation sequence random? N - Randomisation was done by attendee order (first to CB and second to CDP and so on) 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? N – see 1.1 1.3 Did baseline

Study details	Participants	Interventions	Outcomes and Results	Comments
Aim of the study To evaluate the effectiveness of complex decongestive physiotherapy (CDP) and conventional bandaging (CB) on the postamputation oedema of geriatric transtibial amputees **Study dates** Not reported **Source of funding** No financial interest in any commercial companies	the fi rst session and transition to permanent prostheses were recorded in days.") CDP: 33±2.92 CB: 126±33.73 **Inclusion criteria** • >65 years of age • Unilateral transtibial amputee volunteer • Those with good cooperation • Those without any systemic problems • Those being able to use the prothesis **Exclusion criteria** • Bilateral amputees • Amputees suffering from neurologic and orthopedic problems as fractures or endoprotheses	the entire limb before compression bandaging. After skin care is performed, compression bandaging is applied to the limb. This is a multilayer bandage that is worn 24 hours per day during the treatment phase. After compression bandaging is applied, the patients were recommended to perform isometric, isotonic exercises for knee and thigh muscles and dynamic stump exercises 2 times a day, with 15 repetitions for each exercise. The patients performed the exercise at regular intervals throughout the day, to engage the pumping mechanism. These exercises involve movement of the limb through a comfortable range of motion with the bandaging in place, whereas some exercises incorporate diaphragmatic breathing to enhance the lymphatic pumping rate." CB:"the first group received CB techniques utilizing 10-cm bandage. Two or three elastic bandages were used. During application, the bandages were stretched to about two-thirds of the limit of the	CB: 2.75±0.76*	differences between intervention groups suggest a problem with the randomization process? PY Risk-of-bias judgement: High risk • **Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)** 2.1. Were participants aware of their assigned intervention during the trial? NI 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? NI 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? PN 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? NA 2.5 If N/PN/NI to 2.4:

Study details	Participants	Interventions	Outcomes and Results	Comments
		elastic, and the end of the stump had the greatest tension. The stump was kept bandaged at all times, but the bandage was changed every 6 or 8 hours. If throbbing occurred, the bandage had been removed and rewrapped. The geriatrics also participated in an exercise program, which consisted of stretching, dynamic stump exercises, and isotonic and isometric exercises. Exercises were performed twice a day, with 15 repeats."		Were these deviations likely to have affected the outcome? NA 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? Y 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? NA Risk-of-bias judgement: Low risk • **Domain 3: Missing outcome data** 3.1 Were data for this outcome available for all, or nearly all, participants randomized? N - Likely attrition bias due to amount of incomplete outcome data: 4 out of 9 in CB group and 2 out of 8 in CDP group dropped out 3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? N 3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value? NI

Study details	Participants	Interventions	Outcomes and Results	Comments
				3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? NI Risk-of-bias judgement: High risk • **Domain 4: Risk of bias in measurement of the outcome** 4.1 Was the method of measuring the outcome inappropriate? N 4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? N 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? PN 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? NA 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? NA Risk-of-bias judgement: Low risk

Study details	Participants	Interventions	Outcomes and Results	Comments
				• **Domain 5: Risk of bias in selection of the reported result** 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? NI Is the numerical result being assessed likely to have been selected, on the basis of the results, from... 5.2. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain? NI 5.3 ... multiple analyses of the data? NI Risk-of-bias judgement Some concerns **Overall risk of bias** High risk **Other information** Note - • We did not report on change in middle stump circumference measurement as we are

Study details	Participants	Interventions	Outcomes and Results	Comments
				suspicious of first session measurement in CB group (which is significantly higher than the last session).

CB: conventional bandaging; CDP: complex decongestive physiotherapy; GRF: ground reaction force; MIQ-RS: Movement Imagery Questionnaire-Revised second version; MLD: manual lymphatic drainage; MP: mental practice; MTP: medial tibial platol; N: number [or No if answering a risk of bias checklist question]; NA: not applicable; NI: no information; RCT: randomised controlled trial; RoB: risk of bias; PLP: phantom limb pain; PN: probably no; PNF: proprioceptive neuromuscular facilitation group; PY: probably yes; SD: standard deviation; SF-MPQ: Short-form McGill Pain Questionnaire; TPT: traditional prosthetic strength training; VAS: visual analogue scale

Clinical evidence tables for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

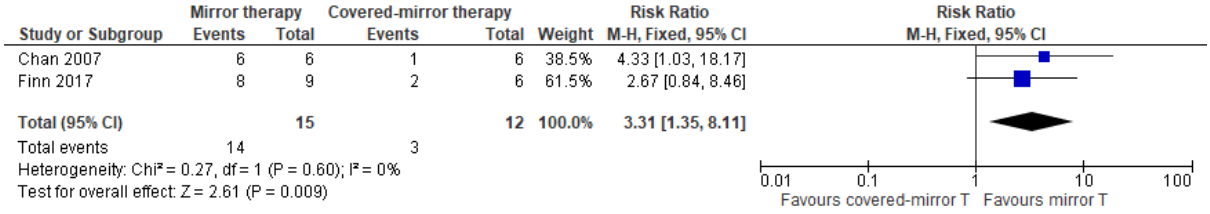
No evidence was identified which was applicable to this review question.

Appendix E – Forest plots

Forest plots for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessment for these outcomes is provided in the GRADE profiles in appendix F.

Figure 3: Mirror therapy versus covered-mirror therapy, Outcomes: pain (number of participants reporting a decrease in pain)



CI: confidence interval; M-H: mantel haenszel; T: therapy

Forest plots for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No evidence was identified which was applicable to this review question.

Appendix F – GRADE tables

GRADE tables for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Table 6: Clinical evidence profile for comparison proprioceptive neuromuscular facilitation (PNF) to traditional prosthetic strength training (TPT) in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PNF	TPT	Relative (95% CI)	Absolute		
Changes in mobility: Mean locomotor capability index[a] (score 0-42; better indicated by lower values) at 4 weeks follow-up												
1 (Anjum 2016)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	31	32	-	MD 5.75 higher (2.67 to 8.83 higher)	VERY LOW	CRITICAL
Changes in mobility: Manual muscle strength knee flexors[a] (Better indicated by lower values) at 4 weeks follow-up												
1 (Anjum 2016)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	31	32	-	MD 0.21 higher (0.05 to 0.37 higher)	VERY LOW	CRITICAL
Changes in mobility: Manual muscle strength knee extensors[a] (Better indicated by lower values) at 4 weeks follow-up												
1 (Anjum 2016)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[6]	none	31	32	-	MD 0.21 higher (0.05 to 0.37 higher)	VERY LOW	CRITICAL
Changes in mobility: Manual muscle strength hip extensors[a] (Better indicated by lower values) at 4 weeks follow-up												
1 (Anjum 2016)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	31	32	-	MD 0.06 higher (0.06 lower to 0.18 higher)	VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.

2 The quality of evidence was downgraded by 1 level because it was unclear whether amputation was due to trauma or not.
3 95% CI crosses 1 MID (MID boundaries locomotor capability index -3.99, +3.99; knee flexors -0.27, +0.27; knee extensors -0.21, +0.21).
a These outcomes were reported as 'mean' values which were measured at the end of 4-weeks intervention.

Table 7: Clinical evidence profile for comparison complex decongestive physiotherapy (CDP) to conventional bandaging (CB) in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CDP	CB	Relative (95% CI)	Absolute		
Changes in mobility: Change in circumferential measurement[a] at medial tibial platol at 4 weeks post-intervention[b] (Better indicated by lower value)												
1 (Topuz 2012)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5	6	-	MD 0.58 lower (1.84 lower to 0.68 higher)	VERY LOW	CRITICAL
Changes in mobility: Change in circumferential measurement[a] at distal stump at 4 weeks post-intervention[b] (Better indicated by lower values)												
1 (Topuz 2012)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	5	6	-	MD 1.02 lower (2.37 lower to 0.33 higher)	VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.
2 95% CI crosses 2 MIDs (MID boundaries -0.54, +0.54).
3 95% CI crosses 1 MID (MID boundaries -0.64, +0.64).
4 These outcomes were collected as the outcome in the protocol "Change in mobility" as it was considered that oedema (assessed by circumferential measurement) can limit the range of movement.
b These outcomes were calculated as 'change or difference in mean values' from the baseline at the end of 4-weeks intervention.

Table 8: Clinical evidence profile for comparison mirror therapy to covered-mirror therapy in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mirror therapy	Covered-mirror therapy	Relative (95% CI)	Absolute		
Pain: Number of subjects reporting a decrease in pain at 4 weeks follow-up (RR>1 favouring mirror therapy over covered-mirror therapy)												
2[1]	randomised trials	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	14/15 (93.3%)	3/12 (25%)	RR 3.31 (1.35 to 8.11)	577 more per 1000 (from 88 more to 1000 more)	VERY LOW	CRITICAL
Pain: Number of people reporting worsening pain at 4 weeks follow-up (RR<1 favouring mirror therapy over covered-mirror therapy)												
1 (Chan 2007)[1]	randomised trials	very serious[2]	no serious inconsistency	serious[4]	very serious[5]	none	0/6 (0%)	3/6 (50%)	RR 0.14 (0.01 to 2.28)	430 fewer per 1000 (from 495 fewer to 640 more)	VERY LOW	CRITICAL
Pain: Change from baseline in VAS pain score at 4 weeks post-intervention (value reported as mean difference measured on 100 millimetre visual analogue scale; better indicated by lower values)												

1 (Finn 2017)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[6]	none	9	6	-	MD 27.2 lower (44.79 to 9.61 lower)	VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference; PLP: phantom limb pain; VAS: visual analogue scale
[1] Chan 2007, Finn 2017
[2] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.
[3] The quality of evidence was downgraded by 1 level because it was unclear from 1 study (Chan 2007) whether amputation was due to trauma or not.
[4] The quality of evidence was downgraded by 1 level because it was unclear whether amputation was due to trauma or not.
[5] 95% CI crosses 2 MIDs (MID boundaries 0.8, 1.25).
[6] 95% CI crosses 1 MID (MID boundaries -25.5, +25.5).

Table 9: Clinical evidence profile for comparison mental-visualisation therapy to covered-mirror therapy in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Mental-visualisation therapy**	**Covered-mirror therapy**	**Relative (95% CI)**	**Absolute**		
Pain: Number of people reporting a decrease in pain at 4 weeks follow-up (RR>1 favouring mental-visualisation therapy over covered-mirror therapy)												
1 (Chan 2007)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/6 (33.3%)	1/6 (16.7%)	RR 2 (0.24 to 16.61)	167 more per 1000 (from 127 fewer to 1000 more)	VERY LOW	CRITICAL
Pain: Number of people reporting worsening pain at 4 weeks follow-up (RR<1 favouring mental-visualisation therapy over covered-mirror therapy)												
1 (Chan 2007)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	4/6 (66.7%)	3/6 (50%)	RR 1.33 (0.5 to 3.55)	165 more per 1000 (from 250 fewer to 1000 more)	VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio;
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.
2 The quality of evidence was downgraded by 1 level because it was unclear whether amputation was due to trauma or not.
3 95% CI crosses 2 MIDs (MID boundaries 0.8, 1.25).

Table 10: Clinical evidence profile for comparison mirror therapy to tactile treatment in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Mirror therapy**	**Tactile treatment**	**Relative (95% CI)**	**Absolute**		
Pain: Phantom pain (VAS difference) at 1 week post-intervention[a] (score 0-10; better indicated by lower values)												
1 (Ol 2018)	randomised	very	no serious	no serious	serious[2]	none	15	15	-	MD 0.7 higher (1.5 lower to		CRITICAL

	trials	serious[1]	inconsistency	indirectness						2.9 higher)	VERY LOW	
Pain: Stump pain (VAS difference) at 1 week post-intervention[a] (score 0-10; better indicated by lower values)												
1 (Ol 2018)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 1.3 higher (0.79 lower to 3.39 higher)	VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference; RR: risk ratio; VAS: visual analogue score
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.
2 95% CI crosses 1 MID (MID boundaries phantom pain -1.54, +1.54; stump pain -1.48, +1.48).
a These outcomes were calculated as 'change or difference in mean value' from the baseline at the end of 1-week intervention.

Table 11: Clinical evidence profile for gait-oriented mental practice to non-motor mental practice in people with amputation due to traumatic injury

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Gait-oriented mental practice**	**Non-motor mental practice**	**Relative (95% CI)**	**Absolute**		
Changes in mobility: First peak of vertical Ground reaction force (GRF V1: heel strike) at 4 weeks post-intervention[a] (Better indicated by lower values)												
1 (Cunha 2017)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	5	-	MD 12.4 lower (17.47 to 7.33 lower)	VERY LOW	CRITICAL
Changes in mobility: Second peak of vertical ground reaction force (GRF V2: propulsion phase) at 4 weeks post-intervention[a] (Better indicated by higher values)												
1 (Cunha 2017)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	5	-	MD 8.2 higher (4.33 to 12.07 higher)	VERY LOW	CRITICAL
Changes in mobility: First peak of anterior-posterior ground reaction force (GRF AP1: braking capacity) at 4 weeks post-intervention[a] (Better indicated by higher values)												
1 (Cunha 2017)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	5	-	MD 9.1 higher (5.74 to 12.46 higher)	VERY LOW	CRITICAL
Changes in mobility: Second peak of anterior-posterior ground reaction force (GRF AP2: acceleration) at 4 weeks post-intervention[a] (Better indicated by higher values)												
1 (Cunha 2017)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	5	-	MD 3.3 higher (1.97 to 4.63 higher)	VERY LOW	CRITICAL
Changes in mobility: Medio-lateral ground reaction force (ML: prosthetic foot position) at 4 weeks post-intervention[a] (Better indicated by lower values)												
1 (Cunha 2017)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	5	-	MD 0.6 lower (0.85 to 0.35 lower)	VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2.
2 The quality of evidence was downgraded by 1 level because it was unclear whether amputation was due to trauma or not.
a These outcomes were calculated as 'change or difference in mean values' from the baseline at the end of 4-weeks intervention.

GRADE tables for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No evidence was identified which was applicable to this review question.

Appendix G – Economic evidence study selection

Economic study selection for:

C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages are effective and acceptable?

A combined search was conducted for both review questions.

Figure 4: Study selection flow chart

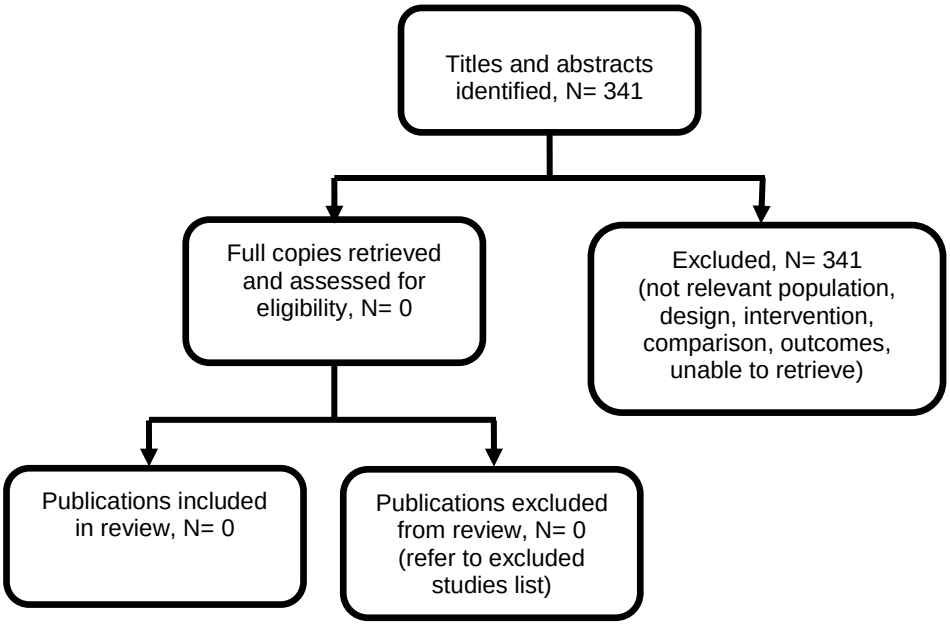
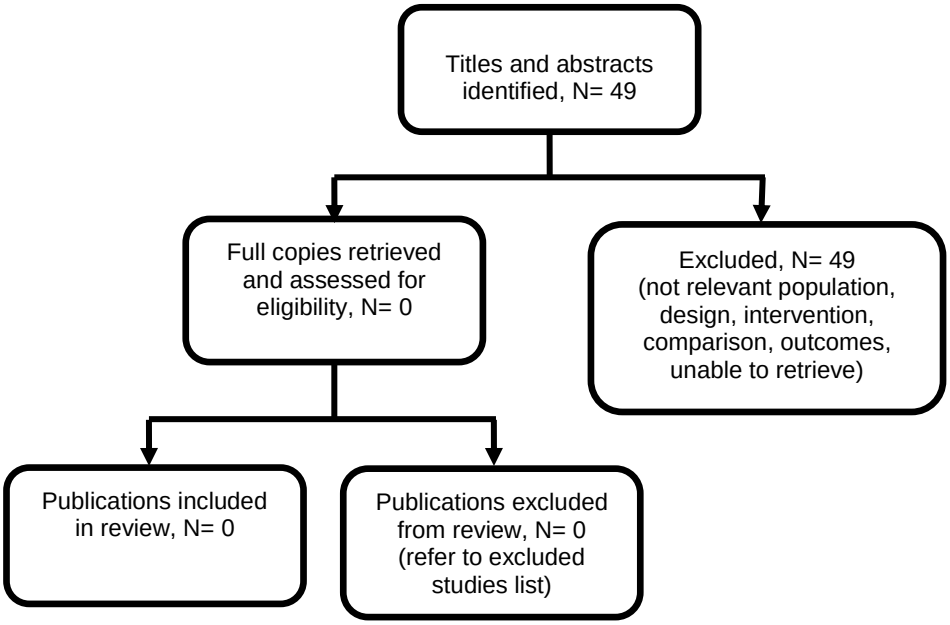


Figure 5: Study selection flow chart



Appendix H – Economic evidence tables

Economic evidence tables for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic studies were identified which were applicable to this review question.

Economic evidence tables for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic studies were identified which were applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic studies were identified which were applicable to this review question.

Economic evidence profiles for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic studies were identified which were applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic analysis was undertaken for this review question.

Economic evidence analysis for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No economic analysis was undertaken for this review question.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Clinical studies

Table 12: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Ali, Mujtaba M., Loretz, Lorraine, Shea, Art, Poorvu, Eli, Robinson, William P., Schanzer, Andres, Messina, Louis M., Baril, Donald T., A contemporary comparative analysis of immediate postoperative prosthesis placement following below-knee amputation, Annals of Vascular Surgery, 27, 1146-53, 2013	None of the patients were amputated for trauma
Anaforoglu Kulunkoglu, Bahar, Erbahceci, Fatih, Alkan, Afra, A comparison of the effects of mirror therapy and phantom exercises on phantom limb pain, Turkish journal of medical sciences, 49, 101-109, 2019	Comparison not in PICO: mirror therapy versus phantom exercises. Intervention not in PICO: Phantom exercises.
Anghelescu, Doralina L., Kelly, Cassandra N., Steen, Brenda D., Wu, Jianrong, Wu, Huiyun, DeFeo, Brian M., Scobey, Kristin, Burgoyne, Laura, Mirror Therapy for Phantom Limb Pain at a Pediatric Oncology Institution, Rehabilitation oncology (American Physical Therapy Association. Oncology Section), 34, 104-110, 2016	Population not in PICO: children with phantom limb pain
Barbin, J., De Angelis, M. P., Paysant, J., Perennou, D., Mirror therapy in the treatment of the phantom limb pain in amputees, Annals of Physical and Rehabilitation Medicine, 57, e127-e128, 2014	Published as an abstract only. Not enough information available to ascertain relevance.
Barbin, J., Seetha, V., Casillas, J. M., Paysant, J., Perennou, D., The effects of mirror therapy on pain and motor control of phantom limb in amputees: A systematic review, Annals of Physical and Rehabilitation Medicine, 59, 270-5, 2016	Systematic review, included studies checked for relevance
Batsford, Sarah, Ryan, Cormac G., Martin, Denis J., Non-pharmacological conservative therapy for phantom limb pain: A systematic review of randomized controlled trials, Physiotherapy theory and practice, 33, 173-183, 2017	Systematic review, included studies checked for relevance.
Brodie, E. E., Whyte, A., Niven, C. A., Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement, Eur J Pain, 11, 428-36, 2007	Mixed population, 26/80 patients had amputations for trauma
Brunelli, Stefano, Morone, Giovanni, Iosa, Marco, Ciotti, Cristina, De Giorgi, Roberto, Foti, Calogero, Traballesi, Marco, Efficacy of progressive muscle relaxation, mental imagery, and phantom exercise training on phantom limb: a randomized controlled trial, Archives of Physical Medicine and Rehabilitation, 96, 181-7, 2015	28/40 patients were amputated due to dysvascular cause
Campo-Prieto, P., Rodriguez-Fuentes, G., Effectiveness of mirror therapy in phantom limb pain: A literature review, Efectividad de la terapia de espejo en el dolor del miembro fantasma. Una revision actual de la literatura., 2018	Unavailable

Cole, J., Crowle, S., Austwick, G., Slater, D. H., Exploratory findings with virtual reality for phantom limb pain; from stump motion to agency and analgesia, Disabil Rehabil, 31, 846-54, 2009	Only 1 out of 14 amputees were amputated for trauma
Darnall, B. D., Self-delivered home-based mirror therapy for lower limb phantom pain, Am J Phys Med Rehabil, 88, 78-81, 2009	Case report
Darnall, Beth D., Li, Hong, Home-based self-delivered mirror therapy for phantom pain: a pilot study, Journal of rehabilitation medicine, 44, 254-60, 2012	Mixed population; 14/31 participants had amputations due to trauma.
Darter, Benjamin J., Nielsen, David H., Yack, H. John, Janz, Kathleen F., Home-based treadmill training to improve gait performance in persons with a chronic transfemoral amputation, Archives of Physical Medicine and Rehabilitation, 94, 2440-7, 2013	Mixed population. Amputations were performed due to cancer or trauma, but unclear how many patients had amputations due to trauma.
De-Rosende Celeiro, Ivan, Simon Sanjuan, Luisa, Santos-Del-Riego, Sergio, Activities of daily living in people with lower limb amputation: outcomes of an intervention to reduce dependence in pre-prosthetic phase, Disability and Rehabilitation, 39, 1799-1806, 2017	Population not in PICO: 45/52 subjects were amputated for vascular cause
Diers, M., Christmann, C., Koeppe, C., Ruf, M., Flor, H., Mirrored, imagined and executed movements differentially activate sensorimotor cortex in amputees with and without phantom limb pain, Pain, 149, 296-304, 2010	No relevant outcomes
Ezendam, Danielle, Bongers, Raoul M., Jannink, Michiel J. A., Systematic review of the effectiveness of mirror therapy in upper extremity function, Disability and Rehabilitation, 31, 2135-49, 2009	Systematic review, included studies checked for relevance
Farsi, Zahra, Azarmi, Somayeh, Effect of Roy's Adaptation Model-Guided Education on Coping Strategies of the Veterans with Lower Extremities Amputation: A Double-Blind Randomized Controlled Clinical Trial, International journal of community based nursing and midwifery, 4, 127-36, 2016	Outcomes not in PICO
Foell, J., Bekrater-Bodmann, R., Diers, M., Flor, H., Mirror therapy for phantom limb pain: brain changes and the role of body representation, European journal of pain (London, England), 18, 729-39, 2014	Single-group study
Geertzen, Jan H. B., Kees, Emmelot, Dijkstra, Pieter U., A randomised trial of rigid stump dressing following trans-tibial amputation for peripheral arterial insufficiency, Prosthetics and Orthotics International, 28, 192, 2004	Letter; the RCT looked at amputation for peripheral arterial insufficiency
Herrador Colmenero, Laura, Perez Marmol, Jose Manuel, Marti-Garcia, Celia, Querol Zaldivar, Maria de Los Angeles, Tapia Haro, Rosa Maria, Castro Sanchez, Adelaida Maria, Aguilar-Ferrandiz, Maria Encarnacion, Effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation: A systematic review, Prosthetics and Orthotics International, 42, 288-298, 2018	Systematic review, included studies checked for relevance
Huang, W. Z., Liu, L., Wang, Z. J., Li, D. D., Cui, S. Y., Yan, W., Effect of mirror therapy on the recovery of hand sensory function in patients with replantation of broken fingers, Basic & clinical pharmacology & toxicology, 125, 4, 2019	Published as abstract only. Not enough information available to ascertain relevance.
Kazemi, A. S., Elahin, F., Moradi, M., Fesharaki, M., Effects of mirror therapy on phantom pain in patients with bilateral amputations admitted to the veterans foundation of Qazvin, Iran, Avicenna journal of phytomedicine., 5, 103, 2015	Published as an abstract only. Not enough information available to ascertain relevance.
MacIver, K., Lloyd, D. M., Kelly, S., Roberts, N., Nurmikko, T.,	Single-group study

Phantom limb pain, cortical reorganization and the therapeutic effect of mental imagery, Brain, 131, 2181-2191, 2008	
Mallik, A. K., Pandey, S. K., Srivastava, A., Kumar, S., Kumar, A., Comparison of Relative Benefits of Mirror Therapy and Mental Imagery in Phantom Limb Pain in Amputee Patients at a Tertiary Care Center, Archives of Rehabilitation Research and Clinical Translation, 100081, 2020	Mixed population; 65/92 had amputations due to trauma, results not presented separately for target population.
McQuaid, J., Peterzell, D., Rutledge, T., Cone, R., Nance, P., Velez, D., Coeshott, R., Ortega, J., Van Duyn, M., Otilingam, P., Atkinson, J., Integrated cognitive-behavioral therapy (CBT) and mirror visual feedback (MVF) for phantom limb pain: A randomized clinical trial, Journal of Pain, 15, S108, 2014	Published as abstract only. Not enough information available to ascertain relevance.
Mercier, Catherine, Sirigu, Angela, Training with virtual visual feedback to alleviate phantom limb pain, Neurorehabilitation and Neural Repair, 23, 587-94, 2009	Mixed population: 2/8 patients were amputee, the rest were brachial plexus avulsion
Morgan, Sara J., McDonald, Cody L., Halsne, Elizabeth G., Cheever, Sarah M., Salem, Rana, Kramer, Patricia A., Hafner, Brian J., Laboratory- and community-based health outcomes in people with transtibial amputation using crossover and energy-storing prosthetic feet: A randomized crossover trial, PLoS ONE, 13, e0189652, 2018	Comparison not in PICO: comparing different types of prostheses
Moseley, G. L., Graded motor imagery for pathologic pain: a randomized controlled trial, Neurology, 67, 2129-34, 2006	Only 9 out of 51 patients were amputee and the rest 37 - complex regional pain syndrome and 5 - bronchial plexus avulsion injury. There is no separate analysis for amputee patients.
Ortiz-Catalan, M., Guethmundsdottir, R. A., Kristoffersen, M. B., Zepeda-Echavarria, A., Caine-Winterberger, K., Kulbacka-Ortiz, K., Widehammar, C., Eriksson, K., Stockselius, A., Ragno, C., Pihlar, Z., Burger, H., Hermansson, L., Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: a single group, clinical trial in patients with chronic intractable phantom limb pain, Lancet, 388, 2885-2894, 2016	Single-group study
Perry, B. N., Hussey-Andersen, L. K., Hughes, K. E., Weeks, S. R., Merritt, V. C., Pasquina, P. F., Tsao, J. W., Mirror therapy as a phantom limb pain treatment for upper-extremity amputees, Journal of neurology., 260, S19, 2013	Published as abstract only. Not enough information available to ascertain relevance.
Ramachandran, V. S., Rogers-Ramachandran, D., Synaesthesia in phantom limbs induced with mirrors, Proc Biol Sci, 263, 377-86, 1996	Mixed population: 5/10 patients were amputated for trauma; results were reported individually (case series)
Ramadugu, Shashikumar, Nagabushnam, Satish C., Katuwal, Nagendra, Chatterjee, Kaushik, Intervention for phantom limb pain: A randomized single crossover study of mirror therapy, Indian Journal of Psychiatry, 59, 457-464, 2017	Cross-over study
Rickard, JA , Effects of Hypnosis in the Treatment of Residual Stump and Phantom Limb Pain (PhD Dissertation). , 2004	Mixed population: 5/20 patients were amputated for trauma. Thesis; no individual analyses for those with trauma-related amputation
Rolin, O., Darter, B. J., Does intensive initial training improve mobility for amputees receiving a new lower extremity prosthesis?, PM and R, 9, S131, 2017	Published as abstract only. Retrospective non-randomised study with 44 participants
Rothgangel, A., Braun, S., Smeets, R., Beurskens, A., Feasibility of a traditional and teletreatment approach to mirror therapy in	Mixed population; 18/51 had amputations due to trauma,

patients with phantom limb pain: a process evaluation performed alongside a randomized controlled trial, Clinical rehabilitation, 33, 1649â€• 1660, 2019	results not presented separately for target population.
Rothgangel, A., Braun, S., Winkens, B., Beurskens, A., Smeets, R., Traditional and augmented reality mirror therapy for patients with chronic phantom limb pain (PACT study): results of a three-group, multicentre single-blind randomized controlled trial, Clinical rehabilitation, 32, 1591â€• 1608, 2018	Mixed population; 25/75 had amputations due to trauma, results not presented separately for target population.
Schmalzl, L., Ragno, C., Ehrsson, H. H., An alternative to traditional mirror therapy: Illusory touch can reduce phantom pain when illusory movement does not, Clinical Journal of Pain, 29, e10-e18, 2013	Single-group study; N=6, 5 of whom had amputations for trauma.
Schon, Lew C., Short, Kelly W., Soupiou, Olga, Noll, Kenneth, Rheinstein, John, Benefits of early prosthetic management of transtibial amputees: a prospective clinical study of a prefabricated prosthesis, Foot & ankle international, 23, 509-14, 2002	Mixed population: amputation was done for infection (16), ischemia (4), acute trauma (4), chronic pain (5), and nonreconstructable Charcot neuroarthropathy (1).
Seidel, S., Kasprian, G., Furtner, J., Schopf, V., Essmeister, M., Sycha, T., Auff, E., Prayer, D., Mirror therapy in lower limb amputees--a look beyond primary motor cortex reorganization, RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin, 183, 1051-7, 2011	Single-group study
Spiliotopoulou, G., Atwal, A., Is occupational therapy practice for older adults with lower limb amputations evidence-based? A systematic review, Prosthetics and Orthotics International, 36, 7-14, 2012	Systematic review, included studies checked for relevance
Sumitani, M., Miyauchi, S., McCabe, C. S., Shibata, M., Maeda, L., Saitoh, Y., Tashiro, T., Mashimo, T., Mirror visual feedback alleviates deafferentation pain, depending on qualitative aspects of the pain: A preliminary report, Rheumatology, 47, 1038-1043, 2008	Mixed population: 5/11 patients had amputations for trauma.
Tilak, Merlyn, Isaac, Serin Anna, Fletcher, Jebaraj, Vasanthan, Lenny Thinagaran, Subbaiah, Rajalakshmi Sankaran, Babu, Andrew, Bhide, Rohit, Tharion, George, Mirror Therapy and Transcutaneous Electrical Nerve Stimulation for Management of Phantom Limb Pain in Amputees - A Single Blinded Randomized Controlled Trial, Physiotherapy research international : the journal for researchers and clinicians in physical therapy, 21, 109-15, 2016	Comparison not in PICO: TENS versus mirror therapy
Timms, J., Carus, C., Mirror therapy for the alleviation of phantom limb pain following amputation: a literature review, Int j ther rehab, 22, 135â€• 145, 2015	Systematic review, included studies checked for relevance
Traballesi, Marco, Porcacchia, Paolo, Averna, Tiziano, Brunelli, Stefano, Energy cost of walking measurements in subjects with lower limb amputations: a comparison study between floor and treadmill test, Gait & posture, 27, 70-5, 2008	Health condition not in PICO: amputation for peripheral vascular disease due to diabetes or atherosclerosis
Ulger, O., Topuz, S., Bayramlar, K., Sener, G., Erbahceci, F., Effectiveness of phantom exercises for phantom limb pain: a pilot study, J Rehabil Med, 41, 582-4, 2009	Intervention not in PICO: Phantom exercises; N=20; non-randomised study.
van Velzen, A. D., Nederhand, M. J., Emmelot, C. H., Ijzerman, M. J., Early treatment of trans-tibial amputees: retrospective analysis of early fitting and elastic bandaging, Prosthetics and Orthotics International, 29, 3-12, 2005	All patients were amputated for vascular insufficiency
White, E., Wheelchair stump boards and their use with lower limb amputees, Br J Occup Ther, 55, 174-178, 1992	Pre-1995 publication
Yildirim, Meltem, Kanan, Nevin, The effect of mirror therapy on the management of phantom limb pain, Agri : Agri (Algoloji)	Mixed population: 7/15 patients were amputated for vascular

Dernegi'nin Yayin organidir = The journal of the Turkish Society of Algology, 28, 127-134, 2016	cause; reasons for amputation for the remaining patients were not reported

Economic studies

All studies were excluded at the initial title and abstract screening stage. See appendix G for further information.

Excluded clinical and economic studies for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

Clinical studies

Table 13: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Ferris, A. E., Aldridge, J. M., Rabago, C. A., Wilken, J. M., Evaluation of a powered ankle-foot prosthetic system during walking, Archives of Physical Medicine and Rehabilitation, 93, 1911-1918, 2012	Single-group study
Onat, Sule Sahin, Unsal-Delialioglu, Sibel, Ozel, Sumru, The importance of orthoses on activities of daily living in patients with unilateral lower limb amputations, Journal of back and musculoskeletal rehabilitation, 30, 829-833, 2017	Comparison of different types of protheses
Osmani-Vllasolli, Teuta, Hundozi, Hajrije, Bytyci, Cen, Kalaveshi, Ariana, Krasniqi, Blerim, Rehabilitation of patients with war-related lower limb amputations, Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria, 20, 39-43, 2011	Unavailable
Otto, Iris A., Kon, Moshe, Schuurman, Arnold H., van Minnen, L. Paul, Replantation versus Prosthetic Fitting in Traumatic Arm Amputations: A Systematic Review, PLoS ONE, 10, e0137729, 2015	Systematic review: included studies checked for relevance
Patzkowski, Jeanne C., Blanck, Ryan V., Owens, Johnny G., Wilken, Jason M., Kirk, Kevin L., Wenke, Joseph C., Hsu, Joseph R., Skeletal Trauma Research, Consortium, Comparative effect of orthosis design on functional performance, The Journal of bone and joint surgery. American volume, 94, 507-15, 2012	Population not in PICO: Patients with lower-extremity dorsiflexion and/or plantar flexion weakness
Pereira, B. P., Kour, A. K., Leow, E. L., Pho, R. W., Benefits and use of digital prostheses, The Journal of hand surgery, 21, 222-8, 1996	Single-group study
Ramadugu, S., Nagabushnam, S. C., Katuwal, N., Chatterjee, K., Intervention for phantom limb pain: A randomized single crossover study of mirror therapy, Indian Journal of Psychiatry, 59, 457-464, 2017	Population not in PICO: Adult population and this study was included in 3.1a
Rosberg, H. E., Disability and health after replantation or revascularisation in the upper extremity in a population in southern Sweden - A retrospective long time follow up, BMC Musculoskeletal Disorders, 15, 73, 2014	Single-group study
Simon, A. L., Apostolou, N., Vidal, C., Ferrero, E., Mazda, K., Ilharreborde, B., Paediatric tibial shaft fractures treated by open reduction and stabilization with monolateral external fixation, Journal of children's orthopaedics, 12, 20-28, 2018	Single-group study
Stoddard, F. J., Therapeutic play in the diagnosis and treatment	Abstract publication only and

of hospitalized children recovering from acute burns, Journal of the American Academy of Child and Adolescent Psychiatry, 56, S118, 2017	case-series study design
Toda, M., Chin, T., Kohno, H., Shibata, Y., Mizobe, F., Hamamoto, Y., Masuda, A., Use of powered prosthesis for children with upper limb deficiency at the Hyogo rehabilitation center, Prosthetics and Orthotics International, 39, 101-102, 2015	Abstract publication only and no outcomes of interest reported

Economic studies

All studies were excluded at the initial title and abstract screening stage. See appendix G for further information.

Appendix L – Research recommendations

Research recommendations for review question: C.1a For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No research recommendations were made for this review question.

Research recommendations for review question: C.1b For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?

No research recommendations were made for this review question.