National Institute for Health and Care Excellence

Final

Early and locally advanced breast cancer: diagnosis and management

[L] Evidence reviews for strategies for reducing arm and shoulder problems after breast cancer surgery or radiotherapy

NICE guideline NG101

Evidence reviews underpinning recommendations 1.12.5 to 1.12.12 and research recommendations in the NICE guideline

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Final

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1.1 Review question

What strategies are effective in reducing arm and shoulder problems after breast cancer surgery or radiotherapy?

1.1.1 Introduction

The NICE guideline on early and locally advanced breast cancer: diagnosis and management (NICE guideline NG101) was reviewed in 2022 as part of NICE's surveillance programme. New evidence was identified that could affect recommendations following the publication of a Health Technology Assessment (HTA) report on a structured exercise programme compared to usual care for women at high risk of upper limb disability after breast cancer surgery (PRevention Of Shoulder ProblEms tRial [PROSPER], Bruce et al. 2022).

The current recommendations highlight that pre-existing shoulder conditions may inform treatment decisions, but do not provide details of potential interventions; and they focus on referring people for physiotherapy only when a persistent reduction in arm and shoulder mobility has been identified after breast cancer treatment, rather than considering how to prevent arm and shoulder mobility problems from occurring. Evidence on potential interventions to prevent or reduce arm and shoulder mobility problems will therefore be reviewed.

The aim of this review was to assess the effectiveness and cost-effectiveness of strategies in reducing arm and shoulder problems after breast cancer surgery or radiotherapy. This review identified randomised controlled trials that fulfilled the conditions specified in Table 1. See Appendix A for full details of the review protocol.

1.1.2 Summary of the protocol

Table 1: PICO table for strategies for reducing arm and shoulder problems after breast cancer surgery or radiotherapy

Population	Adults with early or locally advanced breast cancer (18 and over) who have undergone any of the following treatments alone or in combination: • surgery for breast cancer alone or with: axillary clearance, sentinel lymph node biopsy, or node sampling • radiotherapy for breast cancer alone or with regional lymph node radiotherapy

Intervention	• Prehabilitation provided to patients following their initial diagnosis
	• Post-surgery or post-radiotherapy:
	  ○ Physiotherapy aimed at maximising people's ability to move and function
	  ○ Exercise or rehabilitation classes for people who have undergone surgery or radiotherapy
	  ○ Information/education about unsupervised post-surgical or post-radiotherapy arm/shoulder exercise

Comparator	• All interventions in combination or interventions compared to each other

	• No intervention
Outcome	Primary outcomes: • Upper limb function (includes Disabilities of Arm and Shoulder Hand Scale – DASH and range of movement) • Upper limb muscle strength • Pain • Incidence of lymphoedema • Quality of life • Resource use and cost Secondary outcomes: • Patient adherence

1.1.3 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 the methods section in Appendix L.

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

1.1.4 Effectiveness evidence

1.1.3.1 Methods specific for this review

RCTs were separated into 2 broad categories based on the interventions listed in the protocol as physiotherapy or exercise. Each of these categories was defined as:

- Physiotherapy: physiotherapist-led intervention.
- Exercise: any type of exercise intervention that was not physiotherapist-led.

Data for some outcomes was not published in primary papers. However, data was available for these outcomes in a Cochrane systematic review (McNeely ML, Exercise interventions for upper-limb dysfunction due to breast cancer treatment, Cochrane Database of Systematic Reviews 2010, Issue 6. Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.). The Cochrane review was therefore used as the source of data for the following outcomes and this has been acknowledged in relevant forest plots and GRADE tables:

- range of movement (Chen 1999)
- impaired shoulder mobility (Schultz 1997; van der Horst 1985)
- incidence of lymphoedema (van der Horst 1985; Box 2002)
- range of movement (Box 2002; Hwang 2008; Kilgour 2008)
- pain (Hwang 2008)

Most included RCTs reported multiple time points. Data was collected for all primary and secondary outcomes for all time points. This data can be seen in Appendix E – Forest plots and Appendix F – GRADE tables. This has been summarised to include closest time point to the ones listed in the protocol (see details in the review protocol in Appendix A). This means that only 1 time point was included in the summary for:

- Short term: less or equal to 6 months (for example, if an RCT reported 1, 3 and 6 months, only data at 6 months was reported in the summary)
- Medium term: more than 6 months and less or equal to 12 months (for example, if an RCT reported 7 and 12 months, only data at 12 months was reported in the summary)

- Long term: more than 12 months (the longest time after 12 months was reported in the summary, for example if an RCT reported 18 months and 5 years, only data at 5 years was reported)

1.1.3.2 Protocol deviations

The protocol did not specify 'usual care' but some of the included RCTs reported their comparator as 'usual care' and this was defined based on which country and year the study took place. Therefore, 'usual care' was added as a comparator.

1.1.4.1 Included studies

A systematic search was carried out to identify randomised controlled trials (RCTs) and systemic reviews of RCTs, which found 2814 references (see Appendix B for the literature search strategy). Evidence from the original guideline (19 RCTs) and evidence identified from systematic reviews or in the list of references of included studies (7 references) was also reviewed. In total, 2821 references were identified for screening at title and abstract level with 2676 excluded at this level. Full texts were ordered to be screened for 145 references.

In total 51 RCTs were included based on their relevance to the review protocol (Appendix A). Some RCTs were reported in multiple references, therefore, 64 references were included in total. The clinical evidence study selection is presented as a PRISMA diagram in Appendix C.

Included RCTs reported the following comparisons:

- Early vs delayed physiotherapy (Bendz 2002; Cinar 2008; Flew 1979; Jansen 1990; Schultz 1997; Van Der Horst 1985 = 6 RCTs)
- Physiotherapy and usual care vs usual care (Bruce 2022; Lauridsen 2005; Rafn 2018 = 3 RCTs)
- Physiotherapy (exercise programme) vs usual care (Ammitzboll 2020; Klein 2021 = 1 RCT)
- Physiotherapy (water exercise programme) vs usual care (Cantarero-Villanueva 2012 = 1 RCT)
- Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) vs usual care (Feyzioglu 2020 = 1 RCT)
- Physiotherapy (myofascial release massage) vs usual care (Marshall-Mckenna 2014 = 1 RCT)
- Physiotherapy (group-based educational program and visual material) vs usual care (Simoncini 2017 = 1 RCT)
- Physiotherapy vs information about unsupervised exercise (Beurskens 2007; Box 2002a = 2 RCTs)
- Physiotherapy (free-range exercises) vs physiotherapy (limited-range exercises) (de Almeida Rizzi 2020 = 1 RCT)
- Physiotherapy (directed exercises) vs physiotherapy (free exercises) (De Rezende 2006 = 1 RCT)
- Physiotherapy (water exercise) vs physiotherapy (Pilates) vs physiotherapy (yoga) (Odynets 2019b = 1 RCT comparing 3 interventions)
- Physiotherapy (Pilates) vs physiotherapy (combined exercises) vs physiotherapy (home exercises) (Zengin Alpozgen 2017 = 1 RCT comparing 3 interventions)
- Physiotherapy (manual therapy and upper limb exercises) vs physiotherapy (upper limb exercises) (Pace do Amaral 2012 = 1 RCT)

- Physiotherapy and myofascial therapy vs physiotherapy and placebo – after surgery (De Groef 2017 = 1 RCT)
- Physiotherapy and myofascial therapy vs physiotherapy and placebo – after radiotherapy (De Groef 2018 = 1 RCT)
- Physiotherapy vs no intervention during radiotherapy (Leal 2016 = 1 RCT)
- Physiotherapy (early) vs no intervention (Testa 2014 = 1 RCT)
- Early vs delayed exercise (Abe 1998; Chen 1999; Dawson 1989; Todd 2008 = 4 RCTs)
- Early vs delayed exercise (Chen 1999 = 1 RCT)
- Exercise and usual care vs usual care (Harder 2015; Kilbreath 2006a; Kilbreath 2012; Kilgour 2008; Lee 2007; Majed 2022; Mutrie 2007; Zhou 2019 = 8 RCTs)
- Face to face exercise vs telephone delivered exercise usual care (Hayes 2013 = 1 RCT comparing 3 interventions)
- Rehabilitation vs usual care (da Silveira 2020; Ibrahim 2017 = 2 RCTs)
- Exercise vs exercise (Charati 2022; Giron 2016; Haines2010; Hayes 2013; Hwang 2008; Odynets 2019a; Reis 2013; Wiskemann 2017; Xie 2010 = 6 RCTs)

See 1.1.14 References – included studies for a list of included references.

1.1.4.2 Excluded studies

See Appendix J for a list of excluded studies with reasons for exclusion.

1.1.5 Summary of studies included in the effectiveness evidence

Table 1: Summary of included studies comparing the effectiveness of physiotherapy for reducing arm and shoulder problems after breast cancer surgery or radiotherapy (all interventions in Table 1 were physiotherapist-lead)

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Ammitzboll 2020 **Denmark**	RCT	N=158 women aged 42-63 years with primary unilateral breast cancer and had surgery (including axillary lymph node dissection [ALND])	Exercise programme 2 weeks after surgery for 1 year	Usual care which wasn't standardised and varied in terms of contact with a physiotherapist for 1 year	12 months	**Primary outcomes:** Range of movement Upper limb muscle strength Pain intensity Neuropathic pain

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
						Incidence of lymphoedema Quality of life **Secondary outcome:** Patient adherence
Bendz 2002 **Sweden**	RCT	N= 205 women aged 47-69 years undergoing radical mastectomy or quadrantectomy (including ALND) for breast cancer.	Early arm exercises preoperatively	Delayed arm exercises postoperatively	2 years	**Primary outcomes:** Range of movement Pain intensity Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		Key exclusion criteria: women who underwent bilateral surgery or diseases that affected the outcome				
Beurskens 2007 **The Netherlands**	RCT	N = 30 women aged 34-82 years with breast cancer undergoing surgery with ALND. Key exclusion criteria: participants with	Participants started physiotherapy two weeks following surgery for 3 months	Participants received a flyer with arm/shoulder exercises	6 months	**Primary outcomes:** Upper limb function (DASH score) Range of movement Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		previous contralateral breast cancer surgery.				
Box 2002 **Australia**	RCT	N = 55 women aged 46-69 years undergoing breast conserving surgery (complete local excision and axillary dissection) or modified radical	Physiotherapy management care plan (include preoperative and postoperative assessments) for 2 years	Participants received exercise instruction booklet for 2 years	2 years	**Primary outcomes:** Range of movement Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		mastectomy for breast cancer Key exclusion criteria: elective reconstructive surgery at the same time as initial breast surgery				
Bruce 2022 **United Kingdom**	RCT	N = 350 women aged 46-70 years who were diagnosed with primary breast cancer and scheduled for surgical excision	Usual care and structured exercise programme for 12 months	Usual care (two information leaflets with postoperative advice and exercises)	1 year	**Primary outcomes** Upper limb function (DASH) Pain

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		and considered to be at high risk of upper limb disability after surgery.				Neuropathic pain Incidence of lymphoedema Quality of life Healthcare resource use **Secondary outcome:** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Cantarero-Villanueva 2012	RCT	N= 66 women aged 38-56 years who were diagnosed with breast cancer and received a mastectomy or quadrantectomy Key exclusion criteria: women <25 years and >65 years, had uncontrolled hypertension, had recurrent cancer.	Water exercise programme for 8 weeks	Usual care (recommendations by an oncologist related to a healthy lifestyle) for 8 weeks. Participants received the water exercise programme after 8 weeks	8 weeks	**Primary outcome:** Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Cinar 2008 **Turkey**	RCT	N= 57 women aged 38-64 years who underwent modified radical mastectomy for breast cancer	Directed physiotherapy (1st postoperative day) for 8 weeks	Home physiotherapy after drain removal for 8 weeks	6 months	**Primary outcome:** Range of movement
De Almeida Rizzi 2020 **Brazil**	RCT	N=60 women aged 39-64 years who underwent mastectomy and implant-based reconstruction planning were randomised. Key exclusion criteria: participants with	Participants were allowed to perform free-range exercises and activities of daily living in free amplitude	Participants had the range of movement limited to 90 degrees for 15 days	90 days	**Primary outcomes:** Upper limb function (DASH) Range of movement Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		bilateral breast cancer or reconstruction with autologous flaps.				
De Groef 2017 **Belgium**	RCT	N= 147 women aged 42-66 years who underwent surgery for breast cancer were randomised. Key exclusion criteria: participants who were not able to	Standard physical therapy programme for 4 months and myofascial therapy for 2 months	Standard physical therapy programme for 4 months and a placebo intervention for 2 months	12 months	**Primary outcomes:** Upper limb function (DASH) Pain intensity Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		visit the hospital for the therapeutic sessions and assessments				
De Groef 2018 **Belgium**	RCT	N = 50 women aged 45-63 years who were treated for primary breast cancer and had pain at the upper region within 3 months of the trial start date.	Standard physical therapy programme and myofascial therapy for 12 weeks	Standard physical therapy programme and a placebo intervention for 12 weeks	12 months	**Primary outcomes:** Upper limb function (DASH) Pain intensity Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		Key exclusion criteria: participants with current cancer or metastasis or those who were not able to visit the hospital for the therapeutic sessions				
De Rezende 2006 **Brazil**	RCT	N = 60 women aged 44-66 years who underwent modified radical mastectomy or quadrantectomy with axillary	Directed physiotherapy exercises	Free physiotherapy exercises	28 days	**Primary outcome:** Range of movement **Secondary outcome:**

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		dissection were randomised. Key exclusion criteria: women who had immediate breast reconstruction or bilateral surgery, who showed a difference more than 2 cm in the circumference of the arms before surgery or who showed limitation of movement in the ipsilateral limb before				Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		surgery were excluded				
Feyzioglu 2020 **Turkey**	RCT	N = 40 women aged 42 – 58 years who underwent breast cancer surgery with axillary dissection were randomised. Only women between the ages of 30-60	Kinect-based rehabilitation by a physiotherapist for 6 weeks	Standardised physiotherapy group for 6 weeks	6 weeks	**Primary outcomes:** Upper limb function (DASH) Range of movement Upper limb muscle strength

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		years were included. Key exclusion criteria: women with previous breast cancer surgery on the present or contralateral side, active or metastatic cancer, women with upper extremity Range of movement limitation before surgery.				Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Flew 1979 **United Kingdom**	RCT	N = 64 women aged 27-77 years who underwent radical mastectomy for early breast cancer were admitted.	Early physiotherapy on the 2nd postoperative day	Delayed physiotherapy on the 7th postoperative day	4 months	**Primary outcomes:** Range of movement Incidence of lymphoedema
Jansen 1990 **The Netherlands**	RCT	N = 144 women aged 28-81 years undergoing primary surgical treatment of breast carcinoma. Key exclusion criteria: previous	Early physiotherapy (1st postoperative day)	Late physiotherapy(8th postoperative day)	6 months	**Primary outcomes:** Range of movement Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		disease or operations affecting shoulder movements or previous axillary operations or radiotherapy.				
Klein 2021 **Israel**	RCT	N = 157 women aged 18-85 years scheduled for breast cancer surgery. Key exclusion criteria: cognitive disorders, previous breast	Physical therapy started concomitantly with radiotherapy	Usual care (participants did not receive orientation to perform exercises)	6 months	**Primary outcomes:** Upper limb function (QuickDASH) Range of movement Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		cancer, lymphoedema before surgery or previous shoulder surgery				Incidence of lymphoedema
Lauridsen 2005 **Denmark**	RCT	N = 139 women aged 29-79 years with breast cancer scheduled for surgery. Key exclusion criteria: reported illnesses affecting the	Standard treatment plus physiotherapy from the 6th to 8th postoperative week for 6 weeks	Standard treatment and physiotherapy from 26th postoperative week for 6 weeks	6 weeks	**Secondary outcome:** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		upper extremities preoperatively.				
Leal 2016 **Brazil**	RCT	N = 35 women aged 43-59 years with a diagnosis of unilateral breast cancer and undergoing surgery and radiotherapy. Key exclusion criteria: participants with	Supervised kinesiotherapy of upper limb for 5 weeks	Control (did not receive any intervention) for 5 weeks	2 months	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		orthopaedic and/neurologic disorders				
Marshall-McKenna 2014 **Scotland**	RCT	N = 24 women aged 40-74 years who received a mastectomy or breast conserving treatment and surgery to the axilla. Key exclusion criteria:	Myofascial release massage	Usual care (did not include routine physiotherapy)	3 months	**Primary outcomes:** Upper limb function (DASH score) Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		participants who reported musculoskeletal injuries, had metastatic cancer or any condition associated with pain or reduced upper limb mobility				
Odynets 2019b **Ukraine**	RCT	N = 115 women aged 50-60 years with post-mastectomy pain, who had undergone surgical	Intervention 1: Water exercise interventions for 3 months Intervention 2:	Yoga exercises for 3 months	12 weeks	**Primary outcome:** Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		treatment and adjuvant radiation therapy for breast cancer. Key exclusion criteria: body mass index greater than 25 kg/m^2 and if they had metastasis, bilateral lymphoedema and any contraindications limiting activity.	Pilates exercises for 3 months			

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Oliveira 2009 **Brazil**	RCT	N = 66 women aged 38-62 years who underwent breast surgery for breast cancer. Key exclusion criteria: women who underwent radiotherapy before surgery, upper limb lymphoedema and/or Range of movement limitation prior to radiotherapy, those who underwent	Physical therapy (started concomitantly with radiotherapy) for 6 weeks	Control (no physical therapy during radiotherapy) for 6 weeks	6 months	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		bilateral breast surgery and those with local recurrence.				
Pace de Amaral, 2012 **Brazil**	RCT	N = 131 women aged 44-67 years who underwent axillary lymph node dissection (ALND) for breast cancer treatment. Key exclusion criteria: women who had	Upper limb exercises on the first postoperative day, following by manual therapy foe 1 month	Upper limb exercises on first postoperative day for 1 month	18 months	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		undergone bilateral ALND or had previous radiotherapy				
Rafn 2018 **Canada**	RCT	N = 41 women aged 30-75 years who were scheduled to undergo surgery for breast cancer. Key exclusion criteria: women who were scheduled for lumpectomy and	Prospective surveillance and targeted physiotherapy and usual care	Education and usual care	12 months	**Primary outcomes:** Range of movement Upper limb muscle strength Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		sentinel lymph now dissection, breast cancer surgery, primary lymphoedema.				Quality of life Resource costs
Schultz 1997 **Sweden**	RCT	N = 163 women aged 35-84 years with breast cancer undergoing modified mastectomy.	Early postoperative shoulder exercises	Delayed postoperative shoulder exercises	6 months	**Primary outcome:** Impaired shoulder mobility

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Simoncini 2017 **Italy**	RCT	N = 186 women 37-61 years with breast cancer undergoing radical mastectomy or quadrantectomy with complete unilateral axillary lymph node dissection. Key exclusion criteria: previous axillary surgery, upper extremity physio/pathology, severe heart diseases severe	Group-based educational program and visual material for 6 weeks	Usual rehabilitation (individual) for 6 weeks	3 months	**Primary outcome:** Pain intensity **Secondary outcome:** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		mental disorders and breast reconstruction with flaps.				
Testa 2014 **Italy**	RCT	N = 70 women aged 36-63 years scheduled for modified mastectomy or for segmental mastectomy with axillary dissection. Key exclusion criteria: women	Early physical rehabilitation programme for 1 month	Control (did not receive early physical rehabilitation treatment)	12 months	**Primary outcomes:** Range of movement Pain intensity Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		that underwent segmental mastectomy without axillary dissection, women with only sentinel lymph node biopsy.				
Van der Horst 1985 **The Netherlands**	RCT	N = 57 women aged 17-81 years who underwent axillary dissections for carcinoma of the breast.	Early active mobilisation for 14 days	Late active mobilisation for 14 days	6 months	**Primary outcomes:** Shoulder function Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Zengin Alpozgin 2017 **Turkey**	RCT	N = 57 women aged 35-64 years with stages I-II breast cancer and shoulder Range of movement limitation. Key exclusion criteria: severe cardiac disease, uncontrolled hypertension, lymphoedema, neurological or rheumatological disease	Intervention 1: Pilates-based exercises for 8 weeks Intervention 2: Combined exercises for 8 weeks	Home exercises for 8 weeks	Not reported	**Primary outcomes:** Upper limb function (DASH score) Range of movement Upper limb muscle strength Pain intensity

Table 2: Summary of included studies comparing the effectiveness of exercise for reducing arm and shoulder problems after breast cancer surgery or radiotherapy (all interventions in Table 2 were not physiotherapist-lead)

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Abe 1998 **Japan**	RCT	N = 116 women aged 41-64 years who underwent mastectomy with level I or level II axillary lymph node dissection for breast cancer were randomised.	Early exercise started on the 1st postoperative day	Delayed exercise started on the 8th day postoperatively	1 month	**Primary outcome:** Range of movement
Charati 2022 **Iran**	RCT	N = 70 women aged 28-50 years with non-metastatic non-menopausal breast cancer having surgery on one or both breasts. Key exclusion criteria: women with heart and	Exercise programme for 5 weeks after surgery (starting 2nd postoperative day)	Motor exercise instructions with leaflet for 5 weeks	5 weeks	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		respiratory diseases, women who had experience in psychotherapy				
Chen 1999 **Taiwan**		N= 344 women undergoing primary surgical treatment for breast cancer Key exclusion criteria: women with partial mastectomy or previous axillary operation or radiotherapy, women with bilateral breast cancer.	Early upper arm exercises (3rd postoperative day)	Comparator 1: Later upper arm exercises (6th postoperative day) Comparator 2: Delayed upper arm exercises (after drains were removed)	6 months	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Da Silveira 2020 **Brazil**	RCT	N = 32 women aged 41-60 years who had surgical treatment of breast cancer combined with axillary lymphadenectomy or sentinel lymph node biopsy. Key exclusion criteria: muscle-tendinous lesions or joint injuries in affected limb, skin disorders, diabetes, uncontrolled circulatory disease and lymphoedema	Rehabilitation using the proprioceptive neuromuscular facilitation technique for 4 weeks	Usual care involving conventional rehabilitation for 4 weeks	Not reported	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Dawson 1989 **The Netherlands**	RCT	N = 100 women aged 52-79 years who underwent a radical mastectomy for breast cancer were randomised.	Early exercise started on the 1st post-operative day	Delayed exercise with participants who were immobilised until the 6th day post-operatively	At discharge from hospital	**Primary outcome:** Range of movement
Giron 2016 **Brazil**	RCT	N = 48 women aged 49-60 years who underwent surgical treatment of breast cancer and complained of pain in scapular girdle and upper limb region after 3 months of surgery. Key exclusion criteria: participants with bilateral breast surgery, metastatic disease, vascular	Acupuncture plus kinesiotherapy weekly for 10 weeks	Kinesiotherapy weekly for 10 weeks	10 weeks	**Primary outcomes:** Upper limb function (DASH) Range of movement Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		and tactile sensitivity disorder or with uncompensated diabetes were excluded.				
Haines 2010 **Australia**	RCT	N = 89 women aged 43-66 years with newly diagnosed breast cancer undergoing adjuvant therapy following surgery were randomised. Key exclusion criteria: women with severe cardiac disease, uncontrolled hypertension or	Home-based strength, balance, shoulder mobility and cardiovascular endurance program for 12 months	Active control condition (flexibility and relaxation) for 12 months	12 months	**Primary outcomes:** Pain Quality of life Cost/utilisation of health care services

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		orthopaedic injury were excluded.				
Harder 2015 **United Kingdom**	RCT	N = 92 women aged 44-66 years with early-stage breast cancer were randomised.	Standard care post-operative exercises plus a 10-week self-practise general yoga programme	Standard care post-operative exercises for 10 weeks	6 months	**Primary outcomes:** Upper limb function (QuickDASH) Pain intensity Quality of life **Secondary outcome** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Hayes 2013 **Australia**	RCT	N = 194 women aged 29 – 70 years with a first diagnosis of invasive breast cancer were randomised. Key exclusion criteria: pregnant or lactating women and women who had plans for breast reconstructive surgery during the study period were excluded.	Intervention 1: Face-to-face-delivered physiologist driven exercise for 8 months Intervention 2: Telephone delivered physiologist driven exercise for 8 months	Usual care (no advice given outside of usual care)	12 months	**Primary outcomes:** Upper limb function (DASH) Upper limb muscle strength Neuropathic pain Incidence of lymphoedema Quality of life **Secondary outcome:** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Hwang 2008 **South Korea**	RCT	N = 37 women aged 37-56 years women on a waiting list for radiotherapy for breast cancer were randomised. Key exclusion criteria: women with concurrent major health problems that could affect their participation in an exercise programme.	Supervised exercise for 5 weeks	Unsupervised exercise during radiotherapy	5 weeks	**Primary outcomes:** Range of movement Pain intensity Quality of life
Ibrahim 2017 **Canada**	RCT	N = 59 women aged 18 -45 years with Stage I -II breast cancer. Key exclusion criteria: metastatic disease, significant comorbidities, lymphoedema	Exercise program for 12 weeks	Usual care (included advice on benefits of active lifestyle)	18 months	**Primary outcomes:** Upper limb function (DASH) Pain intensity

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		development postoperatively				
Kilbreath 2006 **Australia**	RCT	N = 22 women aged 41-66 years who underwent surgery in the axilla for breast cancer. Key exclusion criteria: women who presented with baseline infection or any comorbidity.	Exercise group (daily home programme of resistance and stretching shoulder exercises)	Usual care (no additional care or exercises to those provided in hospital)	6 months	**Primary outcome:** Incidence of lymphoedema

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Kilbreath 2012 **Australia**	RCT	N = 160 women aged 40-65 years who had undergone surgery to the axilla for primary breast cancer. Key exclusion criteria: women who presented with baseline infection or any comorbidity.	Weekly supervised exercise sessions at home and in clinics for 8 weeks	No exercise, fortnightly assessment for lymphoedema for 8 weeks	6 months	**Primary outcomes:** Range of movement Upper limb muscle strength Incidence of lymphoedema Quality of life
Kilgour 2008 **Canada**	RCT	N = 188 women aged 43-60 years who were scheduled for breast cancer surgery were randomised Key exclusion criteria: women with a history or presence of	Home-based exercise for 11 days	Usual care (written and verbal material on diet and skincare)	Not reported	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		shoulder dysfunction, women over the age of 65 years or if they had only a sentinel node dissection				
Lee 2007 **Australia**	RCT	N = 64 women aged 4168 years who underwent breast cancer surgery and received radiotherapy to the breast or chest wall. Key exclusion criteria: participants were excluded if they received radiotherapy to the axilla	Usual care and pectoral muscle stretching program for 6 weeks	Usual care without any exercise advice (exercise program outlined in a pamphlet) for 6 weeks	7 months	**Primary outcomes:** Range of movement Incidence of lymphoedema Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Majed 2022 **Lebanon**	RCT	N = 76 women aged 35-55 years diagnosed with breast cancer and undergoing modified radical mastectomy. Key exclusion criteria: women who were pregnant or who co-morbidities that affected their quality of life	Pre-surgery education and training on therapeutic exercises in addition to routine hospital care	Routine hospital care that did not include any exercise training or education	4 weeks	**Primary outcome:** Range of movement
Mutrie 2007 **Glasgow**	RCT	N = 203 women aged 42-60 years with stage 0 – III breast cancer attending chemotherapy and radiotherapy clinics were randomised. Key exclusion criteria: concurrent unstable cardiac,	Usual care and supervised group exercise programme for 12 weeks	Usual care	6 months	**Primary outcome:** Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		hypertensive, or respiratory disease and women with cognitive dysfunction or who regularly exercise.				
Odynets 2019a **Ukraine**	RCT	N = 68 women aged 50-60 years with post-mastectomy pain, who had undergone surgical treatment and adjuvant radiation therapy for breast cancer. Key exclusion criteria: participants with metastatic breast cancer, bilateral lymphoedema,	Water exercised individualised programme for 12 months	Pilates individualised programme for 12 months	12 months	**Primary outcomes:** Range of movement Upper limb muscle strength Quality of life

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		congestive heart failure, primary lymphoedema or infection of the affected limb.				
Reis 2013 **United States**	RCT	N = 41 women aged 34-85 years with stage I-III breast cancer and receiving radiotherapy.	Nia exercise for 12 weeks	Control (maintain exercise regimen for 12 weeks) for 12 weeks	12 weeks	**Primary outcomes:** Range of movement Quality of life Resource costs **Secondary outcome:** Patient adherence

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Todd 2008 **United Kingdom**	RCT	N = 116 women aged 27-87 years with early breast cancer admitted for surgery including ALND. Key exclusion criteria: previous irradiation of the breast or pre-existing lymphoedema.	Early full range shoulder mobilisation	Delayed full shoulder mobilisation	1 year	**Primary outcome:** Incidence of lymphoedema
Wiskemann 2017 **Germany**	RCT	N = 160 women aged 46-64 years, with stage 0-III breast cancer undergoing adjuvant radiotherapy. Key exclusion criteria: concomitant malignant disease, currently participating in	Progressive resistance training for 12 weeks	Control (progressive muscle relaxation) for 12 weeks	12 months	**Primary outcome:** Upper limb muscle strength

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
		systematic exercise training.				
Xie 2010 **China**	RCT	N = 169 women aged 23-71 years with postoperative breast cancer who had adjuvant chemotherapy.	Rehabilitative training by rehabilitation gymnastics	Control (rehabilitative training by themselves)	Not reported	**Primary outcome:** Range of movement

Author / Country	Study design	Population	Intervention	Comparator	Follow-up	Outcome(s)
Zhou 2019 **China**	RCT	N = 102 women aged 40-58 years who underwent mastectomy or breast-conserving surgery with sentinel lymph node biopsy or ALND Key exclusion criteria: other malignant tumours, mastitis, psychiatric or cognitive disorders.	Progressive upper limb exercises and muscle relaxation training for 6 months	Usual care (routine nursing care) for 6 months	6 months	**Primary outcomes:** Upper limb muscle strength Pain Quality of life

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2 See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

This summary shows a single time point for short term (closest to 6 months), medium term (closest to 12 months), and long term (greater than 12 months, reporting the longest point) for RCTs reporting multiple time points.

Early vs delayed physiotherapy

Early physiotherapy: started at 1 or 2 days after surgery. Delayed physiotherapy: started at 1 or 2 weeks after surgery.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Medium term	MD 8.78 higher (0.74 lower to 18.29 higher)	No difference/could not differentiate (6 months, very low quality evidence)
	Long term	MD 2 higher (1.69 lower to 5.69 higher)	No difference/could not differentiate (2 years, low quality evidence)
Range of movement: shoulder abduction in degrees	Medium term	MD 10.26 higher (9.88 lower to 30.4 higher)	No difference/could not differentiate (6 months, very low quality evidence)
	Long term	MD 3 higher (4.72 lower to 10.72 higher)	No difference/could not differentiate (2 years, low quality evidence)
Range of movement: shoulder internal rotation in degrees	Medium term	MD 2.00 higher (1.09 lower to 5.09 higher)	No difference/could not differentiate (6 months, low quality evidence)
	Long term	MD 0 higher (3.31 lower to 3.31 higher)	No difference/could not differentiate (2 years, low quality evidence)
Range of movement: shoulder external rotation in degrees	Medium term	MD 1 higher (2.1 lower to 4.1 higher)	No difference/could not differentiate (6 months, low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
	Long term	MD 2 higher (1.31 lower to 5.31 higher)	No difference/could not differentiate (2 years, very low quality evidence)
Range of movement: shoulder adduction in degrees	Medium term	MD 1.5 higher (2 lower to 5 higher)	No difference/could not differentiate (6 months, low quality evidence)
Range of movement: shoulder extension in degrees	Medium term	MD 1.33 higher (2.59 lower to 5.25 higher)	No difference/could not differentiate (6 months, low quality evidence)
Impaired shoulder mobility	Medium term	RR 0.85 (0.5 to 1.43)	No difference/could not differentiate (6 months, very low quality evidence)
Pain			
Mild or moderate	Medium term	RR 1.77 (0.72 to 4.3)	No difference/could not differentiate (6 months, very low quality evidence)
	Long term	RR 1.01 (0.48 to 2.12)	No difference/could not differentiate (2 years, very low quality evidence)
Incidence of lymphoedema			
Incidence of lymphoedema	Medium term	RR 1.23 (0.47 to 3.23)	No difference/could not differentiate (6 months, very low quality evidence)
	Long term	RR 1.1 (0.53 to 2.26)	No difference/could not differentiate (2 years, very low quality evidence)

Physiotherapy and usual care vs usual care

Physiotherapy interventions: structured exercise programme (physiotherapist-led); team-instructed physiotherapy; prospective surveillance and targeted physiotherapy. Usual care: information leaflets (describing postoperative exercises and advice for recovery

after surgery); standard treatment of the ward; preoperative education by clinic staff and provision of an education booklet (booklet contained a protocol for postsurgical arm exercises).

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 4.6 lower (8.9 to 0.3 lower)	Physiotherapy and usual care better than usual care (moderate quality evidence at 6 months, 12 months)
	Medium term	MD 7.81 lower (12.44 to 3.18 lower)	
DASH – activity limitations domain (0 to 100)	Short term	MD 5.21 lower (9.78 to 0.64 lower)	Physiotherapy and usual care better than usual care (moderate quality evidence at 6 months, 12 months)
	Medium term	MD 8.04 lower (12.93 to 3.15 lower)	
Range of movement: shoulder flexion in degrees	Medium term	MD 1.1 lower (14.33 lower to 12.13 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Range of movement: shoulder abduction in degrees	Medium term	MD 4.9 higher (30.83 lower to 40.63 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Range of movement: shoulder external rotation in degrees	Medium term	MD 15.4 lower (41.66 lower to 10.86 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Upper limb muscle strength			
Shoulder flexion in kg	Medium term	MD 1.5 higher (3.4 lower to 6.4 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Should abduction in kg	Medium term	MD 0 higher (3.07 lower to 3.07 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Shoulder external rotation in kg	Medium term	MD 4.3 higher (1.23 to 7.37 higher)	Physiotherapy and usual care better than usual care (high quality evidence at 12 months)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Pain			
Pain at rest: numerical rating scale (0 to 10)	Short term	MD 0.58 lower (1.09 to 0.07 lower)	Physiotherapy and usual care better than usual care (high quality evidence at 6 weeks)
Pain on movement: numerical rating scale (0 to 10)	Short term	MD 0.55 lower (1.1 lower to 0 higher)	No difference/could not differentiate: 6 weeks (high quality evidence)
Pain: numerical rating scale (0 to 10)	Short term	MD 0.17 lower (0.7 lower to 0.36 higher)	No difference/could not differentiate: 6 months (high quality evidence)
	Medium term	MD 0.68 lower (1.23 to 0.13 lower)	Physiotherapy and usual care better than usual care (high quality evidence at 12 months)
Neuropathic pain	Short term	RR 0.82 (0.51 to 1.32)	No difference/could not differentiate: 6 months, 12 months (moderate to low quality evidence)
	Medium term	RR 0.71 (0.43 to 1.15)	
Pain (FACT-B4)	Short term	MD 1.11 lower (2.01 to 0.21 lower)	Physiotherapy and usual care better than usual care (high to moderate quality evidence at 6 months, 12 months)
	Medium term	MD 2.02 lower (3.11 to 0.93 lower)	
Incidence of lymphoedema			
Incidence of lymphoedema	Short term	RR 0.83 (0.53 to 1.3)	No difference/could not differentiate: 6 months, 12 months (low quality evidence)
	Medium term	RR 0.92 (0.61 to 1.38)	
Quality of life			
EQ-5D (-0.594 to 1)	Short term	MD 0.02 higher (0.02 lower to 0.06 higher)	No difference/could not differentiate: 6 months, 12 months (high to moderate quality evidence)
	Medium term	MD 0.05 higher (0 to 0.1 higher)	
	Short term	MD 2.73 higher (0.24 to 5.22 higher)	

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
SF-12 – physical health composite scale (0 to 100)	Medium term	MD 4.39 higher (1.74 to 7.04 higher)	Physiotherapy and usual care better than usual care (high to moderate quality evidence at 6 months, 12 months)
SF-12 – mental health composite scale (0 to 100)	Short term	MD 2.12 higher (0.37 lower to 4.61 higher)	No difference/could not differentiate: 6 months, 12 months (high quality evidence)
	Medium term	MD 1.99 higher (0.58 lower to 4.56 higher)	
FACT-B+4 (0 to 4)	Short term	MD 1.17 higher (8.8 lower to 11.14 higher)	No difference/could not differentiate: 6 months, 12 months (moderate to low quality evidence)
	Medium term	MD 0.44 lower (9.43 lower to 8.55 higher)	
Adherence			
Number of participants doing arm or shoulder exercises	Short term	RR 1.28 (1.09 to 1.49)	Physiotherapy and usual care better than usual care (high to moderate quality evidence at 6 months)
	Medium term	RR 1.05 (0.91 to 1.21)	No difference/could not differentiate: 12 months (high quality evidence)
Number of participants attending physiotherapy sessions	Short term	RR 1.03 (0.91 to 1.16)	No difference/could not differentiate: 6 weeks (moderate quality evidence)

Physiotherapy (exercise programme) vs usual care

Physiotherapy: physiotherapist-led exercise programme. Usual care: it was not standardised in the postoperative or rehabilitation setting, and varied in terms of contact with a physiotherapist, extent and content of physiotherapy offered.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
QuickDASH – overall score (0 to 100)	Short term	MD 2.10 lower (4.26 lower to 0.06 higher)	No difference/could not differentiate: 6 months (moderate to low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 6.50 higher (2.08 to 10.92 higher)	Physiotherapy (exercise programme) better than usual care (low quality evidence at 6 months)
	Medium term	MD 1.1 lower (8.3 lower to 6.1 higher)	No difference/could not differentiate: 12 months (moderate quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 3.80 higher (0.5 lower to 8.1 higher)	No difference/could not differentiate: 6 months, 12 months (moderate to low quality evidence)
	Medium term	MD 0.8 lower (14.2 lower to 12.6 higher)	
Range of movement: shoulder external rotation (ipsilateral) in degrees	Medium term	MD 2.7 lower (8.4 lower to 3 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Upper limb muscle strength			
Shoulder abduction (ipsilateral) in kg	Medium term	MD 0.3 higher (0.1 lower to 0.7 higher)	No difference/could not differentiate: 12 months (low quality evidence)
Pain			
Pain: numerical rating scale (0 to 10)	Short term	MD 0.50 lower (0.78 to 0.22 lower)	Physiotherapy (exercise programme) better than usual care (moderate quality evidence at 6 months)
	Medium term	MD 0.54 lower (1.11 lower to 0.03 higher)	No difference/could not differentiate: 12 months (moderate to low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Neuropathic pain: NeuPPS (0 to 5)	Short term	MD 0.39 lower (0.68 to 0.1 lower)	Physiotherapy (exercise programme) better than usual care (low quality evidence at 5 months)
	Medium term	MD 0.13 lower (0.88 lower to 0.62 higher)	No difference/could not differentiate: 12 months (moderate quality evidence)
Incidence of lymphoedema			
Incidence of lymphoedema	Short and medium term	RR 1.35 (0.8 to 2.29)	No difference/could not differentiate: 6 and 12 months (very low quality evidence)
Quality of life			
EORTC-QoL-C30 – global scale (0 to 100)	Short term	MD 1.5 higher (5.5 lower to 8.5 higher)	No difference/could not differentiate: 5 months, 12 months (moderate to low quality evidence)
	Medium term	MD 5.8 higher (1 lower to 12.6 higher)	
Adherence			
Any regular exercise (on a weekly basis) in the study period	Medium term	RR 1.28 (1.04 to 1.58)	Physiotherapy (exercise programme) better than usual care (low quality evidence during study period [12 months])

Physiotherapy (water exercise programme) vs usual care

Physiotherapy: water exercise programme supervised by a physical therapist. Usual care: recommendations by an oncologist in relation to a healthy lifestyle including printed recommendations related to nutrition, lifestyle behaviours, and exercise.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Pain			
Neck pain visual analogue scale (0 to 100)	Short term	MD 31 lower (46.5 to 15.5 lower)	Physiotherapy (water exercise programme) better than usual care (moderate quality evidence at 8 weeks)
Shoulder/axillary pain visual analogue scale (0 to 100)	Short term	MD 20 lower (34.64 to 5.36 lower)	Physiotherapy (water exercise programme) better than usual care (low quality evidence at 8 weeks)

Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) vs usual care

Physiotherapy: Kinect-based rehabilitation with tissue massage, passive mobilisation, and Xbox 360 Kinect™ video game program. Usual care: standard upper extremity physiotherapy program including scar tissue massage and passive mobilisation.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 8.34 lower (15.42 to 1.26 lower)	Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) better than usual care (very low quality evidence at 6 weeks)
Range of movement: shoulder flexion in degrees	Short term	MD 2.8 lower (16.48 lower to 10.88 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 2.24 lower (18.88 lower to 14.4 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder external rotation in degrees	Short term	MD 2.56 lower (11.3 lower to 6.18 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)
Upper limb muscle strength			
Shoulder flexion in kg	Short term	MD 0.54 lower (1.36 lower to 0.28 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)
Shoulder abduction in kg	Short term	MD 0.31 lower (1.24 lower to 0.62 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)
Shoulder external rotation in kg	Short term	MD 0.81 lower (1.64 lower to 0.02 higher)	No difference/could not differentiate: 6 weeks (very low quality evidence)
Pain			
Visual analogue scale (0 to 10)	Short term	MD 1.03 higher (0.05 lower to 2.11 higher)	No difference/could not differentiate: 6 weeks (low quality evidence)

Physiotherapy (myofascial release massage) vs usual care

Physiotherapy: myofascial release massage by physiotherapist. Usual care: did not include routine physiotherapy.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 9 lower (17.81 to 0.19 lower)	Physiotherapy (myofascial release massage) better than usual care (low quality evidence at 3 months)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder flexion in degrees	Short term	MD 9.1 higher (3.4 lower to 21.6 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 16.5 higher (5.84 to 27.16 higher)	Physiotherapy (myofascial release massage) better than usual care (moderate quality evidence at 3 months)
Range of movement: shoulder external rotation in degrees	Short term	MD 14.9 higher (2.32 to 27.48 higher)	Physiotherapy (myofascial release massage) better than usual care (low quality evidence at 3 months)
Range of movement: shoulder internal rotation in degrees	Short term	MD 3.1 higher (3.14 lower to 9.34 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: combined movement of abduction/flexion/external rotation in degrees	Short term	MD 9 higher (4.09 lower to 22.09 higher)	No difference/could not differentiate: 3 months (low quality evidence)

Physiotherapy (group-based educational program and visual material) vs usual care

Physiotherapy: group education supported by visual information by physiotherapist. Usual care: usual rehabilitation conducted on an individual basis, and it was not supported by visual information.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Pain			

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Visual analogue scale (0 to 10)	Short term	MD 1 lower (1.73 to 0.27 lower)	Physiotherapy (group-based educational program and visual material) better than usual care (low quality evidence at 3 months)
Adherence			
To advice provided during interventions: ≥80%	Short term	RR 1.45 (0.69 to 3.08)	No difference/could not differentiate: 3 months (very low quality evidence)

Physiotherapy vs information about unsupervised exercise

Physiotherapy: treatment regimen and information by physiotherapists; physiotherapy management care plan. Unsupervised exercise: leaflet flyer or booklet with advice or exercise instructions.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 9 lower (17.2 to 0.8 lower)	Physiotherapy better than information about unsupervised exercise (very low quality evidence at 6 months)
Range of movement: shoulder flexion in degrees	Short term	MD 10.15 higher (1.17 lower to 21.47 higher)	No difference/could not differentiate: 6 months, (very low quality evidence)
	Medium term	MD 5.4 higher (1.13 to 9.67 higher)	Physiotherapy better than information about unsupervised exercise (low quality evidence at 12 months)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
	Long term	MD 4.7 higher (0.32 lower to 9.72 higher)	No difference/could not differentiate: 24 months (low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 14.23 higher (3.85 lower to 32.31 higher)	No difference/could not differentiate: 6 months, (very low quality evidence)
	Medium term	MD 7 higher (1.3 to 12.7 higher)	Physiotherapy better than information about unsupervised exercise (low quality evidence at 12 months)
	Long term	MD 7 higher (0.82 lower to 14.82 higher)	No difference/could not differentiate: 24 months (low quality evidence)
Pain			
Visual analogue scale (0 to 10)	Short term	MD 2.5 lower (3.5 to 1.5 lower)	Physiotherapy better than information about unsupervised exercise (very low quality evidence at 6 months)
Incidence of lymphoedema			
Increase of ≥200 ml	Short term	RR 0.21 (0.03 to 1.67)	No difference/could not differentiate: 6 months, 12 months, 24 months (low to very low quality evidence)
	Medium term	RR 0.52 (0.1 to 2.62)	
	Long term	RR 0.34 (0.1 to 1.16)	

Physiotherapy (free-range exercises) vs physiotherapy (limited-range exercises)

Free-range exercise by physiotherapist: participants were allowed to perform the protocol exercises and activities of daily living in free amplitude). Limited-range group by physiotherapist: range of movement maintenance limited to 90 degrees for 15 more days.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 2.5 lower (8.82 lower to 3.82 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 4.6 higher (2.82 lower to 12.02 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 8.2 higher (3.21 lower to 19.61 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder extension in degrees	Short term	MD 1.4 lower (5.95 lower to 3.15 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder adduction in degrees	Short term	MD 1.2 lower (6.07 lower to 3.67 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 2.1 higher (4.85 lower to 9.05 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Range of movement: shoulder external rotation in degrees	Short term	MD 1.3 higher (2.31 lower to 4.91 higher)	No difference/could not differentiate: 3 months (low quality evidence)
Pain			
Visual analogue scale (0 to 10)	Short term	MD 0.9 lower (2.02 lower to 0.22 higher)	No difference/could not differentiate: 3 months (low quality evidence)

Physiotherapy (directed exercises) vs physiotherapy (free exercises)

Directed exercises: physiotherapy with a regimen of 19 exercises. Free exercises: The exercises following the biomechanical physiological movements of the shoulder including flexion, extension, abduction, adduction and internal and external rotation, either isolated or combined, without a previously defined sequence or number of repetitions - the exercises being done to the rhythm of music.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Short term	MD 10.8 higher (2.15 to 19.45 higher)	Physiotherapy (directed exercises) better than physiotherapy (free exercises) (low quality evidence at 42 days)
Range of movement: shoulder abduction in degrees	Short term	MD 15 higher (3.9 to 26.1 higher)	Physiotherapy (directed exercises) better than physiotherapy (free exercises) (low quality evidence at 42 days)
Range of movement: shoulder extension in degrees	Short term	MD 4.3 higher (0.27 to 8.33 higher)	Physiotherapy (directed exercises) better than physiotherapy (free exercises) (low quality evidence at 42 days)
Range of movement: shoulder adduction in degrees	Short term	MD 2.3 higher (1.77 lower to 6.37 higher)	No difference/could not differentiate: 42 days (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 8.3 higher (0.95 to 15.65 higher)	Physiotherapy (directed exercises) better than physiotherapy (free exercises) (low quality evidence at 42 days)
Range of movement: shoulder external rotation in degrees	Short term	MD 13.9 higher (1.41 to 26.39 higher)	Physiotherapy (directed exercises) better than physiotherapy (free exercises) (low quality evidence at 42 days)
Adherence			
Number of physiotherapy sessions	Short term	MD 0.64 higher (0.65 lower to 1.93 higher)	No difference/could not differentiate: (low quality evidence)

Physiotherapy (water exercise) vs physiotherapy (Pilates)

Water exercises consisted of a wide range of breathing exercises and physical exercises. Pilates exercises were performed on the floor and included warmup, a main part using a resistance band, and cool-down.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Quality of life			
FACT-B+4 (0 to 148)	Short term	MD 0.38 lower (1.41 lower to 0.65 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
	Medium term	MD 5.86 higher (4.88 to 6.84 higher)	Physiotherapy (water exercise) better than physiotherapy (Pilates) (low quality evidence at 12 months)

Physiotherapy (water exercise) vs physiotherapy (yoga)

Water exercises consisted of a wide range of breathing exercises and physical exercises. Yoga exercises consisted of warmup, exercising, and cooling down.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Quality of life			
FACT-B+4 (0 to 148)	Short term	MD 3.06 lower (4.18 to 1.94 lower)	Physiotherapy (water exercise) worse than physiotherapy (yoga) (low quality evidence at 6 months)
	Medium term	MD 1.38 higher (0.27 to 2.49 higher)	Physiotherapy (water exercise) better than physiotherapy (yoga) (very low quality evidence at 12 months)

Physiotherapy (Pilates) vs physiotherapy (yoga)

Pilates exercises were performed on the floor and included warmup, a main part using a resistance band, and cool-down. Yoga exercises consisted of warmup, exercising, and cooling down.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Quality of life			
FACT-B+4 (0 to 148)	Short term	MD 2.68 lower (3.92 to 1.44 lower)	Physiotherapy (Pilates) worse than physiotherapy (yoga) (low quality evidence at 6 months, 12 months)
	Medium term	MD 4.48 lower (5.74 to 3.22 lower)	

Physiotherapy (Pilates) vs physiotherapy (combined exercises)

Pilates: exercise programme consisted of Pilates-based mat exercises and Pilates-based theraband exercises. Combined exercises: exercise programme consisting of stretching, range of movement, strengthening exercises of shoulder and breathing exercise.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 3.07 lower (12.18 lower to 6.04 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 7.36 lower (14.46 to 0.26 lower)	Physiotherapy (Pilates) worse than physiotherapy (combined exercises) (low quality evidence at 8 weeks)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder abduction in degrees	Short term	MD 6.93 lower (20.23 lower to 6.37 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 8.04 lower (13.44 to 2.64 lower)	Physiotherapy (Pilates) worse than physiotherapy (combined exercises) (low quality evidence at 8 weeks)
Range of movement: shoulder external rotation in degrees	Short term	MD 7.87 lower (14.77 to 0.97 lower)	Physiotherapy (Pilates) worse than physiotherapy (combined exercises) (low quality evidence at 8 weeks)
Upper limb muscle strength			
Shoulder flexion in kg	Short term	MD 0.24 higher (0.68 lower to 1.16 higher)	No difference/could not differentiate: 8 weeks (moderate quality evidence)
Shoulder abduction in kg	Short term	MD 0.09 higher (0.8 lower to 0.98 higher)	No difference/could not differentiate: 8 weeks (very low quality evidence)
Shoulder internal rotation in kg	Short term	MD 0.09 lower (1.31 lower to 1.13 higher)	No difference/could not differentiate: 8 weeks (very low quality evidence)
Shoulder external rotation in kg	Short term	MD 0.02 higher (1.19 lower to 1.23 higher)	No difference/could not differentiate: 8 weeks (very low quality evidence)
Pain			
Motion - numerical rating scale (0 to 10)	Short term	MD 0 higher (1.14 lower to 1.14 higher)	No difference/could not differentiate: 8 weeks (moderate quality evidence)
Rest - numerical rating scale (0 to 10)	Short term	MD 0.67 lower (1.94 lower to 0.6 higher)	No difference/could not differentiate: 8 weeks (moderate quality evidence)

Physiotherapy (Pilates) vs physiotherapy (home exercises)

Pilates: exercise programme consisted of Pilates-based mat exercises and Pilates-based theraband exercises. Home exercises: appropriate exercise programme for participants arranged and each exercise was taught by physiotherapist as practical in the clinic, until the exercise was performed properly.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 8.19 lower (19.78 lower to 3.4 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 0.9 lower (11.5 lower to 9.7 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 4 higher (12.7 lower to 20.7 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 1.23 higher (5.31 lower to 7.77 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder external rotation in degrees	Short term	MD 0.6 lower (9.13 lower to 7.93 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Upper limb muscle strength			
Shoulder flexion in kg	Short term	MD 0.63 higher (0.27 lower to 1.53 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder abduction in kg	Short term	MD 0.6 higher (0.25 lower to 1.45 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder internal rotation in kg	Short term	MD 0.85 higher (0.25 lower to 1.95 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder external rotation in kg	Short term	MD 0.92 higher (0.25 lower to 2.09 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Pain			
Motion - numerical rating scale (0 to 10)	Short term	MD 1.01 lower (2.31 lower to 0.29 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Rest - numerical rating scale (0 to 10)	Short term	MD 0.3 lower (1.68 lower to 1.08 higher)	No difference/could not differentiate: 8 weeks (moderate quality evidence)

Physiotherapy (combined exercises) vs physiotherapy (home exercises)

Combined exercises: exercise programme consisting of stretching, range of movement, strengthening exercises of shoulder and breathing exercise. Home exercises: appropriate exercise programme for participants arranged and each exercise was taught by physiotherapist as practical in the clinic, until the exercise was performed properly.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 5.12 lower (15.72 lower to 5.48 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 6.46 higher (3.3 lower to 16.22 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 10.93 higher (4.62 lower to 26.48 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 9.27 higher (2.72 to 15.82 higher)	Effects: Physiotherapy (combined exercises) better than physiotherapy (home exercises) (low quality evidence at 8 weeks)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder external rotation in degrees	Short term	MD 7.27 higher (1.53 lower to 16.07 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Upper limb muscle strength			
Shoulder flexion in kg	Short term	MD 0.39 higher (0.51 lower to 1.29 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder abduction in kg	Short term	MD 0.51 higher (0.3 lower to 1.32 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder internal rotation in kg	Short term	MD 0.94 higher (0.35 lower to 2.23 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Shoulder external rotation in kg	Short term	MD 0.9 higher (0.26 lower to 2.06 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Pain			
Motion - numerical rating scale (0 to 10)	Short term	MD 1.01 lower (2.26 lower to 0.24 higher)	No difference/could not differentiate: 8 weeks (low quality evidence)
Rest - numerical rating scale (0 to 10)	Short term	MD 0.37 higher (0.82 lower to 1.56 higher)	No difference/could not differentiate: 8 weeks (moderate quality evidence)

Physiotherapy (manual therapy and upper limb exercises) vs physiotherapy (upper limb exercises)

Upper limb exercises: inpatient exercise protocol included 3 active exercises (forward flexion, external rotation, and abduction of shoulder); outpatient exercise protocol consisted of movements of flexion, extension, abduction, adduction, internal, and external rotation of the upper limb, alone or combined.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Short term	MD 4.9 higher (4.19 lower to 13.99 higher)	No difference/could not differentiate: 6 months, 12 months (low quality evidence)
	Medium term	MD 3 lower (14.84 lower to 8.84 higher)	
	Long term	MD 10 lower (17.55 to 2.45 lower)	Physiotherapy (manual therapy and upper limb exercises) worse than physiotherapy (upper limb exercises) (low quality evidence at 18 months)
Range of movement: shoulder abduction in degrees	Short term	MD 0.5 higher (8.36 lower to 9.36 higher)	No difference/could not differentiate: 6 months, 12 months, 18 months (moderate to low quality evidence)
	Medium term	MD 7.5 lower (19.55 lower to 4.55 higher)	
	Long term	MD 5.3 lower (12.53 lower to 1.93 higher)	

Physiotherapy and myofascial therapy vs physiotherapy and placebo – after surgery

Physiotherapy: individual standard physical therapy programme. Myofascial therapy: manual myofascial release techniques. Placebo: static bilateral hand placements at the upper body and arm.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 2 lower (9.4 lower to 5.4 higher)	No difference/could not differentiate: 4 months, 12 months (moderate quality evidence)
	Medium term	MD 4 lower (11.9 lower to 3.9 higher)	
Pain			

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Visual analogue scale (0 to 100)	Short term	MD 1.7 higher (7.38 lower to 10.78 higher)	No difference/could not differentiate: 4 months, 12 months (high to moderate quality evidence)
	Medium term	MD 5.6 lower (14.98 lower to 3.78 higher)	
Quality of life			
SF-36 – physical functioning (0 to 100)	Short term	MD 28 higher (19.77 to 36.23 higher)	Physiotherapy and myofascial therapy better than physiotherapy and placebo (high quality evidence at 4 months)
	Medium term	MD 2 lower (10.41 lower to 6.41 higher)	No difference/could not differentiate: 12 months (high quality evidence)
SF-36 – mental functioning (0 to 100)	Short term	MD 3 lower (10.63 lower to 4.63 higher)	No difference/could not differentiate: 4 months, 12 months (high quality evidence)
	Medium term	MD 2 lower (9.48 lower to 5.48 higher)	

Physiotherapy and myofascial therapy vs physiotherapy and placebo – after radiotherapy

Physiotherapy: individual standard physical therapy programme. Myofascial therapy: manual myofascial release techniques. Placebo: static bilateral hand placements.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 1 lower (11.65 lower to 9.65 higher)	No difference/could not differentiate: 6 months, 12 months (low quality evidence)
	Medium term	MD 3 higher (7.97 lower to 13.97 higher)	
Pain			

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Visual analogue scale (0 to 100)	Short term	MD 6 lower (20.98 lower to 8.98 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 13 lower (27.27 lower to 1.27 higher)	
Quality of life			
SF-36 – physical functioning (0 to 100)	Short term	MD 5 lower (19.04 lower to 9.04 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 14 lower (28.39 lower to 0.39 higher)	
SF-36 – mental functioning (0 to 100)	Short term	MD 10 higher (0.52 lower to 20.52 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 10 higher (1.42 lower to 21.42 higher)	

Physiotherapy vs no intervention during radiotherapy

Physiotherapy: kinesiotherapy.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Short term	MD 5.11 higher (0.71 to 9.51 higher)	Physiotherapy better than no intervention (low quality evidence at 6 months)
Range of movement: shoulder abduction in degrees	Short term	MD 7.24 higher (1.72 to 12.76 higher)	Physiotherapy better than no intervention (low quality evidence at 6 months)
Range of movement: shoulder external rotation in degrees	Short term	MD 5.65 higher (5.65 lower to 16.95 higher)	No difference/could not differentiate: 2 months (low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder internal rotation in degrees	Short term	MD 0.3 higher (9.01 lower to 9.61 higher)	No difference/could not differentiate: 2 months (very low quality evidence)
Range of movement: shoulder extension in degrees	Short term	MD 3.2 higher (2.96 lower to 9.36 higher)	No difference/could not differentiate: 2 months (low quality evidence)
Range of movement: shoulder adduction in degrees	Short term	MD 0.31 higher (7.8 lower to 8.42 higher)	No difference/could not differentiate: 2 months (very low quality evidence)

Physiotherapy (early) vs no intervention

Early physical rehabilitation programme by physiotherapist started at day 2 after surgery.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Short term	MD 31 higher (25.96 to 36.04 higher)	Early physiotherapy better than no intervention (low quality evidence at 6 months, 12 months)
	Medium term	MD 26.7 higher (23.59 to 29.81 higher)	
Range of movement: shoulder abduction in degrees	Short term	MD 18 higher (11.75 to 24.25 higher)	Early physiotherapy better than no intervention (low quality evidence at 6 months, 12 months)
	Medium term	MD 21.1 higher (17.98 to 24.22 higher)	
Range of movement: shoulder internal rotation in degrees	Short term	MD 5.1 higher (0.14 lower to 10.34 higher)	No difference/could not differentiate: 6 months, 12 months (very low quality evidence)
	Medium term	MD 2.9 higher (2.14 lower to 7.94 higher)	
	Short term	MD 3.7 higher (1.41 to 5.99 higher)	

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder external rotation in degrees	Medium term	MD 0.9 higher (1.1 lower to 2.9 higher)	Early physiotherapy better than no intervention (very low quality evidence at 6 months) No difference/could not differentiate: 12 months (very low quality evidence)
Pain			
Visual analogue scale	Short term	MD 1.6 lower (1.87 to 1.33 lower)	Early physiotherapy better than no intervention (low quality evidence at 6 months, 12 months)
	Medium term	MD 1.4 lower (1.67 to 1.13 lower)	
Quality of life			
EORTC-QoL-C30 – global scale (0 to 100)	Short term	MD 17.5 higher (11.71 to 23.29 higher)	Early physiotherapy better than no intervention (low quality evidence at 6 months)
EORTC-QoL-C30 – pain (0 to 100)	Short term	MD 6.8 lower (8.28 to 5.32 lower)	Early physiotherapy better than no intervention (low quality evidence 6 months)
EORTC-QoL-BR23 – breast symptoms (0 to 100)	Short term	MD 10.8 lower (16.33 to 5.27 lower)	Early physiotherapy better than no intervention (very low quality evidence at 6 months)
EORTC-QoL-BR23 – arm symptoms (0 to 100)	Short term	MD 28.8 lower (37.03 to 20.57 lower)	Early physiotherapy better than no intervention (low quality evidence at 6 months)

Early vs delayed exercise

Early exercise: started at 1 to 3 days after surgery. Delayed exercise: started at 1 or 2 weeks after surgery.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
Range of movement: shoulder flexion in degrees	Short term	MD 2 higher (1.55 lower to 5.55 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 4 higher (0.8 to 7.2 higher)	Effects: Early exercise better than delayed exercise (very low quality evidence at 6 months)
Range of movement: shoulder external rotation in degrees	Short term	MD 0.5 higher (2.08 lower to 3.08 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
Range of movement: limitation of shoulder flexion in degrees	Short term	MD 1.6 higher (2.28 lower to 5.48 higher)	No difference/could not differentiate: 1 month (very low quality evidence)
Range of movement: limitation of shoulder abduction in degrees	Short term	MD 1 lower (5.12 lower to 3.12 higher)	No difference/could not differentiate: 2 weeks (low quality evidence)
Incidence of lymphoedema			
200 ml or more	Medium term	RR 2.71 (1.14 to 6.44)	Effects: Early exercise worse than delayed exercise (moderate quality evidence at 12 months)

Exercise and usual care vs usual care

Exercise: self-practise general yoga programme; supervised exercise session and a home programme of resistance training and passive stretching for the shoulder muscles; home programme of resistance and stretching shoulder exercises; home exercise video; pectoral muscle stretching program; pre-surgery education and training on therapeutic exercises; supervised group exercise programme; progressive upper limb exercises and muscle relaxation training. Usual care: post-operative exercise materials distributed by the hospital prior to surgery; written information outlining post-operative arm exercises; upper limb exercises outlined in a pamphlet; brochure entitled ‘Exercise Guide after Breast

Surgery'; exercise program outlined in a pamphlet given after breast cancer surgery; routine hospital care included explanation by the surgeon on the surgical procedure; leaflet entitled 'Exercise after cancer diagnosis'; routine health education and physical exercises.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
QuickDASH – overall score (0 to 100)	Short term	MD 3.5 lower (10.94 lower to 3.94 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 1.9 higher (4.41 lower to 8.21 higher)	No difference/could not differentiate: 6 months (moderate quality evidence)
Range of movement: shoulder abduction in degrees	Short term	MD 10 higher (3.59 to 16.41 higher)	Exercise and usual care better than usual care (low quality evidence at 6 months)
Range of movement: shoulder external rotation in degrees	Short term	MD 1.20 lower (6.2 lower to 3.8 higher)	No difference/could not differentiate: 6 months[(a)]
Range of movement: shoulder extension in degrees End of radiotherapy	Short term	MD 0.5 higher (4.14 lower to 5.14 higher)	No difference/could not differentiate: 6 weeks, (low quality evidence)
Range of movement: shoulder extension in degrees After surgery	Short term	MD 5.8 higher (0.63 to 10.97 higher)	Exercise and usual care better than usual care (low quality evidence at 6 months)
Upper limb muscle strength			
Constant Murley Score (0 to 100)	Short term	MD 4.13 higher (1.96 lower to 10.23 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
Shoulder abduction in Newtons	Short term	MD 3 higher (8.56 lower to 14.56 higher)	No difference/could not differentiate: 6 months (moderate quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Shoulder flexion in Newtons	Short term	MD 3.8 higher (5.74 lower to 13.34 higher)	No difference/could not differentiate: 6 months (moderate to low quality evidence)
Shoulder horizontal extension in Newtons	Short term	MD 3 higher (5.92 lower to 11.92 higher)	No difference/could not differentiate: 6 months (moderate to low quality evidence)
Shoulder horizontal flexion in Newtons	Short term	MD 3.8 lower (13.15 lower to 5.55 higher)	No difference/could not differentiate: 6 months (low quality evidence)
Pain			
Pain score (0 to 10)	Short term	MD 1.4 lower (2.34 to 0.46 lower)	Exercise and usual care better than usual care (very low quality evidence at 6 months)
Pain (Oxford Shoulder Score; 12 to 60)	Short term	MD 1.4 lower (4.68 lower to 1.88 higher)	No difference/could not differentiate: 6 months (low quality evidence)
Incidence of lymphoedema			
Difference in arm circumference ≥2cm	Short term	RR 0.28 (0.08 to 0.96)	Exercise and usual care better than usual care (low quality evidence at 6 months)
Interlimb arm volume =>10%	Short term	RR 0.62 (0.23 to 1.65)	No difference/could not differentiate: 6 months (very low quality evidence)
Quality of life			
FACT-B+4 (0 to 144)	Short term	MD 10.19 higher (9.65 lower to 30.03 higher)	No difference/could not differentiate: 6 months (very low quality evidence)
FACT-G (0 to 108)	Short term	MD 2.4 higher (1.83 lower to 6.63 higher)	No difference/could not differentiate: 6 months, 5 years (moderate quality evidence)
	Long term	MD 0.6 lower (6.04 lower to 4.84 higher)	
EORTC and BR23 arm symptoms (0 to 100)	Short term	MD 4 higher (1.96 lower to 9.96 higher)	No difference/could not differentiate: 6 months (low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
EORTC and BR23 breast symptoms (0 to 100)	Short term	MD 4 higher (2.15 lower to 10.15 higher)	No difference/could not differentiate: 6 months (low quality evidence)
EORTC QoL 30 (0 to 100)	Short term	MD 5.3 higher (4.57 lower to 15.17 higher)	No difference/could not differentiate: post-intervention (low quality evidence)
Patient adherence			
Exercise > 5 times a week	Short term	RR 0.46 (0.27 to 0.78)	Exercise and usual care worse than usual care (moderate quality evidence at week 6 to 10)

(a) SDs were not reported. Therefore, MID could not be calculated to judge imprecision and therefore, overall quality could not be evaluated.

Face to face exercise vs usual care

Face-to-face-delivered exercise intervention: exercise physiologist driven. Usual care: this varied depending on treating clinician and/or hospital.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 0.1 lower (5.73 lower to 5.53 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 0.9 lower (6.21 lower to 4.41 higher)	
Strength and endurance test in kg	Short term	MD 1 higher (0.1 lower to 2.1 higher)	No difference/could not differentiate: 6 months (low quality evidence)
	Medium term	MD 1.1 higher (0.03 to 2.17 higher)	Face to face exercise better than usual care (low quality evidence at 12 months)
Pain			
Neuropathic pain (0 to 100)	Short term	MD 4.4 higher (1.8 lower to 10.6 higher)	

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
	Medium term	MD 1.7 higher (4.22 lower to 7.62 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
Incidence of lymphoedema			
Measured by bioimpedance spectroscopy	Short term	RR 0.6 (0.18 to 2.01)	No difference/could not differentiate: 6 months, 12 months (very low quality evidence)
	Medium term	RR 0.8 (0.33 to 1.93)	
Quality of life			
FACT-B+4 (0 to 160)	Short term	MD 3 higher (4.21 lower to 10.21 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 3 higher (3.86 lower to 9.86 higher)	
Patient adherence			
To exercise	Short or medium term	RR 1.12 (0.89 to 1.4)	No difference/could not differentiate: 6 or 12 months (low quality evidence)

Telephone delivered exercise vs usual care

Telephone-delivered exercise intervention: exercise physiologist driven. Usual care: this varied depending on treating clinician and/or hospital.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 6.7 lower (12.09 to 1.31 lower)	Telephone delivered exercise better than usual care (low quality evidence at 6 months, 12 months)
	Medium term	MD 6.7 lower (12 to 1.4 lower)	

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Strength and endurance test in kg	Short term	MD 0.7 higher (0.43 lower to 1.83 higher)	No difference/could not differentiate: 6 months, 12 months (low quality evidence)
	Medium term	MD 0.7 higher (0.38 lower to 1.78 higher)	
Pain			
Neuropathic pain (0 to 100)	Short term	MD 1.7 lower (7.71 lower to 4.31 higher)	No difference/could not differentiate: 6 months, 12 months (moderate quality evidence)
	Medium term	MD 1.5 lower (7.42 lower to 4.42 higher)	
Incidence of lymphoedema			
Measured by bioimpedance spectroscopy	Short term	RR 0.6 (0.18 to 2.01)	No difference/could not differentiate: 6 months, 12 months (very low quality evidence)
	Medium term	RR 0.8 (0.33 to 1.93)	
Quality of life			
FACT-B+4 (0 to 160)	Short term	MD 8.5 higher (1.41 to 15.59 higher)	Telephone delivered exercise better than usual care (low quality evidence at 6 months, 12 months)
	Medium term	MD 7 higher (0.01 to 13.99 higher)	
Patient adherence			
To exercise	Short or medium term	RR 1.12 (0.89 to 1.4)	No difference/could not differentiate: 6 or 12 months (low quality evidence)

Rehabilitation vs usual care

Rehabilitation: conventional rehabilitation, associated with the proprioceptive neuromuscular facilitation technique. Usual care: active kinesiotherapy in active and active-assisted group, strengthening and stretching of the antero-internal shoulder chain.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Long term	MD 5.62 higher (0.29 lower to 11.53 higher)	No difference/could not differentiate: 18 months (low quality evidence)
Range of movement: shoulder flexion in degrees	Short term	MD 24.35 lower (40.37 to 8.33 lower)	Effects: Rehabilitation worse than usual care (low quality evidence at 4 weeks)
Range of movement: shoulder abduction in degrees	Short term	MD 28.45 lower (45.04 to 11.86 lower)	Effects: Rehabilitation worse than usual care (moderate quality evidence at 4 weeks)
Range of movement: shoulder extension in degrees	Short term	MD 1.5 lower (6.69 lower to 3.69 higher)	No difference/could not differentiate: 4 weeks (very low quality evidence)
Range of movement: shoulder adduction in degrees	Short term	MD 1.95 higher (4.54 lower to 8.44 higher)	No difference/could not differentiate: 4 weeks (low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 8.85 lower (20.43 lower to 2.73 higher)	No difference/could not differentiate: 4 weeks (low quality evidence)
Range of movement: shoulder external rotation in degrees	Short term	MD 10.15 lower (19.52 to 0.78 lower)	Effects: Rehabilitation worse than usual care (low quality evidence at 4 weeks)
Pain			
VAS 1 to 10	Long term	MD 0.26 higher (1.05 lower to 1.57 higher)	No difference/could not differentiate: 18 months (low quality evidence)

Exercise vs exercise

Exercise 1: stretching exercises and aerobic exercises, instructional pamphlet and a motor exercise schedule checklist; acupuncture and kinesiotherapy; home-based strength, balance, shoulder mobility and cardiovascular endurance programme; face-to-face-delivered exercise intervention (physiologist driven); supervised exercise programme; water exercise individualised programme; Nia exercise; progressive resistance training; rehabilitation gymnastics.

Exercise 2: unsupervised exercise (motor exercise instruction and the instructional pamphlet); kinesiotherapy; flexibility and relaxation; telephone-delivered exercise intervention (physiologist driven); unsupervised exercise; Pilates individualised programme; current exercise; muscle relaxation; unsupervised exercise.

See Appendix F for full GRADE tables.

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Upper limb function			
DASH – overall score (0 to 100)	Short term	MD 6.6 higher (1.05 to 12.15 higher)	Exercise (face to face) better than exercise (telephone) (low quality evidence at 6 months, 12 months)
	Medium term	MD 5.8 higher (0.57 to 11.03 higher)	
Range of movement: shoulder flexion in degrees	Short term	MD 7.47 higher (1.48 to 13.46 higher)	Exercise (water exercise) better than exercise (Pilates) (very low quality evidence at 12 weeks)
Range of movement: shoulder adduction in degrees	Short term	MD 5.4 higher (0.72 to 10.08 higher)	Exercise (water exercise) better than exercise (Pilates) (very low quality evidence at 12 weeks)
Participants with 180 degrees shoulder abduction	Short term	RR 2.1 (1.54 to 2.87)	Exercise (rehabilitation gymnastics) better than exercise (unsupervised exercise) (moderate quality evidence at 28 days)
Participants with less than 180 degrees shoulder abduction	Short term	RR 0.49 (0.29 to 0.82)	Exercise (rehabilitation gymnastics) better than exercise (unsupervised exercise) (low quality evidence)
Participants with less than 90 degrees shoulder abduction	Short term	RR 0.62 (0.29 to 1.3)	No difference/could not differentiate (rehabilitation gymnastics vs unsupervised exercise): 28 days (very low quality evidence)
Range of movement: shoulder extension in degrees	Short term	MD 0.80 lower (3.74 lower to 2.14 higher)	No difference/could not differentiate (water exercise vs Pilates): 12 weeks (very low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
Range of movement: shoulder adduction in degrees	Short term	MD 2.3 higher (1.76 lower to 6.36 higher)	No difference/could not differentiate (acupuncture + kinesiotherapy vs kinesiotherapy): 10 weeks (very low quality evidence)
Range of movement: shoulder internal rotation in degrees	Short term	MD 0.93 higher (2.65 lower to 4.51 higher)	No difference/could not differentiate (water exercise vs Pilates): 12 weeks (very low quality evidence)
Range of movement: shoulder external rotation in degrees	Short term	MD 0.41 higher (3.96 lower to 4.78 higher)	No difference/could not differentiate (water exercise vs Pilates): 12 weeks (very low quality evidence)
Upper limb muscle strength			
Shoulder internal rotation at 43 degrees (maximal voluntary isometric contraction)	Short term	MD 0.02 higher (0.01 lower to 0.05 higher)	No difference/could not differentiate (exercise training vs muscle relaxation): 13 weeks (moderate quality evidence)
Of the affected side in kg	Short term	MD 0.8 lower (3.32 lower to 1.72 higher)	No difference/could not differentiate (water exercise vs Pilates): 12 weeks (very low quality evidence)
Strength and endurance test in kg	Short term	MD 0.3 higher (0.65 lower to 1.25 higher)	No difference/could not differentiate (face to face vs telephone): 6 months, 12 months (moderate quality evidence)
	Medium term	MD 0.4 higher (0.46 lower to 1.26 higher)	
Pain			
VAS 0 to 100	Short term	MD 5.4 lower (19.16 lower to 8.36 higher)	No difference/could not differentiate (supervised exercise vs unsupervised exercise): after radiotherapy (low quality evidence)

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
VAS 0 to 10	Short term	MD 1.70 lower (2.89 to 0.51 lower)	Effects: Exercise (acupuncture + kinesiotherapy) better than exercise (kinesiotherapy) (very low quality evidence at 10 weeks)
EORTC-C30 pain scale 0 to 100	Short term	MD 7.10 lower (17.36 lower to 3.16 higher)	No difference/could not differentiate (exercise programme vs flexibility and relaxation): 6 months (low quality evidence)
Neuropathic pain (0 to 100)	Short term	MD 6.1 higher (0.09 to 12.11 higher)	Effects: Exercise (face to face) worse than exercise (telephone) (moderate quality evidence at 6 months)
	Medium term	MD 3.2 higher (2.7 lower to 9.1 higher)	No difference/could not differentiate (face to face vs telephone): 12 months (moderate quality evidence)
Incidence of lymphoedema			
Measured by bioimpedance spectroscopy	Short term	RR 1 (0.26 to 3.83)	No difference/could not differentiate (face to face vs telephone): 6 months, 12 months (very low quality evidence)
	Medium term	RR 1 (0.4 to 2.51)	
Quality of life			
EQ-5D VAS (0 to 100)	Short term	MD 6 higher (0.7 lower to 12.7 higher)	No difference/could not differentiate (exercise programme vs flexibility and relaxation): 6 months (low quality evidence)
FACT-B+4 (0 to 160)	Short term	MD 5.5 lower (12.22 lower to 1.22 higher)	No difference/could not differentiate (face to face vs telephone): 6 months, 12 months (low quality evidence)
	Medium term	MD 4 lower (10.4 lower to 2.4 higher)	

Outcome	Time point	Effect estimate (95% confidence interval)	Interpretation of effect (quality)
FACT-G (0 to 108)	Short term	MD 3.6 higher (5.17 lower to 12.37 higher)	No difference/could not differentiate (Nia exercise vs current exercise): 12 weeks (very low quality evidence)
FACIT-F (0 to 160)	Short term	MD 8.9 higher (5.92 lower to 23.72 higher)	No difference/could not differentiate (Nia exercise vs current exercise): 12 weeks (very low quality evidence)
EORTC C30 (0 to 100)	Short term	MD 9 higher (1.61 to 16.39 higher)	Exercise (exercise programme) better than exercise (flexibility and relaxation) (low quality evidence at 6 months)
EORTC BR23 – Arm symptoms (0 to 100)	Short term	MD 2.4 lower (11.17 lower to 6.37 higher)	No difference/could not differentiate (exercise programme vs flexibility and relaxation): 6 months (low quality evidence)
EORTC BR23 - Breast symptoms (0 to 100)	Short term	MD 3.7 higher (3.8 lower to 11.2 higher)	No difference/could not differentiate (exercise programme vs flexibility and relaxation): 6 months (low quality evidence)
WHOQOL (1 to 5)	Short term	MD 0.42 higher (0.05 to 0.79 higher)	Exercise (supervised exercise) better than exercise (unsupervised exercise) (low quality evidence after radiotherapy)
Patient adherence			
To exercise (at 6 or 12 months)	Short or medium term	RR 1.00 (0.82 to 1.22)	No difference/could not differentiate (face to face vs telephone): 6 or 12 months (moderate quality evidence)
Number of days engaged in aerobic exercise	Short term	MD 6 lower (12.63 lower to 0.63 higher)	No difference/could not differentiate (Nia exercise vs current exercise): 12 weeks (very low quality evidence)

1.1.7 Economic evidence

1.1.7.1 Included studies

A search was performed to identify published economic evaluations of relevance to this guideline update (see Appendix B). This search retrieved 1,467 studies. Based on title and abstract screening, 1,462 of the studies were excluded for this question. One of the identified studies was a systemic review of economic evaluations of exercise and physiotherapy for patients treated for breast cancer, and on the basis of this study, we included an additional 5 studies in the full text review. Following the full-text review, we excluded a further 6 studies. Thus, the review for this question includes 3 studies from the existing literature.

1.1.7.2 Excluded studies

See Appendix J for excluded studies and reasons for exclusion.

1.1.8 Summary of included economic evidence

Table 2 provides summary details of the included studies. See Appendix H for a full evidence table and assessment of applicability and limitations.

Table 2 Summary of included economic evidence

Study	Applicability	Limitations	Comparator	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER[1] (Cost/QALY)	
Bruce 2022 UK NHS and PSS perspective Usual care compared to usual care plus a physiotherapist-led exercise programme Women undergoing breast cancer surgery, at risk of postoperative upper limb morbidity	Directly applicable (Table 5)	Potentially serious limitations (Table 6)	Usual care	-£386.78 (95% CI -£2,491.18, £1717.62)	0.029 (95% CI 0.001, 0.056)	Dominant (i.e. Usual care plus a physiotherapist-led exercise programme cost less and was more effective than usual care)	A range of one-way deterministic sensitivity analyses were conducted including complete-case analysis (in the base case, missing data for health-care cost variables and EQ-5D-5L were assumed to be missing at random. Missingness was handled by imputing costs and utility scores jointly through chained equations and predictive mean matching. The authors also included age, ethnicity, marital status, employment status and recruiting sites as co-variates in the imputation model. 35 imputations were calculated to reflect 35% of data being missing for each cost variable.), including societal costs, including training costs, excluding high-cost cancer treatments and using Hospital Episode Statistics costs for

Study	Applicability	Limitations	Comparator	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER[1] (Cost/QALY)	
							hospital care. Physiotherapist-led exercise programmes had lower costs and greater QALYs in most scenarios. At the cost effectiveness threshold values of £20,000 and £30,000 per QALY, the probability was 78% and 84%, respectively, that exercise was the more cost effective of the two arms. The probability of cost effectiveness at a willingness to pay threshold of £20,000 per QALY increased to 97% when the high-cost cancer treatment were excluded.
Haines 2010 Australia Societal perspective Multimodal exercise program comprising strength, balance and endurance training elements, compared with	Partially applicable (Table 5)	Potentially serious limitations (Table 6)	Active sham intervention consisting of flexibility (static stretching) and relaxation activities	$270 (95% CI $134, $2,084) [Calculated as the difference between total costs of the intervention and control from Table 4	-0.01 (95% CI -0.09, 0.11)	Dominated (i.e. Multimodal exercise program cost more and was less effective than sham flexibility and relaxation program)	There was low probability that the intervention would be both less costly and more effective than the control condition over a 6-month time horizon. For the full dataset the likelihood the intervention would be cost-effective was

Study	Applicability	Limitations	Comparator	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER[1] (Cost/QALY)	
sham flexibility and relaxation program Newly diagnosed breast cancer undergoing adjuvant therapy following surgery				in Haines 2010)			0.05%. When outliers were excluded the likelihood the intervention would be cost-effective was 25.55%.
Gordon 2017 Australia 8-month exercise intervention (involving regular contact with an exercise physiologist over the phone, or home delivered face to face), compared with usual care [Although the clinical trial has 3 arms, 1 – Intervention delivered over the phone, 2 – Intervention home-delivered face-to-face, 3 – Usual care. The economic evaluation only reports results for the intervention vs usual care. The intervention arm of the economic evaluation is a product of	Partially applicable (Table 5)	Potentially serious limitations (Table 6)	Usual care	Service provider model: $947 Private model: $818	0.009	Service provider model: A$105,231 Private model: A$90,842	One-way sensitivity analyses were performed for the calculated QALYs, and different cost scenarios. The model was sensitive to using the lower and upper limits of the 95% confidence interval for the EQ-5D-3L weights instead of its point estimate (this was undertaken as part of one-way sensitivity analyses) – with results ranging from $16,685 per QALY gained to usual care being dominant (cheaper and more effective) for the private model. Under a service provider model the results for variations

Study	Applicability	Limitations	Comparator	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER[1] (Cost/QALY)	
the data from the phone trial arm and face-to-face trial arm being pooled. Women who have undergone surgery for primary breast cancer							in the EQ-5D-3L ranged from $19,328 per QALY to usual care being dominant (cheaper and more effective). Variations in car leasing costs resulted in incremental cost-effectiveness ratios of $103,733 and $106,656 per QALY respectively based on whether a small car or larger car was rented. In probabilistic sensitivity analysis, the likelihood of being cost effective was 44.4% and 46.3% for the service provider model and private model respectively.

1.1.9 Economic model

This question was not prioritised for original economic analysis.

1.1.10 Unit costs and examples of physiotherapy roles

Table 3 Unit Costs of Health and Social Care 2021

Resource	Unit costs	Source
Physiotherapy, average cost per group session	£67	Personal Social Services Research Unit (PSSRU) – Unit Costs of Health and Social Care
Physiotherapy, average cost per one-to-one session	£69	Personal Social Services Research Unit (PSSRU) – Unit Costs of Health and Social Care

Table 4 Example of Physiotherapist roles in each Agenda for Change band with annual and hourly salaries

Band	Example of Role	Agenda for change Annual Salary (range reflects the lowest pay point and highest pay point based on years of experience)	Agenda for change Hourly Salary (based on 37 hours of work per week)
2	Clinical support worker (physiotherapy)	£20,270-£21,318	£10.54-£11.08
3	Clinical support worker higher level (physiotherapy)	£21,730-£23,177	£11.29-£12.05
5	Physiotherapist	£27,055-£32,934	£14.06-£17.12
6	Physiotherapist specialist	£33,706-£40,588	£17.52-£21.10
7	Physiotherapist advanced, specialist physiotherapist, physiotherapy team manager	£41,659-£47,672	£21.65-£24.78
8a	Physiotherapist principal	£48,526-£54,619	£25.22-£28.39
8a-b	Physiotherapist consultant	£48,526-£65,262	£25.22-£33.92

1.1.11 Evidence statements

- One cost-utility analysis from the UK (Bruce et al. 2022) found that in women undergoing breast cancer surgery, at risk of postoperative upper limb morbidity, usual care plus a physiotherapist-led exercise programme was likely to be an effective use of NHS resources as it was both cheaper and more effective than usual care alone.
- One cost-utility analysis from Australia (Haines et al. 2010) found that in people with newly diagnosed breast cancer undergoing adjuvant therapy following surgery, a multimodal

exercise program was unlikely to be an effective use of resources as it was more expensive and less effective than a sham flexibility and relaxation program.

- One cost-utility analysis from Australia (Gordon et al. 2017) found that in women who have undergone surgery for primary breast cancer, an 8-month exercise intervention was unlikely to be an effective use of resources. Although the intervention was more effective than usual care (a health gain of 0.009 quality-adjusted life-years), it was also more expensive (an increased cost of $818 and $947 for a private and service provider model respectively). Thus, when the authors calculated the incremental cost-effectiveness ratio by dividing the costs by the changes in health, the result, around $100,000, was larger than $50,000 (the threshold by which the authors were considering if the intervention was an effective use of resource). These results are driven by the gain in health being relatively small compared with the increased costs.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The committee agreed that the critical outcomes for adults with early or locally advanced breast cancer who have undergone either surgery or radiotherapy for breast cancer were upper limb function and muscle strength, reduction of pain, reduction of lymphoedema, and improvement of quality of life. These outcomes are likely to have an impact on people's daily activities. It is also important that people have a good enough range of shoulder movement (upper limb function) before they start radiotherapy. Another important outcome was patient adherence to interventions as this could indicate that an intervention was working, and the more likely someone is to take part in the intervention, the more likely they are to experience the benefits. The committee thought that both short-term and long-term information about these outcomes were important.

1.1.12.2 The quality of the evidence

Overall, the quality of the evidence ranged from high to very low with the main reasons for downgrading being due to imprecision of the evidence and risk of bias. In some of the evidence, imprecision was considered to be serious or very serious with the 95% confidence intervals crossing one or two ends of the defined minimally important differences (MIDs) thresholds. Some of the included RCTs were downgraded for risk of bias due to lack of information on randomisation, allocation concealment and blinding. There was a wide range of different interventions and comparators, with different follow-up times reported for each comparison. This made it difficult for meta-analysis to be carried out, meaning that most outcomes were based on the results from single studies. The wide range of interventions, and imprecision in the results meant that the committee could not recommend one specific intervention as the best method of reducing arm and shoulder mobility problems after surgery or radiotherapy.

The committee highlighted that very few outcomes were high quality, and most of the evidence was of low to very low quality. The committee did not feel confident in making recommendations based on low quality evidence with limited meta-analysis. Therefore, they based most of their decisions on the high-quality evidence that could also be feasible to implement in the UK (see section of 'Benefits and harms' for more details).

Decision-making based on the lower quality evidence was problematic. The lower quality evidence compared interventions to each other and showed significant results at short term (6 months or less) and medium term (more than 6 months and up to 12 months) in most of the outcomes but without a clear overall effect of any particular intervention. For example, quality of life was shown to improve more with yoga than water exercise at short term (Figure 55) but improved more with water exercises compared to yoga at medium term. Therefore, the committee found it difficult to draw conclusions about which components of

physiotherapy or which specific type of exercise was required for efficacy. The committee agreed that there could be flexibility in the type of physiotherapy or exercises used after breast cancer surgery as long as this decision is made between a trained member of the team and the person receiving the intervention.

The committee noted that some data on range of movement was skewed because some measures had a maximum of 90 degrees (for example internal and external rotation) and in some studies participants' range of movement for internal and external rotation was close to 90 degrees. In these situations, confidence intervals were very narrow, and the mean difference was close to zero (Figure 3). This was likely to account for some of the heterogeneity in the data.

The committee highlighted that there was a lack of long-term evidence (only 4 studies reported more than 12 months follow-up [Bendz 2002, Box 2002a, Ibrahim 2017, Mutrie 2012, Pace do Amaral 2012]). They discussed the importance of investigating outcomes at longer follow-up times (beyond 12 months) to understand how each intervention benefits people in the long term, such as the ability to remain independent and to carry out activities of daily living effectively and without pain. Therefore, a research recommendation was developed to cover this gap in the evidence and to find the most effective and cost-effective way of delivering the intervention (type of physiotherapy or exercise, mode of delivery, number of sessions).

It was also noted that all of the evidence was for women, with no male participants in the included studies. Therefore, the committee could not be certain whether the effectiveness of different interventions would differ for men and women. However, while the content of information may need to differ for each gender, the most effective methods of providing physiotherapy or exercise rehabilitation were not expected to differ greatly and so the committee did not think that recommending upper limb exercises would cause equality issues for men who have had breast cancer.

There was limited, low quality, evidence on long-term outcomes and no evidence on outcomes for different population subgroups, such as people from minority ethnic family backgrounds, disabled people and neurodiverse people. These populations were discussed in the equality and health inequalities assessment (EHIA) form and the health inequalities briefing. The committee discussed the importance of understanding which interventions were the most effective, at short, medium and longer-term follow-up, for different populations and included these groups in the research recommendations to cover this gap in the evidence.

The evidence showed that there was no difference between interventions and comparators for patients' adherence in the long term (beyond 12 months). Only 2 RCTs found a significant difference in patients' adherence between comparisons at short and medium term but none of the RCTs provided data about whether patients' adherence had an effect on effectiveness. There was no evidence on factors affecting adherence, but the committee highlighted that lack of adherence is likely to be linked to lack of confidence of people to do the exercises given to them in written materials (for example leaflets) or because instructions were not clear (for example, instructions about how long interventions should be continued for). They made a research recommendation exploring whether adherence and satisfaction was impacted by the format of the intervention (individual, group, virtual, and face to face) because they expect that people who regularly take part in the interventions are more likely to experience the benefits.

1.1.12.3 Benefits and harms

The committee discussed evidence comparing interventions (either alone or in addition of usual care) to usual care. These comparisons showed a significant effect at short (6 months or less) or medium term (more than 6 months and up to 12 months) but none at long term (more than 12 months) in all outcomes in favour of the intervention. There were also significant effects on range of movement, pain and quality of life from physiotherapy

compared to no intervention at short and medium term but none at long term. However, the quality of this evidence was moderate to very low. Therefore, the committee focused on the high-quality UK-based evidence from 1 RCT (the PROSPER trial [Bruce 2022]). The trial compared usual care to a physiotherapy-led structured supervised exercise programme in addition to usual care. All participants received best practice usual care (written information leaflets recommending exercises after surgery and generic postoperative advice). In addition, participants randomised to the active intervention were referred to a physiotherapy-led structured exercise programme. High quality evidence showed improved outcomes with physiotherapy-led structured exercise programme in addition to usual care for:

- Reduction of pain in the breast and armpit (pain at rest at 6 weeks measured with a numerical rating scale [NRS]; MD -0.58 [95% CI -1.09 to -0.07]) and at 6 months (measured by FACT-B4; MD -1.11 [95% CI -2.01 to -0.21]) and at 12 months (measured with NRS; MD -0.68 [95% CI -1.23 to -0.13])
- Quality of life improvement (measured with SF-12 for physical health composite scale at 6 months [MD 2.73 [95% CI 0.24 to 5.22] and at 12 months [MD 4.39 [95% CI 1.74 to 7.04])
- Adherence (to arm or shoulder exercises) improvement (relative risk [RR] 1.07 [95% CI 1.01 to 1.14]) at 6 weeks

The committee discussed these effect sizes in the context of the agreed minimally important differences (see Appendix L for details on minimally important differences and clinical decision thresholds). None of these effects reached the MIDs, but as published MIDs were not available for most of these outcomes, discussions were based on the default MIDs. While the outcomes did not meet these default values, the committee considered that any reduction in pain or in quality of life was important.

The UK-based trial provided all participants with information leaflets about exercises to help with arm and shoulder mobility after breast cancer surgery. This reflects standard practice in the UK, and the committee thought it was important to reflect this in the recommendations. They therefore made a recommendation about giving people instructions on upper limb exercises. The recommendation highlighted that instructions on upper limb exercises and information should be discussed, explained and clarified with the person, before breast cancer surgery and radiotherapy because the exercises should have been well established before starting this treatment. After surgery or radiotherapy, the person may be more fatigued and already in some discomfort, so they may find it more difficult to maintain the concentration needed to learn and understand the exercises. Additionally, people who have other cognitive or sensory challenges may need longer to become confident in performing the exercises, so starting before treatment is also helpful for this group.

The committee discussed health inequalities, including how people have different needs that should be taken into account when providing care. This includes people who have a learning disability, impairment or sensory loss, people who are neurodiverse, people whose first language is not English, or people from religions or cultural backgrounds with specific needs. Therefore, instructions on upper limb exercises should be available in other formats to ensure they are accessible to a range of people with different needs (other formats could include easy read, different languages, audio translation, video, large print, signing, or Braille).

The committee were aware that instructions on upper limb exercises are not always given out by someone who is a specialist in physiotherapy (for example, breast care nurses), so they also recommended that breast care units have documented local guidelines in place that include details about who and how to deliver this information effectively. They thought it was important that the information included details on when the exercises should be started. For most people this will be the day after surgery but it may be later for others, such as those who have certain surgical procedures (for example, free flap reconstruction or implant reconstruction) because exercising the day after surgery could interfere with their recovery. Exercises should be tailored for each person based on their needs (for example,

comorbidities and side effects of cancer treatment) but for the majority of patients, a standard programme of upper limb exercises will be suitable. The committee also agreed it was important that instructions on upper limb exercises should be available in other formats to be accessible to people with different needs (for example, video or large print and various languages). There are already recommendations on communication in the NICE guideline on patient experience in adult NHS services and so a link to this was included as part of the recommendation.

Based on the effectiveness of the intervention in the UK-based trial, the committee agreed that people who met the same criteria as those included in the trial should be identified as being at higher risk of developing shoulder problems and made a recommendation offering supervised support to apply the upper limb exercises. The committee also made a recommendation which lists risk factors of developing shoulder problems and should be identified preoperatively in people who are having surgery for breast cancer. These factors are pre-existing shoulder conditions (such as: history of shoulder surgery, shoulder trauma injury [fracture or shoulder dislocation], frozen shoulder, osteoarthritis or rheumatoid arthritis affecting the shoulder, non-specific shoulder pain, stiffness, decreased function), BMI (over 30), axillary node clearance planned, or radiotherapy to the axilla or supraclavicular nodes planned. The baseline shoulder identification of someone as high risk of developing shoulder problems could be done by a member of the clinical team (for example, a clinical nurse specialist) and could be done by looking at a person's medical history and asking the person if they have experienced any of the issues listed in the recommendation (for example asking if they have stiffness of their shoulder or if the function of their shoulder is reduced). The evidence did not specify that these risk factors were only relevant to the affected side and the committee noted that people should be considered at high risk if they have any of the pre-existing shoulder conditions in the contralateral side. It was also highlighted that for most people radiotherapy to the axilla or supraclavicular nodes is decided before surgery. However, for some people this may be decided after postoperative pathology review. For this reason, they recommended that people who are identified as needing radiotherapy to the axilla or supraclavicular nodes after surgery should also be considered as being at higher risk of developing shoulder problems. This ensures that people would not miss out from supervised support if the need for radiotherapy was not identified before surgery.

People who were not considered at higher risk of developing shoulder problems, and people who had radiotherapy, were not included in the UK-based trial. However, the committee also agreed that, in their experience, other people having surgery for breast cancer who did not meet the high risk criteria in the recommendations could benefit from supervised support. This includes, for example, people with learning or sensory disabilities, which could adversely affect their ability to carry out exercises without supervision and make them more likely to develop shoulder problems as a result. It also includes people having breast cancer surgery who have side effects from additional cancer treatments or who have other commonly performed adjunct surgeries in addition to breast cancer surgery, as well as people who are having radiotherapy without surgery.

Based on their experience, the committee recommended that supervised support should be delivered by a physiotherapy staff member or other appropriately trained allied health professional (for example an occupational therapist). This should include checking the performance of the exercises and correcting them as needed. The committee agreed that many people may not feel confident in translating written exercise instructions into physical movement, so would benefit from having confirmation they are doing them correctly. This also allows healthcare staff to identify people who might be experiencing difficulties both with the exercises and with shoulder function early after surgery or before radiotherapy. This support will ensure that they are able to receive the full benefit from the exercises, and may increase adherence if someone is confident they are doing the exercises correctly.

Supervised exercises and physiotherapy support should also be available in different formats (for example virtual or group sessions), and the format of the information should be tailored

to individual circumstances and needs. The number of sessions should be decided based on each person's needs and wishes. There was no evidence about interventions delivered virtually but the committee agreed to recommend this as an option as it may help to reduce health inequalities and address access options for people where other interventions are not locally available. The committee were aware that some people may not be able to access virtual services for a range of reasons, such as a lack of access to suitable devices, living in areas of poor connectivity and difficulties with using the technology. However, including virtual services in the recommendations should not provide barriers to these people accessing support, as they can be given the option of face-to-face sessions. The committee were mindful that, while their experience shows that virtual interventions are beneficial, there is a lack of evidence for this and so it was added to the research recommendation. The committee also acknowledged that a person's ability to adhere to any exercise programme offered may be impacted by the person's individual needs (for example, mental health and learning needs), so recommended tailoring programmes to the individual.

One group that may have particular concerns about undertaking post-surgery exercises are those who have multiple surgeries and/or reconstruction. In addition to the people that have had reconstruction, some people may have multiple re-excisions or have sentinel node biopsy followed by axillary lymph node clearance. Another group may be those with significant lymphoedema. All these groups may be afraid of doing the exercises wrongly and potentially causing themselves harm. This strengthens the recommendation why people need supervised support in how to do post-surgery exercises safely and effectively.

The committee highlighted that neurodiverse people and people with disabilities may particularly benefit from receiving a demonstration on how to do the exercises and a confirmation that they are doing the exercises correctly. It would also be helpful for people to have a clear guideline of what to do if a problem happens once the supervised support has finished (for example, who they should contact).

The committee discussed that offering supervised exercise or physiotherapy to all people having surgery and/or radiotherapy for breast cancer may increase cost. However, supervised exercise or physiotherapy could be virtual (individual or group) which is likely to have less economic impact than if it had to be in-person individual 1-to-1 sessions (like the PROSPER trial). This may mean that a person could be referred to an out of area service that offers virtual support if the support is not available in their local service.

The committee also recommended that people should be referred to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment. This allows people to continue to seek support if it is needed. The committee noted that the research recommendation will gather evidence about the long-term effects of strategies to reduce arm and shoulder problems, and this may reduce the number of people who have to be referred to the physiotherapy department in future.

1.1.12.4 Cost effectiveness and resource use

The committee reviewed economic evidence on the cost effectiveness of strategies to reduce arm and shoulder problems after breast cancer surgery and radiotherapy from the existing literature. The evidence from the literature came from 3 cost-effectiveness analyses, one from the UK (Bruce et al. 2022) and two from Australia (Gordon et al. 2017 and Haines et al. 2010).

The committee decided not to recommend the interventions that were evaluated in each of the two Australian studies, as the studies were less applicable to the UK setting, and the interventions were not considered to be cost effective. The intervention evaluated in Gordon et al. 2017 was an 8-month exercise intervention, and the economic analysis estimated that it was not an effective use of resources. It was more effective than usual care and more expensive, and that the additional costs outweighed the additional benefits. In addition, there were concerns over cost and capacity, and this programme would not currently be possible

to implement in the NHS. The comparison in Haines et al. 2010, between a multimodal exercise program and a flexibility and relaxation program showed no evidence of effectiveness. The committee discussed that they would not recommend a program that is not effective, but also discussed it is difficult to draw any conclusions from this comparison because in the NHS, people are usually given a breast cancer care information leaflet and not a flexibility and relaxation program. Therefore, this trial is looking at a comparison that is not reflective of UK clinical practice and is of limited value for decision making.

The committee discussed the economic evidence from the UK study, which it did consider suitable for decision making. In this study's base case analysis, the PROSPER physiotherapist-led exercise intervention plus breast cancer care information leaflets results in more QALYs (better health) and is less costly than giving leaflets alone. Although improvements in utility are reported for the PROSPER exercise intervention, a detailed breakdown of EQ-5D scores is not provided, making it impossible to identify exactly which domains were different between the two groups in order to see where the intervention had the most impact on people. With regards to costs, the largest cost saving associated with the PROSPER exercise intervention is medication costs, however, this was not statistically significant ($p = 0.79$). The authors note there is a great deal of uncertainty around the costs of the intervention: this can be seen with the wide confidence interval around the total incremental costs (95% CI -£2,491.18, £1,717.62). Despite the uncertainty around cost, the PROSPER exercise intervention had a 78% likelihood of being an effective use of NHS resources in this population, if we value a QALY at £20,000. Therefore, the committee felt confident to make a strong recommendation for a supervised exercise programme for the high-risk population.

However, there are several limitations with the UK study. Firstly, the enrolled study population was restricted to people undergoing surgery who were considered at high risk of developing shoulder problems, including those with pre-existing shoulder problems, a BMI over 30, undergoing ancillary node clearance (ANC). These people are likely to have greater capacity to benefit from the intervention than those not at high risk of developing shoulder problems, and so it is unclear if the results of this study are generalizable to the wider population. The committee discussed this and agreed that if one were to expand the PROSPER exercise intervention as detailed in the study to those not at high risk of shoulder problems or those undergoing radiotherapy only, this may result in increased costs per person, with the effect on health unclear, and it was less clear whether it would be a cost effective intervention. Others highlighted that due to the exclusion criteria of PROSPER, a significant number of people who were excluded may actually stand to benefit a lot from the exercise intervention; however, they noted that we did not have sufficient evidence to make a strong recommendation. Given the uncertainty regarding the effect on health a wider population might see, the committee felt that it was likely that the benefits of a programme would outweigh the costs and made a weaker recommendation for a supervised exercise intervention for population not at high risk of developing shoulder problems.

Secondly, the PROSPER study was designed in a way to maximize adherence, with 75% attending the minimum three physiotherapy contacts. If levels of adherence in the wider population are lower than those seen in this study, it is possible that the benefits in health observed in reality will be lower than those seen in the trial. The committee was confident with the assumption that adherence is likely to be one of the key factors associated with any potential health benefits observed and were mindful that any recommendations they make should strive to ensure such interventions are implemented in a way to maximize adherence and therefore the health benefit people see. Lay members of the committee highlighted their experience that a program with supervision means they are more likely to be adherent to their exercises, and so it was felt that other supervised exercise programmes would be able to deliver similar levels of benefit to the PROSPER exercise programme.

Finally, this study only assessed the impact of the intervention over a one-year time-horizon. That is to say, only one year of health and costs were modelled, and assumes that there are

no further impacts on cost or benefits. The recommendation to refer people to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment was developed in order to allow people to continue to seek support if it is needed. Notably, in PROSPER, there was a small proportion of participants with ongoing, protracted, treatment-related problems who were permitted additional physiotherapy contacts. The committee noted this as an area of uncertainty and made a research recommendation about the long-term effects of strategies to reduce arm and shoulder problems.

In view of these considerations, the committee were confident in making a strong recommendation for supervised exercise programme to reduce arm and shoulder problem after breast cancer surgery in the population at high risk of developing arm and shoulder problems. Given uncertainties in whether these benefits would be realised outside of this population, the committee agreed to make a weaker recommendation for supervised support for the population who were not at risk of developing arm and shoulder problems.

The committee considered the potential resource impact of its recommendation. They suggested that the intervention did not need to be delivered in person or one-to-one for all people to see the benefits of the intervention. Alternatively, the intervention could be delivered either in a group setting or in a virtual session to those people for whom it would be acceptable. These suggestions were to help mitigate the increased cost of making an intervention available to a wider population. There is no specific evidence of the effectiveness of a programme in these formats, and included a research recommendation on this topic.

The committee believed that both clinically and personally, it is important that a supervisor can see the exercises someone is doing, and to be able to correct them if they are doing it inappropriately. This can be achieved in a group or virtual setting, provided there is a face-to-face opportunity for populations with more complex needs or are at higher risk. The committee believed that an intervention delivered in a group setting or virtually would be able to provide similar benefits to an intervention delivered in one-to-one or in-person sessions as per the PROSPER trial, but would have a substantial ability to keep costs low while offering the program to more people. The committee also noted both group and virtual therapy are associated with positive benefits that would not have been captured by a one-to-one in-person therapy such as a sense of community built through group sessions, and also for those unable to join in-person, such as carers, the ability to still access treatment.

The committee said that, in their experience, a physiotherapy assistant would be capable of delivering the intervention in a group setting, particularly for those who are not at high risk of arm and shoulder problems. The benefit of allowing a physiotherapy assistant practitioner (alternatively referred to as a clinical support worker in Table 4) to deliver the intervention is further cost savings. This is because a physiotherapy assistant practitioner is band 2 or 3 on the NHS agenda for change, and is therefore cheaper to employ than a physiotherapist who are band 5 or higher. Who will lead the intervention is a decision that will remain with individual NHS trusts, as capacity is likely to vary. However, areas that are able to utilize physiotherapy assistant practitioners to deliver the intervention in a group setting are likely to incur reduced costs compared to areas that utilize physiotherapists.

The committee did note that some areas may not have the infrastructure currently in place to support virtual sessions. However, it was also noted that this is something to address with commissioners, especially given newly developed hybrid ways of working and remote meetings are unlikely to disappear. The committee therefore thought being able to provide such services will be an essential part of a health service moving forward.

1.1.12.5 Other factors the committee took into account

The committee highlighted that video support may be a useful option to many people, as it is easier than attending a physiotherapy or exercise class in person. However, they noted that

there might be some people who may have vision and or hearing problems or may not have access to technology to receive virtual support. They acknowledged that since the COVID pandemic, video consultations are more common, and in their experience it is likely that very few people are not able to use this format. They therefore thought that the option of virtual consultations should not cause any major equalities issues.

The committee also highlighted that face to face physiotherapy may be more beneficial for people with complex needs or those at higher risk (for example people from minority ethnic family backgrounds, people with disabilities, neurodiverse people, those who experience physical difficulties with recovery or rehabilitation) because they might need specific instructions and feedback.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.12.5 to 1.12.12 and the research recommendations on strategies to reduce arm and shoulder problems, and adherence and satisfaction to interventions to reduce arm and shoulder problems.

1.1.14 References – included studies

1.1.14.1 Effectiveness

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1.1.14.2 Economic

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1 Appendices

Appendix A – Review protocols

Review protocol for effective strategies for reducing arm and shoulder problems after breast cancer surgery or radiotherapy

ID	Field	Content
1.	Review title	Effective strategies for reducing arm and shoulder problems after breast cancer surgery or radiotherapy
2.	Review question	1.1 What strategies are effective in reducing arm and shoulder problems after breast cancer surgery or radiotherapy?
3.	Objective	To assess the effectiveness and cost-effectiveness of strategies in reducing arm and shoulder problems after breast cancer surgery or radiotherapy.
4.	Searches	The following databases will be searched for the clinical review: • Cochrane Central Register of Controlled Trials (CENTRAL) (including ongoing trials) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Emcare

ID	Field	Content
		For the economics review the following databases will be searched on population only: • Embase • MEDLINE • Medline in Process • Medline EPub Ahead of Print • Econlit • HTA (legacy records) • NHS EED (legacy records) • INAHTA Searches will be restricted by: • Studies reported in English • Study design RCT and systematic review will be applied • Animal studies will be excluded from the search results • Conference abstracts will be excluded from the search results

ID	Field	Content
		The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Early and locally advanced breast cancer
6.	Population	Inclusion: Adults with early or locally advanced breast cancer (18 and over) who have undergone any of the following treatments alone or in combination: • surgery for breast cancer alone or with: axillary clearance, sentinel lymph node biopsy, or node sampling • radiotherapy for breast cancer alone or with regional lymph node radiotherapy No exclusion criteria.
7.	Intervention	• Prehabilitation provided to patients following their initial diagnosis to prepare and optimise them for their forthcoming surgery or radiotherapy

ID	Field	Content

		(interventions will only be included if they contain at least one of the intervention types listed in the post-surgery or post-radiotherapy section)
		• Post-surgery or post-radiotherapy:
		  ○ Physiotherapy aimed at maximising people's ability to move and function
		  ○ Exercise or rehabilitation classes for people who have undergone surgery or radiotherapy
		  ○ Information/education about unsupervised post-surgical or post-radiotherapy arm/shoulder exercise
		Consideration will be given to the timing of the intervention pre or post-surgery or radiotherapy and its content, delivery, duration and intensity.

8.	Comparator	• All interventions and combination of interventions compared to each other • No intervention
9.	Types of study to be included	• RCTs • Systematic reviews of RCTs

ID	Field	Content
10.	Other exclusion criteria	• Abstracts, conference presentations and theses • Non-human studies • Non-English language studies • Studies of interventions that are not started within a year of the end of active treatment (i.e., breast surgery or radiotherapy) • Pilot studies may also be excluded due to small samples sizes. • Interventions solely aimed at managing lymphedema.
11.	Context	This is an update of existing NICE guidance (NG101) on strategies for reducing arm and shoulder mobility problems after breast cancer surgery. The current update is being undertaken based on identification of the PROSPER trial (Bruce et al 2022) by the NICE surveillance team, which was judged to have the potential to alter the existing recommendations. Reference: Bruce J, Mazuquin B, Mistry P, et al. (2022) Exercise to prevent shoulder problems after breast cancer surgery: the PROSPER RCT. Health Technol Assess. 2022 Feb;26(15):1-124. Doi: 10.3310/JKNZ2003. PMID: 35220995.
12.	Primary Outcomes (critical outcomes)	Data will be collected for all primary and secondary outcomes at the following time points: Short term: <=6 months

ID	Field	Content

		Medium term: >6 to <=12
		Long term: >12
		• Upper limb function:
		  ○ Disabilities of the Arm, Shoulder and Hand scale (DASH; activity limitations domain will be presented separately where reported)
		  ○ Range of movement (ROM), for example: shoulder flexion and abduction
		• Upper limb muscle strength
		• Pain (validated scales for example: numerical rating scale [NRS])
		• Incidence of lymphoedema
		• Quality of life (EQ-5D, FACT-B+4, EORTC-QoL-C30)
		• Resource use and cost

13.	Secondary outcomes (important outcomes)	• Patient adherence
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be

ID	Field	Content
		reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. This review will make use of the priority screening functionality within the EPPI-reviewer software. 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). Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the Cochrane Risk of Bias v.2.0 checklist as described in Developing NICE guidelines: the manual.
16.	Strategy for data synthesis	Where possible, meta-analyses of outcome data will be conducted for all comparators that are reported by more than one study, with reference to the Cochrane Handbook for Systematic Reviews of Interventions. Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below).

ID	Field	Content
		Continuous outcomes will be analysed as mean differences, unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all comparators, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions is met: Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. The presence of significant statistical heterogeneity in the meta-analysis, defined as I2≥50%. In any meta-analyses where some (but not all) of the data comes from studies at high risk of bias, a sensitivity analysis will be conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses will be reported. Similarly, in any meta-analyses where some (but not all) of the data comes from indirect studies, a sensitivity analysis will be conducted, excluding those studies from the analysis.

ID	Field	Content
		GRADE will be used to assess the quality of the outcomes. All outcomes in this review will come from RCTs and will be rated as high quality initially and downgraded from this point. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias.
17.	Analysis of sub-groups	• risk of upper limb problems (high versus low) • type of treatment (radiotherapy, surgery, etc.) • format of intervention (for example, timing of the intervention pre or post-surgery or radiotherapy and its content, delivery, duration and intensity, etc.)
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)

ID	Field	Content		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	19 September 2022		
22.	Anticipated completion date	23 February 2023		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐ ☐	☐ ☐
		Piloting of the study selection process	☐ ☐	☐ ☐
		Formal screening of search results against eligibility criteria	☐ ☐	☐ ☐
		Data extraction	☐ ☐	☐ ☐

ID	Field	Content		
		Risk of bias (quality) assessment	☐ ☐	☐ ☐
		Data analysis	☐ ☐	☐ ☐
24.	Named contact	**5a. Named contact** Centre for Guidelines, NICE. **5b Named contact e-mail** breastcancerupdate2@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and Guideline Development Team.		
25.	Review team members	From the Guideline Development Team: • Marie Harrisingh, Technical adviser • Clare Dadswell, Senior technical analyst • Yolanda Martinez, Technical analyst • Lindsay Claxton, Health economist adviser • Jeremy Dietz, Health economist analyst • Andrea Heath, Information specialist		

ID	Field	Content
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team 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: Breast cancer – reducing arm and shoulder mobility problems after breast cancer surgery.
29.	Other registration details	None
30.	Reference/URL for published protocol	None
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts

ID	Field	Content
		• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Breast cancer surgery; arm mobility; shoulder mobility
33.	Details of existing review of same topic by same authors	Not applicable
34.	Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	None
36.	Details of final publication	www.nice.org.uk

Appendix B – Literature search strategies

What strategies are effective in reducing arm and shoulder problems after breast cancer surgery or radiotherapy?
Database: Ovid MEDLINE(R) ALL <1946 to September 08, 2022>
Search Strategy:
---

1 exp Breast Neoplasms/ (330783)
2 Carcinoma, Ductal, Breast/ (16756)
3 Carcinoma, Lobular/ (5983)
4 Carcinoma, Medullary/ (3360)
5 Carcinoma, Intraductal, Noninfiltrating/ (10411)
6 or/1-5 (334607)
7 exp Breast/ (51590)
8 breast*.ti,ab,kw. (525932)
9 7 or 8 (535749)
10 (breast adj milk).ti,ab,kw. (14835)
11 (breast adj tender*).ti,ab,kw. (573)
12 10 or 11 (15406)
13 9 not 12 (520343)
14 exp Neoplasms/ (3732453)
15 13 and 14 (343457)
16 (breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)).ti,ab,kw. (388709)
17 (mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)).ti,ab,kw. (35554)
18 Paget's Disease, Mammary/ (797)
19 (paget* and (breast* or mammary or nipple*)).ti,ab,kw. (1408)
20 or/15-19 (444235)
21 6 or 20 (485422)
22 exp Upper Extremity/ (182379)
23 Shoulder Pain/ (5640)
24 Shoulder Joint/ (20961)
25 Elbow Joint/ (13722)
26 "Range of Motion, Articular"/ (58191)
27 (arm* or shoulder* or upper limb* or upper extremit* or musculoskeletal*).ti,ab,kw. (461628)
28 or/22-27 (640750)
29 Preoperative Care/ (64999)
30 Preoperative Exercise/ (290)
31 Physical Therapy Modalities/ (39859)
32 exp Exercise/ (235819)
33 exp Exercise Therapy/ (60690)
34 Exercise Movement Techniques/ (842)
35 exp Massage/ (6759)
36 Electric Stimulation Therapy/ (21730)
37 Acupuncture/ (1963)
38 Self Care/ or Self-Management/ (39889)
39 Musculoskeletal Manipulations/ (2136)
40 Patient Education Handout/ (5557)

41 Patient Education as Topic/ (88127)
42 Nutrition Therapy/ (3095)
43 Diet, Healthy/ (6505)
44 (exercis* or physical activit* or physical therap* or movement* or resistance train* or kinesiotherap* or kinesitherap* or kinesiatric* or physiotherap* or massage* or electric stimulation therap* or electrotherap* or manual therap* or prehab* or rehab* or nutrition* or diet* or wellbeing or well being or advi* or leaflet* or brochure* or booklet* or factsheet* or information* or educat*).ti,ab,kw. (3894133)
45 (lymph* adj2 drain*).ti,ab,kw. (14575)
46 SLD.ti,ab,kw. (1262)
47 or/29-46 (4126864)
48 and/21,28,47 (3515)
49 (MEDLINE or pubmed).tw. (288916)
50 systematic review.tw. (234947)
51 systematic review.pt. (206391)
52 meta-analysis.pt. (167048)
53 intervention$.ti. (185015)
54 or/49-53 (617790)
55 randomized controlled trial.pt. (576561)
56 randomi?ed.mp. (1020624)
57 placebo.mp. (238987)
58 or/55-57 (1083895)
59 54 or 58 (1537776)
60 48 and 59 (1281)
61 animals/ not humans/ (5009892)
62 60 not 61 (1281)
63 limit 62 to english language (1259)

Database: Embase <1974 to 2022 September 09>
Search Strategy:
---
1 exp breast cancer/ (531237)
2 exp breast carcinoma/ (92189)
3 exp medullary carcinoma/ (11694)
4 ductal breast carcinoma in situ/ (970)
5 exp breast tumor/ (607527)
6 lobular carcinoma/ (3004)
7 or/1-6 (617872)
8 exp breast/ (123991)
9 breast*.ti,ab,kw. (721336)
10 8 or 9 (752931)
11 (breast adj milk).ti,ab,kw. (18699)
12 (breast adj tender*).ti,ab,kw. (721)
13 11 or 12 (19415)
14 10 not 13 (733516)
15 exp neoplasm/ (5181226)
16 14 and 15 (556604)
17 (breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)).ti,ab,kw. (553333)

18 (mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)).ti,ab,kw. (41717)
19 exp Paget nipple disease/ (8045)
20 (paget* and (breast* or mammary or nipple*)).ti,ab,kw. (1763)
21 or/16-20 (627455)
22 7 or 21 (737589)
23 exp upper limb/ (330796)
24 exp arm pain/ (9080)
25 exp shoulder pain/ (19661)
26 exp arm disease/ (178311)
27 "range of motion"/ (55753)
28 joint mobility/ (19275)
29 (arm* or shoulder* or upper limb* or upper extremit* or musculoskeletal*).ti,ab,kw. (648553)
30 or/23-29 (963606)
31 preoperative care/ (44241)
32 preoperative exercise/ (749)
33 exp physiotherapy/ (100412)
34 exp exercise/ (399962)
35 exp kinesiotherapy/ (92629)
36 exp physical activity/ (500166)
37 cancer rehabilitation/ (1562)
38 exp massage/ (16570)
39 electrotherapy/ (2222)
40 acupuncture/ (44927)
41 exp manipulative medicine/ (41118)
42 patient education/ (121502)
43 self care/ (70197)
44 nutrition education/ (6448)
45 healthy diet/ (5782)
46 patient information/ (29593)
47 lymphatic drainage/ (7030)
48 (exercis* or physical activit* or physical therap* or movement* or resistance train* or kinesiotherap* or kinesitherap* or kinesiatric* or physiotherap* or massage* or electric stimulation therap* or electrotherap* or manual therap* or prehab* or rehab* or nutrition* or diet* or wellbeing or well being or advi* or leaflet* or brochure* or booklet* or factsheet* or information* or educat*).ti,ab,kw. (4962734)
49 (lymph* adj2 drain*).ti,ab,kw. (20746)
50 SLD.ti,ab,kw. (1739)
51 or/31-50 (5499711)
52 and/22,30,51 (5896)
53 (MEDLINE or pubmed).tw. (358825)
54 exp systematic review/ or systematic review.tw. (439777)
55 meta-analysis/ (256008)
56 intervention$.ti. (243882)
57 or/53-56 (864147)
58 random:.tw. (1831381)
59 placebo:.mp. (500916)
60 double-blind:.tw. (233437)
61 randomized controlled trial/ (726538)
62 or/58-61 (2186528)

63 57 or 62 (2776660)
64 52 and 63 (2553)
65 nonhuman/ not human/ (5048794)
66 64 not 65 (2547)
67 limit 66 to english language (2502)
68 (conference abstract* or conference review or conference paper or conference proceeding or preprint).db,pt,su. (5342798)
69 67 not 68 (1471)

Database: Cochrane Library <1974 to 08 September 2022)
Search strategy

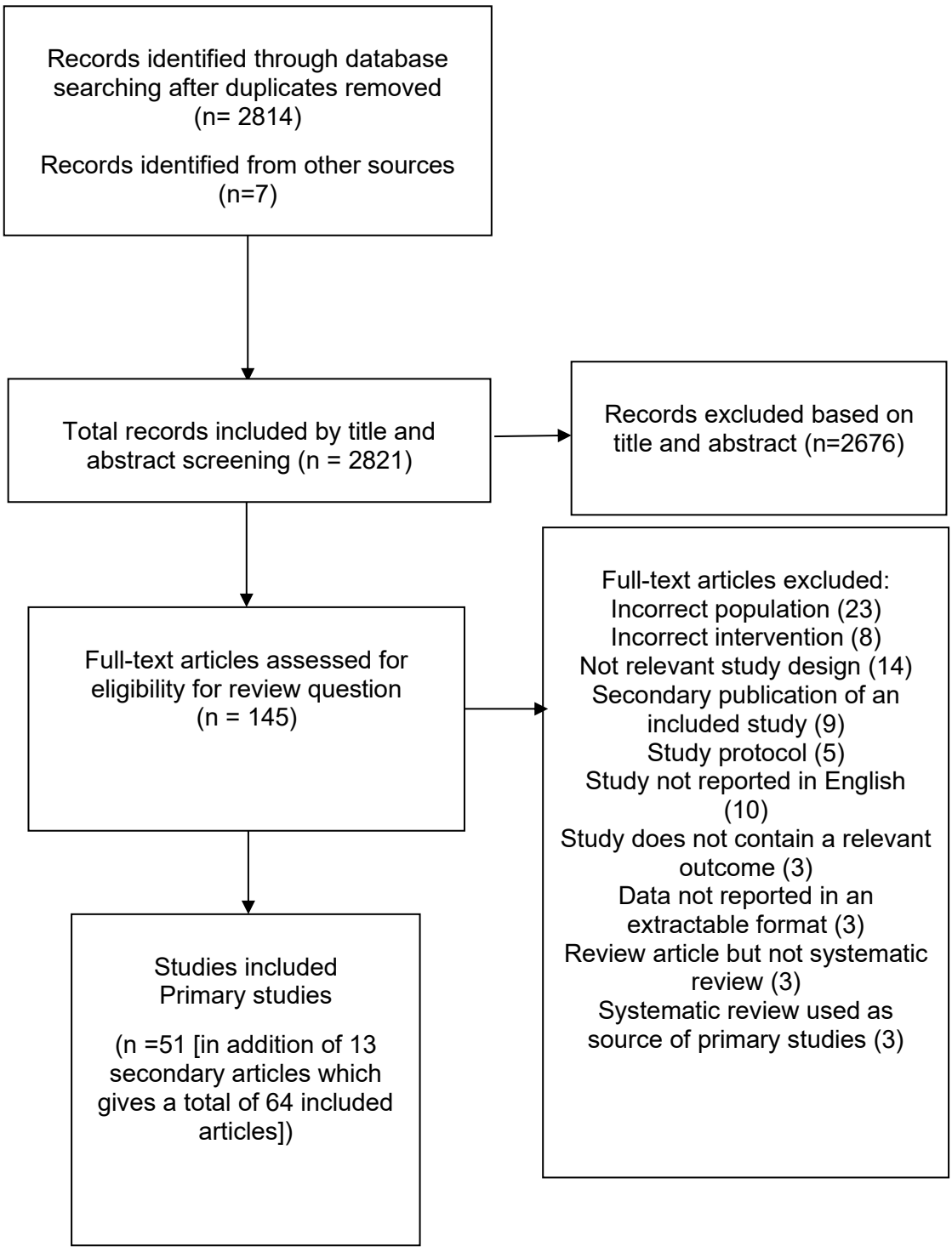
#1 MeSH descriptor: [Breast Neoplasms] explode all trees 14754
#2 MeSH descriptor: [Carcinoma, Ductal, Breast] this term only 377
#3 MeSH descriptor: [Carcinoma, Lobular] this term only 176
#4 MeSH descriptor: [Carcinoma, Medullary] this term only 16
#5 MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] this term only 209
#6 {OR #1-#5} 14786
#7 MeSH descriptor: [Breast] explode all trees 845
#8 breast*:ti,ab 54342
#9 #7 or #8 54429
#10 (breast NEXT milk):ti,ab 2430
#11 (breast NEXT tender*):ti,ab 238
#12 #10 or #11 2668
#13 #9 not #12 51761
#14 MeSH descriptor: [Neoplasms] explode all trees 89520
#15 #13 and #14 15019
#16 (breast* NEAR/5 (neoplasm* or cancer* or tumor* or tumour* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)):ti,ab 39165
#17 (mammar* near/5 (neoplasm* or cancer* or tumor* or tumour* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)):ti,ab 268
#18 MeSH descriptor: [Paget's Disease, Mammary] explode all trees 3
#19 (paget* and (breast* or mammary or nipple*)):ti,ab 18
#20 {OR #15-#19} 39928
#21 #6 or #20 40686
#22 MeSH descriptor: [Upper Extremity] explode all trees 8080
#23 MeSH descriptor: [Shoulder Pain] this term only 1131
#24 MeSH descriptor: [Shoulder Joint] this term only 827
#25 MeSH descriptor: [Elbow Joint] this term only 277
#26 MeSH descriptor: [Range of Motion, Articular] this term only 5312
#27 (arm* or shoulder* or upper limb* or upper extremit* or musculoskeletal*):ti,ab 168318
#28 {OR #22-#27} 176634
#29 MeSH descriptor: [Preoperative Care] this term only 4447
#30 MeSH descriptor: [Preoperative Exercise] this term only 43
#31 MeSH descriptor: [Physical Therapy Modalities] this term only 4157
#32 MeSH descriptor: [Exercise] explode all trees 28693
#33 MeSH descriptor: [Exercise Therapy] explode all trees 16366
#34 MeSH descriptor: [Exercise Movement Techniques] this term only 287

#35 MeSH descriptor: [Massage] explode all trees 1298
#36 MeSH descriptor: [Electric Stimulation Therapy] this term only 2041
#37 MeSH descriptor: [Acupuncture] this term only 164
#38 MeSH descriptor: [Self Care] this term only 4376
#39 MeSH descriptor: [Self-Management] this term only 714
#40 MeSH descriptor: [Musculoskeletal Manipulations] this term only 559
#41 MeSH descriptor: [Patient Education Handout] this term only 0
#42 MeSH descriptor: [Patient Education as Topic] this term only 9239
#43 MeSH descriptor: [Nutrition Therapy] this term only 220
#44 MeSH descriptor: [Diet, Healthy] this term only 639
#45 (exercis* or physical activit* or physical therap* or movement* or resistance train* or kinesiotherap* or kinesitherap* or kinesiatric* or physiotherap* or massage* or electric stimulation therap* or electrotherap* or manual therap* or prehab* or rehab* or nutrition* or diet* or wellbeing or well being or advi* or leaflet* or brochure* or booklet* or factsheet* or information* or educat*):ti,ab 433854
#46 (lymph* near/2 drain*):ti,ab 668
#47 SLD:ti,ab 144
#48 {OR #29-#47} 447300
#49 #21 and #28 and #48 in Cochrane Reviews, Cochrane Protocols 32
#50 #21 and #28 and #48 2767
#51 "conference":pt 202391
#52 #50 not #51 in Trials 2031

ID Search Hits
#1 MeSH descriptor: [Breast Neoplasms] explode all trees 14754
#2 MeSH descriptor: [Carcinoma, Ductal, Breast] this term only 377
#3 MeSH descriptor: [Carcinoma, Lobular] this term only 176
#4 MeSH descriptor: [Carcinoma, Medullary] this term only 16
#5 MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] this term only 209
#6 {OR #1-#5} 14786
#7 MeSH descriptor: [Breast] explode all trees 845
#8 breast*:ti,ab 54342
#9 #7 or #8 54429
#10 (breast NEXT milk):ti,ab 2430
#11 (breast NEXT tender*):ti,ab 238
#12 #10 or #11 2668
#13 #9 not #12 51761
#14 MeSH descriptor: [Neoplasms] explode all trees 89520
#15 #13 and #14 15019
#16 (breast* NEAR/5 (neoplasm* or cancer* or tumor* or tumour* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)):ti,ab 39165
#17 (mammar* near/5 (neoplasm* or cancer* or tumor* or tumour* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignanc*)):ti,ab 268
#18 MeSH descriptor: [Paget's Disease, Mammary] explode all trees 3
#19 (paget* and (breast* or mammary or nipple*)):ti,ab 18
#20 {OR #15-#19} 39928
#21 #6 or #20 40686
#22 MeSH descriptor: [Upper Extremity] explode all trees 8080
#23 MeSH descriptor: [Shoulder Pain] this term only 1131

#24 MeSH descriptor: [Shoulder Joint] this term only 827
#25 MeSH descriptor: [Elbow Joint] this term only 277
#26 MeSH descriptor: [Range of Motion, Articular] this term only 5312
#27 (arm* or shoulder* or upper limb* or upper extremit* or musculoskeletal*):ti,ab 168318
#28 {OR #22-#27} 176634
#29 MeSH descriptor: [Preoperative Care] this term only 4447
#30 MeSH descriptor: [Preoperative Exercise] this term only 43
#31 MeSH descriptor: [Physical Therapy Modalities] this term only 4157
#32 MeSH descriptor: [Exercise] explode all trees 28693
#33 MeSH descriptor: [Exercise Therapy] explode all trees 16366
#34 MeSH descriptor: [Exercise Movement Techniques] this term only 287
#35 MeSH descriptor: [Massage] explode all trees 1298
#36 MeSH descriptor: [Electric Stimulation Therapy] this term only 2041
#37 MeSH descriptor: [Acupuncture] this term only 164
#38 MeSH descriptor: [Self Care] this term only 4376
#39 MeSH descriptor: [Self-Management] this term only 714
#40 MeSH descriptor: [Musculoskeletal Manipulations] this term only 559
#41 MeSH descriptor: [Patient Education Handout] this term only 0
#42 MeSH descriptor: [Patient Education as Topic] this term only 9239
#43 MeSH descriptor: [Nutrition Therapy] this term only 220
#44 MeSH descriptor: [Diet, Healthy] this term only 639
#45 (exercis* or physical activit* or physical therap* or movement* or resistance train* or kinesiotherap* or kinesitherap* or kinesiatric* or physiotherap* or massage* or electric stimulation therap* or electrotherap* or manual therap* or prehab* or rehab* or nutrition* or diet* or wellbeing or well being or advi* or leaflet* or brochure* or booklet* or factsheet* or information* or educat*):ti,ab 433854
#46 (lymph* near/2 drain*):ti,ab 668
#47 SLD:ti,ab 144
#48 {OR #29-#47} 447300
#49 #21 and #28 and #48 in Cochrane Reviews, Cochrane Protocols 32
#50 #21 and #28 and #48 2767
#51 "conference":pt 202391
#52 #50 not #51 in Trials 2031

Appendix C – Effectiveness evidence study selection



Appendix D – Effectiveness evidence

Abe, 1998

Bibliographic Reference	Abe, Makoto; Iwase, Takuji; Takeuchi, Toru; Murai, Hiroshi; Miura, Shigeto; A randomized controlled trial on the prevention of seroma after

partial or total mastectomy and axillary lymph node dissection; Breast Cancer; 1998; vol. 5 (no. 1); 67-69

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Japan
Study setting	Hospital and out-patient settings
Study dates	April 1996 to September 1996
Sources of funding	Not reported
Inclusion criteria	Women who underwent mastectomy with Level I and Level II ALND
Exclusion criteria	Not reported
Intervention(s)	The immediate exercise group started shoulder exercises on the first postoperative day. This included anterior flexion of the ipsilateral shoulder joint to 90 degrees on the first day, without massage of the ipsilateral axillary region or skin flap and flexion was extended to 180 degrees on the second day.
Comparator	The delayed exercise group's movement was limited to their usual daily activities during the first postoperative week. In the second week, the same exercise regime used in the immediate exercise group was started.
Outcome measures	Range of movement
Number of participants	116 patients

Duration of follow-up	One month
Loss to follow-up	Not reported
Methods of analysis	The degree of anteflexion was measured at the end of the second postoperative week, and a month after the operation. The corrected chi-square test and Mann-Whitney's U test were used for statistical analysis
Additional comments	• All participants were women. • Baseline characteristics were balanced between groups. • There was no reporting of exclusion criteria.

Study arms

Immediate exercise (N = 58)

Delayed exercise (N = 58)

Characteristics

Arm-level characteristics

Characteristic	Immediate exercise (N = 58)	Delayed exercise (N = 58)
Mean age (SD) Mean (SD)	51.9 (10.1)	53.8 (11.6)
Standard radical No of events	n = 0 ; % = 0	n = 1 ; % = 1.7
Modified radical No of events	n = 43 ; % = 74.1	n = 48 ; % = 82.8
Breast conserving No of events	n = 15 ; % = 25.9	n = 10 ; % = 17.2
Adjuvant radiation No of events	n = 15 ; % = 25.9	n = 10 ; % = 17.2
Patients with positive nodes No of events	n = 20 ; % = 34.5	n = 19 ; % = 32.8

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study did not report on randomisation, masking and blinding methodology. The study did not detail a specific analysis plan and as such, there are concerns about the reporting of outcomes.)*
Overall Directness	Directly applicable

Ammitzboll, 2020

Bibliographic Reference	Ammitzboll, Gunn; Andersen, Kenneth Geving; Bidstrup, Pernille Envold; Johansen, Christoffer; Lanng, Charlotte; Kroman, Niels; Zerahn, Bo; Hyldegaard, Ole; Andersen, Elisabeth Wreford; Dalton, Susanne Oksbjerg; Effect of progressive resistance training on persistent pain after axillary dissection in breast cancer: a randomized controlled trial.; Breast cancer research and treatment; 2020; vol. 179 (no. 1); 173-183

Study details

Secondary publication of another included study- see primary study for details	Complete reporting of results from two previous publications in 2019.
Other publications associated with this study included in review	Ammitzboll 2019a and 2019b
Trial registration number and/or trial name	LYCA study NCT02518477
Study type	Randomised controlled trial (RCT)
Study location	Denmark
Study setting	Out-patient settings

Study dates	Participants were recruited from August 2015 to January 2017. Data collection ended by January 2018
Sources of funding	The Danish Cancer Society Tryg Fonden
Inclusion criteria	Aged 18-75 Diagnosed with primary unilateral breast cancer Had no known distant metastases Understood spoken and written Danish Were physically and mentally able to participate in a group exercise regimen
Exclusion criteria	Not reported
Intervention(s)	Consisted of 2 phases, in phase 1 (3rd post-operative week), 20 weeks of twice-weekly supervised exercise in groups offered at set times in study hospitals and once weekly self-administered exercise at home or at a chosen facility. Phase 2 comprised 30 weeks of self-administered exercise 3 times a week.
Comparator	Consisted of 2 phases, in phase 1 (3rd post-operative week), 20 weeks of twice-weekly supervised exercise in groups offered at set times in study hospitals and once weekly self-administered exercise at home or at a chosen facility. Phase 2 comprised 30 weeks of self-administered exercise 3 times a week.
Outcome measures	Range of movement Upper limb muscle strength Pain intensity Neuropathic pain Incidence of lymphoedema Quality of life Patient adherence
Number of participants	158
Duration of follow-up	12 months
Loss to follow-up	Not reported
Methods of analysis	Sample size was calculated with α=0.05 and a power of 0.90, allowing a 15% loss to follow-up, the estimated sample size was 158 women. Baseline characteristics were presented separately for each group as

	numbers with proportions (%) and means with standard deviation (SD). All statistical analyses were performed on the groups. First, we examined the effect of the intervention on the intensity of pain outcomes using linear mixed models including an interaction between the visit and allocated group at 20 weeks and 12 months allowing for a different intervention effect at the two follow-up assessments. A possible correlation between measures from the same person was considered using an unstructured covariance matrix. The analyses were repeated with multiple data imputations to explore the effect of missing data. The imputations were carried out using chained equations on the three outcomes per person using normal regression models and including auxiliary variables in the model (age, BMI, surgery type and lymphoedema) for improved imputations. Furthermore, based on analyses of the complete data, the absolute effects for both groups were estimated separately and for both follow-ups. The result was graphed as estimated means and 95% confidence intervals (CI). Second, to examine the effect of the intervention according to clinically meaningful cut-off, NRS scores were categorised in three levels; “no” (0), “mild” [1–3] and “moderate/severe” [4–10], and NeuPPS in two categories; “no” (0) and “yes” [1-5], and multinomial logistic regression models on complete cases were used for analyses of the efect. To take the repeated measures into account, the variance was adjusted using the person as a cluster. Results were presented as conditional odds ratios (COR) with “mild” as a reference. The COR represents the odds of experiencing “no” versus “mild”, and “moderate/severe” versus “mild” of the outcome, and the odds are conditional on not being in another category than the two categories compared. For neuropathic pain, the COR represents the odds of reporting “yes” versus “no”. Based on the results, probabilities of each outcome were estimated and presented graphically with CI. All analyses were carried out using Stata version 14.2.
Additional comments	Baseline characteristics were balanced across study arms. There are two publications relevant to this trial; one reports on quality of life and the second reports on early outcomes (both published in 2019).

Study arms

Intervention (N = 82)

Control (N = 76)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 82)	Control (N = 76)
Mean age (SD) Mean (SD)	53 (10)	52 (10)

Characteristic	Intervention (N = 82)	Control (N = 76)
<25 No of events	n = 39 ; % = 48	n = 33 ; % = 43
> 25 - <=30 No of events	n = 22 ; % = 27	n = 26 ; % = 34
≤30 No of events	n = 21 ; % = 26	n = 17 ; % = 22
Lumpectomy No of events	n = 43	n = 41
Mastectomy No of events	n = 39 ; % = 48	n = 35 ; % = 46
Adjuvant No of events	n = 48 ; % = 59	n = 45 ; % = 59
Neoadjuvant No of events	n = 25 ; % = 30	n = 21 ; % = 28
Hormone treatment No of events	n = 64 ; % = 78	n = 41 ; % = 67

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation, allocation concealment and blinding . There may be differences baseline differences between participants and as such the intervention and outcome measures may be impacted.)*
Overall Directness	Directly applicable

Bendz, 2002

Bibliographic Reference	Bendz, I.; Fagevik Olsen, M.; Evaluation of immediate versus delayed shoulder exercises after breast cancer surgery including lymph node dissection - A randomised controlled trial; Breast; 2002; vol. 11 (no. 3); 241-248

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Sweden
Study setting	In hospital and out-patient settings
Study dates	November 1994 to December 1996
Sources of funding	Not reported
Inclusion criteria	Undergoing radical mastectomy or quadrantectomy with complete unilateral ALND
Exclusion criteria	Age >80 years Senility Bilateral surgery Women with diseases affecting the outcome
Intervention(s)	Early shoulder exercises: these participants received preoperatively a shoulder/arm exercise programme to be started on the first postoperative day. On the first and the second day, the exercise programme included intermittent hand contractions with a ball in the hand, elbow

	flexion/extension and hand pro- and supination in a supine position with the arm resting on a wedge pillow. From day 3 the exercises were increased to include arm elevation and abduction to 90 degrees with bent elbow in the sitting position. From day 8 also arm elevation and abduction to 90 degrees with straight elbows as well as internal rotation with the hand on the back trying to reach as high as possible were included. After 14 days, in the outpatient clinic, patients from both groups received an exercise programme including the following exercises in the sitting position: • arm elevation to 180 degrees with straight elbows, • internal rotation with the hand on the back trying to reach as high as possible, • abduction with the fingertips on the shoulders, • elbows together and apart with the hands behind the neck, • lift the right and left shoulder as high as possible with the arms elevated to 180 degrees. And the following exercises in the standing position: • arm extension with a stick held horizontally behind the back, • shoulders forward, backward, upwards and downwards, • shoulder circles with the fingertips on the shoulder, • arm elevation standing in a corner with the back of the hand gliding along the wall. Patients were told to perform each exercise 5 times in every set and repeat the session 3 times daily.
Comparator	Delayed exercises group: these participants received preoperative instructions to follow after the operation, they were advised to use the arm as much as comfortable but to avoid lifting and carrying heavier items and to avoid forced movements for 14 days. Postoperatively, no further information was given during their hospital stay. After 14 days, in the outpatient clinic, patients from both groups received an exercise programme including the following exercises in the sitting position: • arm elevation to 180 degrees with straight elbows, • internal rotation with the hand on the back trying to reach as high as possible, • abduction with the fingertips on the shoulders, • elbows together and apart with the hands behind the neck,

	• lift the right and left shoulder as high as possible with the arms elevated to 180 degrees. And the following exercises in the standing position: • arm extension with a stick held horizontally behind the back, • shoulders forward, backward, upwards and downwards, • shoulder circles with the fingertips on the shoulder, • arm elevation standing in a corner with the back of the hand gliding along the wall. Patients were told to perform each exercise 5 times in every set and repeat the session 3 times daily.
Outcome measures	Range of movement Pain intensity Incidence of lymphoedema
Number of participants	205
Duration of follow-up	2 years (with 2 week, 1 month, 6 months and 2 year appointments)
Loss to follow-up	49 participants • 5 died • 6 moved from the area • 3 had other diseases • 3 had surgery on the opposite side • 8 had personal reasons
Methods of analysis	Results are reported as mean and standard deviation (SD) or range. Differences within and between the groups were analysed with Pitman's non-parametric permutation test for groups and for matched pairs. Differences between proportions in each group were calculated using Fisher's exact test. Probability values less than 0.05 were considered significant.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Early shoulder exercises (N = 101)

Delayed shoulder exercises (N = 104)

Characteristics

Arm-level characteristics

Characteristic	Early shoulder exercises (N = 101)	Delayed shoulder exercises (N = 104)
Mean age (SD) Mean (SD)	58 (11)	58 (11)
Right No of events	n = 39 ; % = 38.6	n = 60 ; % = 57.7
Left No of events	n = 62 ; % = 61.4	n = 44 ; % = 42.3
Mastectomy only No of events	n = 31 ; % = 30.7	n = 22 ; % = 21.2
Mastectomy and radiotherapy No of events	n = 5 ; % = 5	n = 7 ; % = 6.7
Quadrant resection only No of events	n = 20 ; % = 19.8	n = 23 ; % = 22.1
Quadrant resection and radiotherapy No of events	n = 45 ; % = 44.6	n = 52 ; % = 50

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding was reported. There were some baseline differences between the groups and as such outcome measures and intervention administration may have been impacted.)*
Overall Directness	Directly applicable

Beurskens, 2007

Bibliographic Reference	Beurskens, C.H.G.; van Uden, C.J.T.; Strobbe, L.J.A.; Oostendorp, R.A.B.; Wobbes, T.; The efficacy of physiotherapy upon shoulder function following axillary dissection in breast cancer, a randomized controlled study; BMC Cancer; 2007; vol. 7; 166

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	ISRCTN31186536
Study type	Randomised controlled trial (RCT)
Study location	The Netherlands
Study setting	Hospital and out-patient settings
Study dates	July 2003 to January 2005
Sources of funding	Not reported
Inclusion criteria	Had surgery including ALND Age 18 years or older Patients with a VAS pain score of 1 or more Moderate shoulder disabilities in daily life
Exclusion criteria	Previous contralateral breast surgery
Intervention(s)	Patients assigned to the treatment group started physiotherapy two weeks following surgery in a private practice of their own choice. The research

	assistant contacted the individual physiotherapists (n = 15) who had agreed to comply with the treatment regime and supplied them with information regarding the project and treatment guidelines. This information consisted of: • guidelines with advice and exercises for arm/shoulder, posture correction, coordination exercises, exercises for muscular strength and improvement of general physical condition; • exercises to prevent lymphedema; • instruction for soft tissue massage of the surgical scar if required; • a form to report the content of the treatment sessions and a 3-point scale to indicate whether the number of treatment sessions was sufficient. The total number of treatments was nine (nine being usually covered by the healthcare insurance), once or twice weekly for the first three weeks, and thereafter once a fortnight or less. The total amount of sessions had to be given within three months. Patients were asked to perform home exercises for ten minutes each day.
Comparator	Participants received a leaflet flyer with advice and exercises for the arm/shoulder for the first weeks following surgery and had no further contact with a physiotherapist.
Outcome measures	Upper limb function (DASH score) Range of movement Pain intensity
Number of participants	30
Duration of follow-up	One to three months
Loss to follow-up	1 participant from the control group died.
Methods of analysis	Data was analysed using the SPSS version 12.1. Univariate analysis of variance was used to test differences in outcome variables between the control group and physiotherapy group. Baseline data were entered in the analysis as covariates. Level of significance was set at 0.05.
Additional comments	Baseline characteristics between both trial arms were balanced. The study included patients who already suffered from pain/shoulder disability.

Study arms

Intervention (N = 15)

Control (N = 15)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 15)	Control (N = 15)
Mean age (SD) Mean (SD)	53.7 (13)	55.4 (9.3)
Breast conserving and ALND No of events	n = 3 ; % = 20	n = 4 ; % = 26.7
Mastectomy and ALND No of events	n = 12 ; % = 75	n = 11 ; % = 73.3
None No of events	n = 3 ; % = 20	n = 0 ; % = 0
Radiotherapy No of events	n = 0	n = 2 ; % = 13.3
Chemotherapy No of events	n = 2 ; % = 13.3	n = 2 ; % = 13.3
Hormonal therapy No of events	n = 1 ; % = 6.7	n = 1 ; % = 6.7
Radiation and chemotherapy No of events	n = 6 ; % = 40	n = 8 ; % = 53.3
Chemotherapy and hormonal therapy No of events	n = 1 ; % = 6.7	n = 1 ; % = 6.7
Radiation and hormonal therapy No of events	n = 1 ; % = 6.7	n = 1 ; % = 6.7
Radiotherapy, chemotherpay and hormonal therapy No of events	n = 1 ; % = 6.7	n = 0 ; % = 0

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(Details on randomisation, allocation concealment and blinding were not reported.)*
Overall Directness	Partially applicable *(The study included participants with pre-existing shoulder disabilities in daily life VAS score 1-3)*

Box, 2002

Bibliographic Reference	Box, R.C.; Reul-Hirche, H.M.; Bullock-Saxton, J.E.; Furnival, C.M.; Shoulder movement after breast cancer surgery: Results of a randomised controlled study of postoperative physiotherapy; Breast Cancer Research and Treatment; 2002; vol. 75 (no. 1); 35-50

Study details

Secondary publication of another included study- see primary study for details	Primary study
Other publications associated with this study included in review	A secondary study published in 2002 explored the effects of physiotherapy to minimise lymphoedema
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Australia

Study setting	In hospital and outpatient settings
Study dates	July 1996 to July 1999
Sources of funding	Not reported
Inclusion criteria	Women with breast cancer Undergoing breast conserving surgery with complete local excision and axillary dissection Undergoing modified radical mastectomy
Exclusion criteria	Confused mental state or inability to independently follow exercise guidelines Permanent residence beyond a 50km radius of hospital and no monitoring in outpatients
Intervention(s)	Participants received a physiotherapy management care plan (PMCP) - includes preoperative assessment and explanation with inpatient and outpatient postoperative reviews
Comparator	The control group received an exercise instruction booklet.
Outcome measures	Range of movement Incidence of lymphoedema Patient adherence (Data not reported in an extractable format)
Number of participants	65 participants
Duration of follow-up	2 years
Loss to follow-up	Not reported
Methods of analysis	The nominal significance level is p=0.045, corresponding to an overall significance level of p<0.05. Frequency distributions were considered for all variables to detect outliers and categories with few responses that were suitable for collapsing. For variables that the data were identified as having normal distribution, mean responses for continuous outcome variables were compared over time in the study using ANOVA models in which differences across time, randomised groups, surgical procedure and dominant operation arm were considerd. Categorical outcome variables were similarly modelled using logistic and log-linear modelling techniques were two or more than two categories were involved, respectively. The data for other variables not meeting the criteria for normal distribution were analysed using non-parametric tests. The recovery of shoulder range of motion was examined using a number of multivariate repeated measureANOVA models. The recovery of functional status was analysing using the MULTILOG procedure outlined in the SUDAAN statistical package to implement an ordinal logistic regression model within a genearlised estimating equations framework, accounting for the repeated scores.

Additional comments	Baseline characteristics were balanced between participants.

Study arms

Intervention (N = 32)

Control (N = 33)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 32)	Control (N = 33)
Mean age (SD) Mean (SD)	53.03 (9.49)	59 (10.95)
BMI (kg/m2) Median (IQR)	24.3 (19.2 to 35.8)	27.2 (19.2 to 48.7)
Complete local excision and axillary dissection No of events	% = 46.9	% = 51.5
Modified radical mastectomy No of events	% = 53.1	% = 48.5
Radiotherapy No of events	% = 65.6	% = 48.5
Chemotherapy No of events	% = 43.8	% = 21.2
Hormone therapy No of events	% = 46.9	% = 57.6

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer

Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Bruce, 2022

Bibliographic Reference	Bruce, J.; Mazuquin, B.; Mistry, P.; Rees, S.; Canaway, A.; Hossain, A.; Williamson, E.; Padfield, E.J.; Lall, R.; Richmond, H.; Chowdhury, L.; Lait, C.; Petrou, S.; Booth, K.; Lamb, S.E.; Vidya, R.; Thompson, A.M.; Exercise to prevent shoulder problems after breast cancer surgery: The PROSPER RCT; Health Technology Assessment; 2022; vol. 26 (no. 15)

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Bruce 2018 - study protocol Bruce 2021 - secondary publication
Trial registration number and/or trial name	PROSPER Trial ISRCTN35358984
Study type	Randomised controlled trial (RCT)
Study location	United Kingdom
Study setting	Community
Study dates	1 March 2015 to 14 March 2020
Sources of funding	National Institute for Health Research Health Technology Assessment program

Inclusion criteria	Women >18 years Histologically confirmed or non-invasive primary breast cancer scheduled for surgery Considered high risk of developing shoulder problems after surgery
Exclusion criteria	Psychiatric or cognitive disorders Bilateral surgery Elective reconstructive surgery at the same time as the initial breast cancer surgery Males Detectable metastatic disease
Intervention(s)	Best practice usual care in addition to a physiotherapy-led exercise programme incorporating behavioural strategies. The intervention package involved different phases to encourage early restricted movement, progression of exercises to incorporate range of motion and strengthening, followed by a maintenance phase to ensure that flexibility and strength are maintained over time.
Comparator	Best practice usual care
Outcome measures	Upper limb function (DASH) Pain Neuropathic pain Incidence of lymphoedema Quality of life Healthcare resource use Patient adherence
Number of participants	392 participants
Duration of follow-up	12 months
Loss to follow-up	Control: 32 Intervention: 31
Methods of analysis	Statistical analyses were carried out using Stata® version 15 (StataCorp LP, College Station, TX, USA). All statistical tests were two-sided and performed at the 5% significance level. Two levels of analysis: using intention to treat (ITT), as per CONSORT guidelines,32 and complier-average causal effect (CACE) were completed. PROSPER, defined ‘complete’ compliance with the intervention as three or more sessions with

	the physiotherapist. This was the specified minimum number of recommended contacts that would ensure that all elements of the exercise programme were introduced and progressed. Non-compliance was defined as none or fewer than three physiotherapy sessions. All baseline demographic and pre-randomisation clinical measures were summarised by treatment allocation. Continuous data were summarised using mean, SD, median and range values. Categorical data were summarised by number and proportion (%) by treatment group. For both types of data, CIs were also specified. The primary analysis compared the DASH score at 12 months between the control and the exercise intervention. The clustering effect was assessed prior to data analysis and was found to be negligible. For this reason, the primary outcome was assessed using ordinary linear regression. In each case, the mean DASH change score from baseline to 6 and 12 months respectively, were summarised by treatment group and for differences between treatment groups using unadjusted and adjusted estimates. PROSPER adjusted for baseline scores, age, type of breast surgery (BCS vs. mastectomy), type of axillary surgery (ANC vs. SNLB), radiotherapy (yes/no) and chemotherapy (yes/no). For the primary analyses, a post hoc sensitivity analysis was undertaken to assess the impact of adjusting for age only at baseline, given that participants had not completed adjuvant therapy on recruitment. Mean changes and 95% CIs were plotted graphically to assess change over 12 months
Additional comments	Baseline characteristics were balances between trial arms. The trial excluded males with cancer.

Study arms

Intervention (N = 196)

Control (N = 196)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 196)	Control (N = 196)
Mean age (SD) Mean (SD)	58.4 (12.1)	57.9 (11.7)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Low *(The study reported details on randomisation, blinding and allocation concealment.)*
Overall Directness	Directly applicable

Cantarero-Villanueva, 2012

Bibliographic Reference	Cantarero-Villanueva, I.; Fernandez-Lao, C.; Fernandez-de-las-Penas, C.; Lopez-Barajas, I.B.; Del-Moral-Avila, R.; de la-Llave-Rincon, A.I.; Arroyo-Morales, M.; Effectiveness of Water Physical Therapy on Pain, Pressure Pain Sensitivity, and Myofascial Trigger Points in Breast Cancer Survivors: A Randomized, Controlled Clinical Trial; Pain Medicine (United States); 2012; vol. 13 (no. 11); 1509-1519

Study details

Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Spain
Study setting	In hospital and outpatient settings
Study dates	June 2010 to September 2011
Sources of funding	• Health Institute Carlos III • PN I+D+I

	• Andalusian Health Service
Inclusion criteria	Women with breast cancer Mastectomy or simple quadrantectomy with posterior breast reconstruction Between 25 - 65 years Finished adjuvant therapy, except hormone therapy, 3 months before the start of the study Have neck and shoulder pain that began after breast cancer surgery
Exclusion criteria	Receiving chemotherapy or radiotherapy at the time of the study Suffer from orthopaedic disease that hinders them following the water program Had uncontrolled hypertension Presence of lymphoedema Recurrent cancer Previous diagnosis of fibromyalgia
Intervention(s)	Water exercise program. The WATER exercise group trained in a warm pool (32°C), 3 times/week over 8 consecutive weeks (total number of sessions: 24). This study used a deep water pool frequently used for swimming (water temperature: 28–31°C; depth: 1.40 m in the lowest part and 1.80 m in the deepest part). All participants were immersed in water up to the neck. Each 1-hour session included a 10-minute warm-up consisting of slow aerobic, mobility, and stretching exercise; 35 minutes of aerobic, low-intensity endurance, and core stability training; and a 15-minute cool-down period including stretching and relaxation exercises focusing on the neck/ shoulder region. The intensity of the training was established following the recommendations of the American College of Sports Medicine and the American Heart Association. Participants used the “Borg Rating of Perceived Exertion Scale” for rating their fatigue during the exercise. Progression in the aerobic training was performed throughout the 8 weeks by gradually increasing the intensity and the duration. The program was supervised by two physical therapists with clinical experience in the management of patients with different cancer conditions, and there were 10–12 participants per group. Progression was individualized by a physical therapist with a rate of 4–5 participants for one therapist.
Comparator	Usual care treatment included a document relating to nutrition, lifestyle behaviours and exercise.
Outcome measures	Pain intensity
Number of participants	66 participants

Duration of follow-up	8 weeks
Methods of analysis	Statistical analyses were performed using SPSS statistical software, version 17.0 (SPSS, Inc., Chicago, IL, USA), and were conducted according to intention-to-treat analysis principle. Chi-square tests and Student's t-tests were used to examine the differences in sociodemographic, medical and clinical features, and PPT levels between the water and control groups. A 2x2 mixed-model repeated-measure analysis of variance (ANOVA) with time (pre- and post-intervention) as the within-subject variable and intervention (water-control) as the between-subjects variable was used to examine the effects of the intervention on neck and shoulder/axillary pain. A 2x3 mixed-model repeated-measure ANOVA with time (pre- and post-intervention) and side (affected or unaffected) as within-subject factors and intervention (water-control) as a between-subjects factor was used to analyse differences in PPT. Separate ANOVAs were done with each outcome as the dependent variable. The main hypothesis of interest was the groupxtime interaction. Intergroup effect sizes were calculated according to Cohen's d statistic. An effect size <0.2 reflects a negligible difference, between 0.2 and 0.5 a small difference, between 0.5 and 0.8 a moderate difference, and >0.8 a large difference. A P value less than 0.05 was considered statistically significant
Additional comments	Baseline characteristics were balanced between study arms. Study recruited participants with pre-existing shoulder pain.

Study arms

Water therapy (N = 33)

Control (N = 33)

Characteristics

Arm-level characteristics

Characteristic	Water therapy (N = 33)	Control (N = 33)
Mean age (SD) Mean (SD)	48 (8)	47 (9)
Quadrantectomy No of events	n = 22 ; % = 67	n = 21 ; % = 64
Mastectomy No of events	n = 11 ; % = 33	n = 12 ; % = 36

Characteristic	Water therapy (N = 33)	Control (N = 33)
Radiation No of events	n = 1 ; % = 3	n = 1 ; % = 3
Chemotherapy No of events	n = 2 ; % = 7	n = 1 ; % = 3
Radiation and chemotherapy No of events	n = 30 ; % = 90	n = 31 ; % = 94
Hormone therapy No of events	n = 5 ; % = 15	n = 4 ; % = 12

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation but not blinding and allocation concealment. There were also differences in patient adherence to the intervention which were not adjusted for neither was physical activity performed controlled between participants.)*
Overall Directness	Directly applicable

Charati, 2022

Bibliographic Reference	Charati, F.G.; Shojaee, L.; Haghighat, S.; Esmaeili, R.; Madani, Z.; Charati, J.Y.; Hosseini, S.H.; Shafipour, V.; Motor Exercises Effect on Improving Shoulders Functioning, Functional Ability, Quality of Life, Depression and Anxiety For Women With Breast Cancer; Clinical Breast Cancer; 2022

Study details

Secondary publication of another	Not applicable

included study- see primary study for details	
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	IRCT20200228046637N1
Study type	Randomised controlled trial (RCT)
Study location	Iran
Study setting	Hospital and out-patient settings
Study dates	October 2019 to May 2020
Sources of funding	Not reported
Inclusion criteria	Women >18 years Women with non-metastatic, non-menopausal breast cancer Past 4 weeks since chemotherapy treatment No experience in psychotherapy No drug addiction No heart or respiratory diseases No history of regular exercise within 1 year of the study Surgery on one or both breasts Score of over 11 on HADS questionnaire
Exclusion criteria	Physical incapability to perform intervention due to treatment courses Inability to walk or stand during intervention Pregnancy
Intervention(s)	Motor exercises for five weeks
Comparator	Usual care
Outcome measures	Range of movement

	Quality of life (only 1 score was reported for each measure: EORTC QOL-C30 and QLQ-BR23 but it was unclear whether higher or lower scores meant better quality of life)
Number of participants	70 participants
Duration of follow-up	5 weeks
Loss to follow-up	Not reported
Methods of analysis	Data analysis was carried out by using SPSS v3.24 software, with descriptive statistics methods consisting of mean and standard deviation for quantitative variables. A frequency table was used for qualitative variables. The T-test and Chi-Square were used for demographic information comparison in both arms the t-hotelling model for a comparison of the effects of anxiety and depression, and generalised linear models for comparison of effects of quality of life.
Additional comments	Baseline characteristics were balanced between both arms.

Study arms

Intervention (N = 35)

Control (N = 35)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 35)	Control (N = 35)
Mean age (SD) Mean (SD)	38.14 (10.7)	42.63 (8.11)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not reported details on randomisation, blinding and allocation concealment.)*

Characteristic	Intervention (N = 35)	Control (N = 35)
Overall Directness	Directly applicable	

Chen, 1999

Bibliographic Reference	Chen, S.C.; Chen, M.F.; Timing of shoulder exercise after modified radical mastectomy: a prospective study; Changgeng yi xue za zhi / Changgeng ji nian yi yuan = Chang Gung medical journal / Chang Gung Memorial Hospital; 1999; vol. 22 (no. 1); 37-43

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	In hospital and out-patient settings
Study dates	January 1994 to December 1995
Sources of funding	Not reported
Inclusion criteria	Undergoing modified radical mastectomy
Exclusion criteria	Previous axillary operation or radiotherapy Bilateral breast cancer

	Persistent haematoma Serious infection of surgical wound
Intervention(s)	On the first day after operation and on each additional day, all the patients performed the following lower arm exercises four times daily: a hand squeezing exercise, and elevation of the forearm not beyond 40°. Patients in the early group, started upper arm exercises on the third post-operative day as described below, gradually increasing the range of motion (ROM) until the patient experienced the painful shoulder.
Comparator	Patients in the later group patients started the same exercises on the sixth post-operative day and patients in the delayed group did not perform any upper arm exercises until after the drains were removed. The active and active-assisted exercise was done under the supervision of a nurse with instructions. The nurse measured the shoulder function (abduction, anteflexion, exo-rotation) of each patient.
Outcome measures	Range of movement
Number of participants	344 participants
Duration of follow-up	Not reported
Loss to follow-up	Not reported
Methods of analysis	To analyse axillary drainage, a t-test was used if the normal distribution was apparent. Univariate analysis of various exercise groups was performed using ANOVA. A significance of 0.05 was chosen.
Additional comments	Baseline characteristics were balanced. Details on follow-up and missing data were not reported.

Study arms

Early (N = 116)

Later (N = 115)

Delayed (N = 113)

Characteristics

Arm-level characteristics

Characteristic	Early (N = 116)	Later (N = 115)	Delayed (N = 113)
Mean age (SD) Mean (SD)	50.9 (13.6)	48.3 (10.6)	47.9 (11.2)
BMI Mean (SD)	24.2 (3.5)	24.9 (4.1)	24.4 (3.8)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding were reported. There were some baseline differences between the groups and as such outcome measures and intervention administration may have been impacted.)*
Overall Directness	Partially applicable

Cinar, 2008

Bibliographic Reference	Cinar, N.; Seckin, U.; Keskin, D.; Bodur, H.; Bozkurt, B.; Cengiz, O.; The effectiveness of early rehabilitation in patients with modified radical mastectomy; Cancer Nursing; 2008; vol. 31 (no. 2); 160-165

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications	Not applicable

associated with this study included in review	
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	In hospital and out-patient settings
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Undergoing modified radical mastectomy
Intervention(s)	In the treatment group, the shoulder was positioned at 65 degrees flexion, 45 degrees to 65 degrees abduction, and 65 degrees internal rotation on a wedge pillow on the first postoperative day and the exercise scheme prescribed active hand and elbow ROM exercises under the supervision of a physiotherapist. On the second postoperative day, isometric hand and forearm exercises were started. On the third and fourth days, the exercises included active assistive and active flexion, abduction, and internal and external rotation ROM exercises of the shoulder joint. In the following days, passive stretching exercises were performed. When the drains were removed, the patients in TG received individual 15 sessions of a physiotherapy program in physical medicine and rehabilitation department, including pendulum, wall climbing, overhead pulley, horizontal abduction, posture, wand, dorsal strengthening, and stretching exercises for levator scapula. The patients performed the exercises at home in the following 8 weeks
Comparator	The home exercises group received a form to perform the exercises by themselves after removal of the drains. Each exercise was taught by a physiotherapist until the exercise was performed properly. Detailed forms showing and explaining the exercises were given to the home exercises group.
Outcome measures	Range of movement (study reported SD as 0.00 for shoulder internal and external rotation at 3 months; this means there was no variability and the mean difference could not be estimated for these 2 outcomes at 3 months) Incidence of lymphoedema
Number of participants	57 participants
Duration of follow-up	6 months
Loss to follow-up	Not reported

Methods of analysis	All analyses were performed using the SPSS version 11.5. The demographic and clinical parameters of the patients were evaluated by using descriptive statistics. Fisher exact test was used for categorical comparisons. Student t-test was used to compare baseline values between the groups. Pearson and Spearman correlation tests were performed to evaluate the differences between baseline and follow-up evaluations for each group. Repeated measures of analysis of variance (1- and 2-way) tests were performed to evaluate whether the varied measurements were depending on time within groups; P<0.05 was considered as statistically significant
Additional comments	Baseline characteristics between both arms were balanced. Study did not report on exclusion criteria

Study arms

Treatment (N = 27)

Home exercise (N = 30)

Characteristics

Arm-level characteristics

Characteristic	Treatment (N = 27)	Home exercise (N = 30)
Mean age (SD) Mean (SD)	52.6 (12.2)	51.1 (*empty data*)
BMI Median (IQR)	28.7 (24 to 76)	27.72 (23.1 to 32.8)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*

Overall Directness	Directly applicable

da Silveira, 2020

Bibliographic Reference	da Silveira, D.S.P.; dos Santos, M.J.; da Silva, E.T.; Sarri, A.J.; das Neves, L.M.S.; Guirro, E.C.D.O.; Proprioceptive neuromuscular facilitation in the functionality and lymphatic circulation of the upper limb of women undergoing breast cancer treatment; Clinical Biomechanics; 2020; vol. 80; 105158

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Brazil
Study setting	In hospital and out-patient settings
Study dates	Not reported
Sources of funding	Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior Brasil (CAPES)
Inclusion criteria	Women who had surgical treatment of breast cancer combined with ALND and SLNB
Exclusion criteria	Receiving chemotherapy or radiotherapy at the time of the study

	Presence of lymphoedema Muscle tendinous lesions and/or joint injuries in the affected limb Skin disorders Diabetes Uncontrolled circulatory disorders Submitted to bilateral axillary emptying Had a diagnosis of metastasis in the upper limb during pregnancy
Intervention(s)	The muscle training protocol consisted of proprioceptive neuro-muscular facilitation (PNF) exercises, in which the movement was manually resisted by the researcher on the upper limb of surgery side. Proprioceptive neuromuscular facilitation was performed with the volunteer lying in a supine position, and hip joint in flexion of 30° with the lower limbs supported in semiflexion, the technique of proprioceptive neuromuscular facilitation was applied involving the diagonals of flexion-abduction-external rotation and extension-adduction-internal rotation maintaining extension of elbows, associated with a verbal command, aiming to stimulate mechanisms of contraction, muscle relaxation, and stretching in the upper limb of surgery side. The therapeutic exercises of proprioceptive neuromuscular facilitation were applied with isolated or combined movements, with three sets of ten repetitions of each movement, finishing the sequence of movements with stretching. The intervention was applied three times a week, for four weeks, aiming at stretching the adjacent muscles of the shoulder, as well as training and muscle strength gain.
Comparator	Standard breast cancer treatment - conventional rehabilitation, considered the standard for surgical treatment of breast cancer involving active kinesiotherapy in active and active-assisted group, strengthening and stretching of the antero-internal shoulder chain
Outcome measures	Range of movement
Number of participants	32 participants
Duration of follow-up	4 weeks
Loss to follow-up	None
Methods of analysis	Initially, the quantitative variables were compared between the study groups, and the student t-test was applied to independent samples, the data show variance and normal distribution. Fisher's Exact Test was applied to compare the qualitative variables between the study groups, a test that aims to verify an association between two qualitative variables. For comparison between the variables between the time periods of each group and between the groups for each time, the linear model of mixed-effects (random and fixed effects) was used. The following covariates of the mixed model were considered as covariates: age, BMI (body mass index), type of surgery, and level of emptying. This methodology is used in

	data analysis, where the responses of the same individual are grouped, and the assumption of independence between observations in the same group is not adequate. The effects estimated by the mixed model showed that the factors that influenced most of the variables were time, surgical side and group, side and time interaction. The analyses were performed in the statistical software SAS 9.4, and the graphs were constructed in the statistical software R 3.6.1. The significance level α = 0.05 was fixed for all analyses.
Additional comments	Baseline characteristics were balanced between both treatment arms. No participants were lost at follow-up.

Study arms

Intervention (N = 20)

Control group (N = 12)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 20)	Control group (N = 12)
Mean age (SD) Mean (SD)	52.2 (8.3)	48.4 (7.1)
BMI Mean (SD)	28.1 (4.4)	27.2 (4.9)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Dawson, 1989

Bibliographic Reference	Dawson, I.; Stam, L.; Heslinga, J.M.; Kalsbeek, H.L.; Effect of shoulder immobilization on wound seroma and shoulder dysfunction following modified radical mastectomy: A randomized prospective clinical trial; British Journal of Surgery; 1989; vol. 76 (no. 3); 311-312

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	The Netherlands

Study setting	Not reported
Study dates	March 1984 to October 1986
Sources of funding	Not reported
Inclusion criteria	Undergoing modified radical mastectomy
Exclusion criteria	Not reported
Intervention(s)	Started exercise on the first postoperative day
Comparator	The ipsilateral as immobilised in a sling for 5 days and then the same shoulder exercises were started.
Outcome measures	Range of movement
Number of participants	100 participants
Duration of follow-up	Not reported
Loss to follow-up	Not reported
Methods of analysis	The corrected chi-squared test and the student's two-tailed t-test were used for statistical analysis.
Additional comments	Baseline characteristics were balanced between treatment arms.

Study arms

Exercise group (N = 51)

Immobilized group (N = 49)

Characteristics

Arm-level characteristics

Characteristic	Exercise group (N = 51)	Immobilized group (N = 49)
Mean age (SD) Mean (SD)	64 (12)	65 (14)
Adjuvant irradiation No of events	n = 24 ; % = 47	n = 21 ; % = 43

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on allocation concealment and blinding.)*
Overall Directness	Directly applicable

de Almeida Rizzi, 2020

Bibliographic Reference	de Almeida Rizzi, S.K.L.; Haddad, C.A.S.; Giron, P.S.; Figueira, P.V.G.; Estevao, A.; Elias, S.; Nazario, A.C.P.; Facina, G.; Early Free Range-of-Motion Upper Limb Exercises After Mastectomy and Immediate Implant-Based Reconstruction Are Safe and Beneficial: A Randomized Trial; Annals of Surgical Oncology; 2020; vol. 27 (no. 12); 4750-4759

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number	NCT02480842

and/or trial name	
Study location	Brazil
Study setting	In hospital and outpatient settings
Study dates	July 2015 to April 2019
Sources of funding	Not reported
Inclusion criteria	Women with breast cancer Women >18 years Women who were scheduled for mastectomy and immediate reconstruction with breast implant
Exclusion criteria	Breast reconstruction with flaps Bilateral breast cancer People with cognitive, motor or neurologic alterations that would not allow exercise or assessments
Intervention(s)	The patients started physical therapy at the hospital the day following surgery after they had learned and performed six exercises (1–6 of protocol) and had undergone new physical therapy evaluations 7, 15, 30, 60, and 90 days after surgery, performed at the mastology outpatient clinic. At post operative day 15, two exercises were included (7 and 8 of the protocol), and the patients were randomised into two groups: (1) the ‘‘free-range group’’ (intervention), which was allowed to perform the protocol exercises and activities of daily living (ADLs) in free amplitude (i.e., at the limit of pain or the sensation of tightening of the scar). Free Exercises After Breast Reconstruction 1. Lateral neck stretch, each side held for 10 s 2. Posterior neck stretch, held for 10 s 3. Pectoral stretch, with fingers intertwined behind the body, held for 10 s 4. Upper limb pendulum exercises (back and forth), each side 10 times 5. Upper limb flexion with fingers interlaced in front of the body, 10 times. 6. Circular movements with the shoulder from front to back and the arms dropped along the body, 10 times. 7. Upper limbs flexion running fingers up the wall, held for 10 s 8. Upper limbs abduction running fingers up the wall, held for 10 s each side.
Comparator	The limited-range group (control-standard center protocol), which had range of motion maintenance limited to 90degrees for 15 more days (i.e., until the post operative day30), when free-range exercises also were allowed. The exercise protocol consisted of the following exercises:

	Free Exercises After Breast Reconstruction 1. Lateral neck stretch, each side held for 10 s 2. Posterior neck stretch, held for 10 s 3. Pectoral stretch, with fingers intertwined behind the body, held for 10 s 4. Upper limb pendulum exercises (back and forth), each side 10 times 5. Upper limb flexion with fingers interlaced in front of the body, 10 times. 6. Circular movements with the shoulder from front to back and the arms dropped along the body, 10 times. 7. Upper limbs flexion running fingers up the wall, held for 10 s 8. Upper limbs abduction running fingers up the wall, held for 10 s each side. In all the sessions, the proposed exercises were reviewed, and the patients were encouraged to perform them at home. As soon as the patients had been instructed to perform the exercises in free range, they also were allowed to perform ADLs without the restriction of movement.
Outcome measures	Upper limb function (DASH) Range of movement Pain intensity
Number of participants	62 participants
Duration of follow-up	90 days
Loss to follow-up	4 participants from free range group 3 participants from the limited range group
Methods of analysis	Sample size calculation was performed considering the outcomes, dehiscence and seroma, with the Chi square test using an alpha value of 0.05, a power of 0.8, and an effect size of 0.4. The results called for a sample of 61 participants to be divided into two groups. Statistical analysis was performed using the TIBCO Statistica Software Inc., Palo Alto, California (version 13.5). Sample distribution was evaluated for normality analysis using the Shapiro–Wilk test. The t-test was used to compare normal distribution data, and the Mann–Whitney test was used for non-normal distribution data. Categorical data differences between groups were assessed by Chi square or Fisher's exact test. Skewness and kurtosis tests were performed, and repeated measures analysis of variance (ANOVA) was used for differences over time and between groups during the follow-up period, with Tukey's post hoc test used to evaluate intragroup differences.
Additional comments	Baseline characteristics were balanced between both treatment arms.

Study arms

Free range exercises (N = 31)

Limited range exercises (N = 31)

Characteristics

Arm-level characteristics

Characteristic	Free range exercises (N = 31)	Limited range exercises (N = 31)
Mean age (SD) Mean (SD)	49.9 (10.11)	54.46 (10.68)
Arterial hypertension No of events	n = 4 ; % = 13.3	n = 11 ; % = 36.7
Diabetes No of events	n = 3 ; % = 10	n = 1 ; % = 3.3
Skin/nipple-sparing mastectomy No of events	n = 14 ; % = 46.7	n = 10 ; % = 33.3
Mastectomy No of events	n = 16 ; % = 53.3	n = 20 ; % = 66.7
Neoadjuvant chemotherapy No of events	n = 13 ; % = 43.3	n = 10 ; % = 33.3

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on allocation concealment and blinding.)*

Overall Directness	Directly applicable

De Groef, 2017

Bibliographic Reference	De Groef, A.; Van Kampen, M.; Vervloesem, N.; De Geyter, S.; Christiaens, M.-R.; Neven, P.; Vos, L.; De Vrieze, T.; Geraerts, I.; Devoogdt, N.; Myofascial techniques have no additional beneficial effects to a standard physical therapy programme for upper limb pain after breast cancer surgery: a randomized controlled trial; Clinical rehabilitation; 2017; vol. 31 (no. 12); 1625-1635

Study details

Secondary publication of another included study- see primary study for details	Primary study
Other publications associated with this study included in review	de Groef 2018 - physiotherapy following radiotherapy
Trial registration number and/or trial name	Trial register.nl (TC = 3610)
Study type	Randomised controlled trial (RCT)
Study location	Belgium
Study setting	In hospital and out-patient settings
Study dates	October 2012 to February 2015
Sources of funding	Agency for Innovation by Science nad Technology
Inclusion criteria	Undergoing radical mastectomy or quadrantectomy with complete unilateral ALND
Exclusion criteria	Not able to visit the hospital for therapeutic sessions and assessments

Intervention(s)	All participants attended an individual standard physical therapy programme immediately after surgery for four months (two sessions per week, reducing to once a week after the first two months) at the Department of Physical Medicine and Rehabilitation of the University Hospitals Leuven. The sessions were individual, lasted 30 minutes and consisted of different physical therapy modalities: (1) passive mobilisations, including angular mobilisations combined with tractions and translations of the shoulder to improve passive and active shoulder range of motion (ROM) (10 minutes on average); (2) stretching and transverse strain of pectoral muscles to improve muscle flexibility and passive and active shoulder ROM; (3) scar tissue massage by gripping scar tissue between thumb and index fingers and moving hands in opposite direction to improve flexibility of the scar(s) (together with stretching 10 minutes on average) and (4) exercise schemes to restore and improve muscle flexibility, endurance and strength, posture and movement control and active shoulder ROM. Schemes built steadily and incrementally in difficulty (10 minutes on average). Patients were asked to perform these exercises twice daily at home. Patients in the intervention group received, in addition to the standard physical therapy programme, myofascial therapy consisting of manual myofascial release techniques on (1) active myofascial trigger points at the upper limb region and (2) myofascial adhesions in the pectoral, axillary and cervical regions, diaphragm and scars. The pressure applied by the therapist hands proceed from the superficial to the deep layers of the myofascial tissues. Where a resistance was felt, the barrier was softly maintained until a release was felt. This approach was repeated until a soft end-feel was reached in every direction and layer. One session of myofascial therapy lasted 30 minutes with a frequency of once a week for two months (eight sessions).
Comparator	All participants attended an individual standard physical therapy programme immediately after surgery for four months (two sessions per week, reducing to once a week after the first two months) at the Department of Physical Medicine and Rehabilitation of the University Hospitals Leuven. The sessions were individual, lasted 30 minutes and consisted of different physical therapy modalities: (1) passive mobilisations, including angular mobilisations combined with tractions and translations of the shoulder to improve passive and active shoulder range of motion (ROM) (10 minutes on average); (2) stretching and transverse strain of pectoral muscles to improve muscle flexibility and passive and active shoulder ROM; (3) scar tissue massage by gripping scar tissue between thumb and index fingers and moving hands in opposite direction to improve flexibility of the scar(s) (together with stretching 10 minutes on average) and (4) exercise schemes to restore and improve muscle flexibility, endurance and strength, posture and movement control and active shoulder ROM. Schemes built steadily and incrementally in difficulty (10 minutes on average). Patients were asked to perform these exercises twice daily at home. Patients in the control group received a placebo treatment consisting of static bilateral hand placements at the upper body and arm. This session

	took 30 minutes as well, with a frequency of once a week for two months (eight sessions). Myofascial/placebo interventions were performed from two months up to four months post-surgery
Outcome measures	Upper limb function (DASH) Pain intensity Quality of life
Number of participants	147 participants
Duration of follow-up	12 months
Loss to follow-up	3 from intervention group
Methods of analysis	Data were analysed according to the intention to treat principle. The Fisher exact test was used to compare prevalence rates at baseline and 4, 9 and 12months post-surgery. The independent t-test was used to compare continuous outcome parameters at baseline. At 4, 9 and 12 months post-surgery, analysis of covariance (ANCOVA) were performed to correct for differences at baseline (i.e. two months after surgery). For the prevalence rates, relative risk reduction and its 95% confidence interval were calculated as measure of effect size. For continuous outcome parameters, the difference in means between groups and its 95% confidence interval is given as measure of effect size. Statistical significance was taken as P<0.05. All data were analysed with SPSS 22.0.><0.05. All data were analysed with SPSS v22.0.
Additional comments	Baseline characteristics were balanced between both study arms.

Study arms

Intervention (N = 72)

Control (N = 75)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 72)	Control (N = 75)
Mean age (SD) Mean (SD)	53.9 (11.5)	54.7 (11.9)

Characteristic	Intervention (N = 72)	Control (N = 75)
BMI Mean (SD)	25.8 (*empty data*)	24.8 (5.4)
Mastectomy No of events	n = 46 ; % = 64	n = 50 ; % = 67
Breast conserving No of events	n = 26 ; % = 36	n = 25 ; % = 33
Radiotherapy No of events	n = 72 ; % = 100	n = 75 ; % = 100
Chemotherapy No of events	n = 60 ; % = 83	n = 55 ; % = 73
Neo-adjuvant chemotherapy No of events	n = 29 ; % = 29	n = 21 ; % = 28
Target therapy No of events	n = 22 ; % = 31	n = 9 ; % = 12
Endocrine No of events	n = 57 ; % = 79	n = 62 ; % = 83

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Low *(The study reported details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

De Groef, 2018

Bibliographic Reference	De Groef, A.; Van Kampen, M.; Vervloesem, N.; Dieltjens, E.; Christiaens, M.-R.; Neven, P.; Vos, L.; De Vrieze, T.; Geraerts, I.; Devoogdt, N.; Effect of myofascial techniques for treatment of persistent arm pain after breast cancer treatment: randomized controlled trial; Clinical rehabilitation; 2018; vol. 32 (no. 4); 451-461

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	de Groef 2017, effect of physiotherapy on arm pain after breast cancer surgery
Trial registration number and/or trial name	Trial register.nl T=3610
Study location	Belgium
Study setting	In hospital and outpatient settings
Study dates	March 2013 to February 2015
Sources of funding	Agency for Innovation by Science and Technology
Inclusion criteria	Women treated for a primary breast cancer Radiation therapy was terminated more than 3 months ago More than 3 months of pain at the upper region (VAS score 40/100) in the past week Presence of myofascial dysfunction at the upper body region
Exclusion criteria	Detectable metastatic disease Not able to visit the hospital for therapeutic sessions and assessments Presence of shoulder pathologies for which surgical indications exist

Intervention(s)	All participants attended an individual standard physical therapy program of 12 weeks (week 1–8 two sessions per week, week 9–12 one session per week) at the Department of Physical Medicine and Rehabilitation of the University Hospital Leuven. The sessions were individual, lasted 30 minutes and consisted of different physical therapy modalities including: (1) passive mobilisations of the shoulder to improve passive and active shoulder range of motion (ROM); (2) stretching of pectoral muscles to improve muscle flexibility and passive and active shoulder ROM; (3) scar tissue massage to improve flexibility of the scar(s) and (4) exercise therapy to improve muscle flexibility, endurance and strength, posture and movement patterns and active shoulder ROM. Patients in the intervention group received myofascial therapy consisting of manual myofascial release techniques on (1) active myofascial trigger points at the upper body and (2) on myofascial adhesions in the pectoral, axillary and cervical region, diaphragm and scars. The pressure applied by the therapist's hands proceed from the superficial to the deep layers of the myofascial tissue. Where a resistance is felt, the barrier is softly maintained until a release is felt. This approach is repeated until a soft end-feel is reached in every direction and layer. One session of myofascial therapy lasted 30 minutes with a frequency of once a week for 12 weeks.
Comparator	All participants attended an individual standard physical therapy program of 12 weeks (week 1–8 two sessions per week, week 9–12 one session per week) at the Department of Physical Medicine and Rehabilitation of the University Hospital Leuven. The sessions were individual, lasted 30 minutes and consisted of different physical therapy modalities including: (1) passive mobilisations of the shoulder to improve passive and active shoulder range of motion (ROM); (2) stretching of pectoral muscles to improve muscle flexibility and passive and active shoulder ROM; (3) scar tissue massage to improve flexibility of the scar(s) and (4) exercise therapy to improve muscle flexibility, endurance and strength, posture and movement patterns and active shoulder ROM. Patients in the control group received a placebo treatment consisting of static bilateral hand placements. Therapist's hands were placed up and down the upper body and arm on the affected side and lasted for 10–15 seconds at one location. During this hand placements, the therapist made sure myofascial tissue were not moved and minimal pressure was given. In contrast, the myofascial techniques were more firm and dynamic. This session took 30 minutes as well, with a frequency of once a week for 12 weeks.
Outcome measures	Upper limb function (DASH) Pain intensity Quality of life
Number of participants	50 participants

Duration of follow-up	12 months
Loss to follow-up	2 from the intervention from
Methods of analysis	Data were analysed according to the intention-to-treat principle. First, overall treatment effects (i.e. change over time) were analysed by a multivariate linear model for repeated (longitudinal) measurements, using an unstructured covariance matrix. The primary end-point was change in pain intensity at short term (i.e. three months). As secondary analysis, long-term effects (i.e. 6 and 12months) were analysed. The effect size for continuous outcomes is given by the difference in mean change and its 95% confidence interval (CI). Second, Fisher's exact test was used to compare point prevalence rates at different points in time. For binary outcomes, relative risk reduction (%) and its 95% CI is given as measures of effect size. Statistical significance was taken as P<0.05. All data were analyzed with SPSS 22.0><0.05.
Additional comments	Baseline characteristics were balanced between study arms. Study included participants with arm sho/shoulder pain at baseline.

Study arms

Intervention (N = 25)

Control (N = 25)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 25)	Control (N = 25)
Mean age (SD) Mean (SD)	55.3 (7.5)	53.1 (7.5)
BMI Mean (SD)	28.5 (4.7)	25.4 (4.1)
Mastectomy No of events	n = 17 ; % = 68	n = 18 ; % = 72
Breast conserving No of events	n = 8 ; % = 32	n = 7 ; % = 28
Axillary level I-III	n = 25 ; % = 100	n = 25 ; % = 100

Characteristic	Intervention (N = 25)	Control (N = 25)
No of events		
Radiotherapy No of events	n = 18	n = 21 ; % = 84
Chemotherapy No of events	n = 17 ; % = 68	n = 15 ; % = 60
Neoadjuvant chemotherapy No of events	n = 2 ; % = 8	n = 3 ; % = 12
Target therapy No of events	n = 4 ; % = 16	n = 3 ; % = 12
Endocrine therapy No of events	n = 22 ; % = 88	n = 23 ; % = 92

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Low *(The study reported details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

De Rezende, 2006

Bibliographic Reference	De Rezende, L.F.; Franco, R.L.; De Rezende, M.F.; Beletti, P.O.; Morais, S.S.; Costa Gurgel, M.S.; Two exercise schemes in postoperative breast cancer: Comparison of effects on shoulder movement and lymphatic disturbance; Tumori; 2006; vol. 92 (no. 1); 55-61

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Brazil
Study setting	In hospital and outpatient settings
Study dates	March 23 2003 to July 13 2003
Sources of funding	Fundo de Apoio ao Ensino, Pesquisa e Extensao - State University of Campinas
Inclusion criteria	Preparing to undergo first surgery for invasive breast cancer
Exclusion criteria	Bilateral surgery Elective reconstructive surgery at the same time as the initial breast cancer surgery Women who showed a difference more than 2cm in circumference of arms before surgery Women who showed limitation of movement in the ipsilateral limb before surgery Women with a greater than 20 degree difference in flexion and abduction before surgery
Intervention(s)	The physiotherapy technique used was kinesiotherapy based on spontaneous exercises including movements for flexion, extension, abduction, adduction and internal and external rotation of the shoulder, either isolated or combined. The intervention group performed physiotherapy with a regiment of 19 exercises. All of the movements were performed 10 times and there was a 60-second interval between exercises.

Comparator	The free group performed exercises following biomechanical physiological movements of the shoulder including flexion, extension, abduction, adduction and internal and external rotation, either isolated or combined, without a previously defined sequence or number of repetitions - the exercises were being done to the rhythm fo the music.
Outcome measures	Range of movement Patient adherence
Number of participants	60 participants
Duration of follow-up	42 days
Loss to follow-up	Not reported
Methods of analysis	In the analysis of age, BMI, number of sampled lymph nodes, number of lymph nodes in a location and number of physiotherapy sessions, Student's t test and the Mann-Whitney test were used if a normal distribution was apparent. In the analysis of type of surgery, clinical stage, surgical stage and previous chemotherapy the Fisher exact test and the chi-square test were used. Univariate analysis of the exercises done (flexion, extension, abduction, adduction and external and internal rotation) was performed using MANOVA. MANOVA was the main instrument for the evaluation of the data, having been used in the verification of trends in the movements and comparison of times in each group. A significance level of 0.05 was chosen.
Additional comments	Baseline characteristics were balanced between treatment arms.

Study arms

Directed (N = 30)

Free (N = 30)

Characteristics

Arm-level characteristics

Characteristic	Directed (N = 30)	Free (N = 30)
Mean age (SD) Mean (SD)	54 (10.1)	55.4 (11.24)
BMI Mean (SD)	27.1 (3.7)	28.9 (6.8)

Characteristic	Directed (N = 30)	Free (N = 30)
Halsted No of events	n = 5 ; % = 16.7	n = 1 ; % = 3.3
Patey/Madden No of events	n = 16 ; % = 53.3	n = 21 ; % = 70
Quadrantectomy No of events	n = 9 ; % = 30	n = 8 ; % = 26.7
Previous chemotherapy No of events	n = 8 ; % = 26.7	n = 9 ; % = 30

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Feyzioglu, 2020

Bibliographic Reference	Feyzioglu, O.; Dincer, S.; Akan, A.; Algun, Z.C.; Is Xbox 360 Kinect-based virtual reality training as effective as standard physiotherapy in patients undergoing breast cancer surgery?; Supportive Care in Cancer; 2020; vol. 28 (no. 9); 4295-4303

Study details

Secondary publication of another included study- see primary study for details	Not applicable

Trial registration number and/or trial name	NCT03618433
Study location	Turkey
Study setting	In hospital and outpatient settings
Study dates	August 2018 to July 2019
Sources of funding	Not reported
Inclusion criteria	Had surgery including ALND Female aged 30 to 60 years In the second postoperative week Absence of hearing, visual or speech impairment
Exclusion criteria	Previous contralateral breast surgery Detectable metastatic disease Women who showed limitation of movement in the ipsilateral limb before surgery Presence of pacemaker, infection, open wounds or wound drains Mental disorders or cooperation issues
Intervention(s)	Participants used Kinect Sports I (darts, bowling, boxing) for the first 3 weeks of the 6-week treatment and in the last 3 weeks, Kinect Sports I (beach volleyball, table tennis) and Fruit Ninja were played for 30 min. Before starting each session, patients had a warm-up session for 5 min with Dance Central 3: Macarena. All the games required active upper extremity movements from the patients including shoulder flexion, abduction, extension, internal and external rotation, elbow flexion, extension, forearm supination, pronation, and wrist flexion and extension on the affected side. The treatment program consisted of playing Kinect video games for 35 min, scar tissue massage for 5 min, and passive shoulder joint mobilisation for 5 min. The treatment program was performed by an experienced physiotherapist.
Comparator	Standard physical therapy which involved breathing exercises, upper limb exercises, shoulder flexion and abduction, in the first postoperative 2 weeks. From the 2nd week onwards resistance training, as well as climbing exercises and strengthening exercises were added until the 8th week.
Outcome measures	Upper limb function (DASH) Range of movement Upper limb muscle strength

	Pain intensity
Number of participants	40 participants
Duration of follow-up	6 weeks
Loss to follow-up	1 participant in Kinect based rehabilitation group 3 participants in standard physical therapy group
Methods of analysis	The Shapiro–Wilk test was used to evaluate whether continuous variables were normally distributed. An independent t test was used for comparisons between the groups in terms of mean values. The paired t test was used for intragroup comparisons of pre-intervention and post-intervention mean values. General linear model repeated measures variance analysis (time × group interaction) was used to determine whether the differences between pre-intervention and post-intervention measurements varied by group. Cohen's d was used to calculate the effect size. Fisher's exact test was used for the analysis of categorical variables. A p value of 0.05 was considered to be significant in the analysis. An IBM SPSS 21 Statistics software package was used to analyse the study data
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Kinect-based rehabilitation group (N = 19)

Standardised physiotherapy group (N = 17)

Characteristics

Arm-level characteristics

Characteristic	Kinect-based rehabilitation group (N = 19)	Standardised physiotherapy group (N = 17)
% Female No of events	n = 20 ; % = 100	n = 20 ; % = 100
Mean age (SD) Mean (SD)	50.88 (8.53)	51 (7.06)
BMI Mean (SD)	30.06 (4.73)	28.97 (6.14)

Characteristic	Kinect-based rehabilitation group (N = 19)	Standardised physiotherapy group (N = 17)
Chemotherapy No of events	n = 4 ; % = 21	n = 2 ; % = 11.8
Radiotherapy No of events	n = 13 ; % = 68.4	n = 13 ; % = 76.5
Targeted and endocrine therapy No of events	n = 2 ; % = 10.5	n = 2 ; % = 11.8

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*
Overall Directness	Partially applicable *(Participants were included if they already had an existing range of movement limitation.)*

Flew, 1979

Bibliographic Reference	Flew, T.J.; Wound damage following radical mastectomy: The effect of restriction of shoulder movement; British Journal of Surgery; 1979; vol. 66 (no. 5); 302-305

Study details

Secondary publication of another included study- see	Not applicable

primary study for details	
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	United Kingdom
Study setting	In hospital and outpatient settings
Study dates	1973
Sources of funding	Not reported
Inclusion criteria	Undergoing modified radical mastectomy
Exclusion criteria	Not reported
Intervention(s)	Participants had the shoulder on the side of the operation held immobile by a triangular bandage postoperation and on the 7th-day arm movement exercises commenced under a physiotherapist's instruction
Comparator	Participants had their operation arm left unrestricted and arm movement exercises commenced under a physiotherapist's instruction
Outcome measures	Range of movement Incidence of lymphoedema
Number of participants	64 participants
Duration of follow-up	4 months
Loss to follow-up	Not reported
Methods of analysis	Not reported
Additional comments	Statistical analysis details not reported.

Study arms

Fixed shoulder postoperatively (N = 29)

Free shoulder postoperatively (N = 35)

Characteristics

Arm-level characteristics

Characteristic	Fixed shoulder postoperatively (N = 29)	Free shoulder postoperatively (N = 35)
% Female No of events	n = 29 ; % = 100	n = 35 ; % = 100
Age Mean (SD)	53.5 (12.25)	51.4 (11.25)
Postoperative radiotherapy No of events	n = 21 ; % = 72.4	n = 24 ; % = 68.6

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study did not report information on randomisation, allocation concealment and blinding as well as data analysis methods.)*
Overall Directness	Directly applicable

Giron, 2016

Bibliographic Reference	Giron, P.S.; Haddad, C.A.S.; Lopes de Almeida Rizzi, S.K.; Nazario, A.C.P.; Facina, G.; Effectiveness of acupuncture in rehabilitation of physical and functional disorders of women undergoing breast cancer surgery; Supportive Care in Cancer; 2016; vol. 24 (no. 6); 2491-2496

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study location	Brazil
Study setting	Outpatient settings
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Age 18 years or older Undergoing radical mastectomy or quadrantectomy with complete unilateral ALND Undergoing breast conserving surgery with complete local excision and axillary dissection
Exclusion criteria	Bilateral surgery Detectable metastatic disease Vascular and tactile sensitivity disorders Uncompensated diabetes mellitus type I and II

	Lower education level than 4 years]
Intervention(s)	Participants were treated with predefined standard kinesiotherapy, based on stretching of the neck muscles and scapular girdle, exercises for ROM and UL muscle strength, lasting 30 minutes followed by another 30 minutes of acupuncture applied at predefined points.
Comparator	—treated with predefined standard kinesiotherapy, based on stretching of the neck muscles and scapular girdle, exercises for ROM and UL muscle strength, lasting 30 minutes.
Outcome measures	Upper limb function (DASH) Range of movement Pain intensity
Number of participants	48 participants
Duration of follow-up	10 weeks
Loss to follow-up	Not reported
Methods of analysis	Statistical analysis was performed using Statistica 12. For groups, characterisation descriptive analysis (mean ± standard deviation) was used. The Shapiro-Wilk test was used to verify the normality of the variables and then the student t-test for independent groups. For the analysis of qualitative variables, the Pearson chi-square test and the Cochran Q test were performed. Regarding quantitative variables, ANOVA with repeated measures and post hoc Tukey's test were used.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Kinesiotherapy and acupuncture (N = 24)

Kinesiotherapy (N = 48)

Characteristics

Study-level characteristics

Characteristic	**Study (N = 48)**
% Female No of events	n = 48 ; % = 100

Characteristic	Study (N = 48)
Mean age (SD) Mean (SD)	53.7 (11.1)
BMI (kg/m) Mean (SD)	27.6 (6)
Hypertension No of events	n = 19 ; % = 39.5
Diabetes mellitus % No of events	n = 8 ; % = 16.6

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study did not report information on randomisation, allocation concealment and blinding.)*
Overall Directness	Partially applicable *(The study included participant with existing complains about upper limb region; VAS score =>3).*

Haines, 2010

Bibliographic Reference	Haines, T.P.; Sinnamon, P.; Wetzig, N.G.; Lehman, M.; Walpole, E.; Pratt, T.; Smith, A.; Multimodal exercise improves quality of life of women being treated for breast cancer, but at what cost? Randomized trial with economic evaluation; Breast Cancer Research and Treatment; 2010; vol. 124 (no. 1); 163-175

Study details

Secondary publication of	Not applicable

another included study- see primary study for details	
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Australia New Zealand Clinical Trials Registry: ACTRN12606000047594
Study type	Randomised controlled trial (RCT)
Study location	89 participants were randomised
Study setting	Community settings
Study dates	May 2006 to September 2007
Sources of funding	Princess Alexandra Hospital Cancer Collaborative Group.
Inclusion criteria	Women with breast cancer Women undergoing adjuvant therapy (radiation, chemotherapy and hormonal therapy)
Exclusion criteria	Severe cardiac disease Uncontrolled hypertension or orthopaedic injury precluding participation in exercise program
Intervention(s)	Participants were allocated to a home-based strength, balance and shoulder mobility and cardiovascular endurance programme. They received a multimedia instructional package along with equipment to facilitate the completion of the program. A range of exercise approaches was selected for physical improvements. The DVD included general safety precautions related to exercise, health advice related to the post-surgical period, a description of how to use the materials that had been provided with the program, a description of how to perform and progress each exercise in the program and a description of how to record data in logbooks related to adherence, adverse events and use of health care resources. Strategies of progression were recommended to make exercises harder every 2–4 weeks particularly if muscles were not feeling tired after completing the second set of exercises (for strength exercises), If the minimum number of repetitions within a set could not be completed, then the participants were recommended to try an easier version of that exercise. Participants were recommended to complete one set of each exercise, then complete a second set so that specific muscle groups could rest between sets.

Comparator	An active (sham intervention) control condition was employed consisting of flexibility and relaxation activities. Patients were provided with what looked like an exercise program with an equivalent amount of supporting material. The video material was of similar content to that in the intervention program (though the actual exercises described differed). There was no progression of activities performed in this condition
Outcome measures	Pain Quality of life Patient adherence (Data not reported in an extractable format) Cost/utilisation of health care services
Number of participants	89 participants
Duration of follow-up	12 months
Loss to follow-up	9 participants in the intervention group 7 participants in the control group
Methods of analysis	Health-related quality of life assessments gleaned from the EQ-5D instrument were converted to utility scores, and EORTC items were converted to subscale scores. Outcome measures were compared between groups using maximum likelihood Linear Mixed Models (LMMs). The analyses were conducted using raw data (not change scores). Group (intervention vs. control), assessment (baseline, 3, 6 and 12 month for EQ-5D and VAS only) and group-by-assessment interaction terms were entered as independent variables, such that a positive effect of the intervention at a specific assessment time point would be revealed by significant group-by-assessment interaction terms. Group, assessment, and the group-by-assessment interaction were treated as fixed effects, and participants were treated as random. The economic evaluation examined the cost per quality-adjusted life year (QALY) gained per patient provided with the intervention. Both utility-based and value-based cost-effectiveness analyses were undertaken using a societal perspective and a 6-month time horizon. QALY measurement used the EQ-5D utility component (Dolan conversion formula) for the utility-based cost-effectiveness analysis, and the EQ-5D VAS component for the value-based analysis. The health-benefits derived from the intervention were calculated using an area under the curve approach. Factors considered were: the LMM coefficients modelling the difference between groups (intervention minus control) in change the EQ-5D and EQ-5D VAS components from baseline to 3 month (A) and baseline to 6-month assessments (B) and a constant (C) representing the proportion of a year that a 3-month assessment time period represented (ie., 0.25). Costs of program provision and direct health costs were valued for each participant using market prices. Hospitalisation costs were calculated using Australian Diagnosis Related Grouping cost weights. Productivity costs through paid employment were calculated by multiplying loss or gain in work-time over the follow-up period relative to the baseline assessment using individual wage rates or the study median wage rate if the participant chose not to provide their individual wage rate. Productivity costs through unpaid employment were calculated by

	multiplying loss or gain in hours worked by others to complete tasks normally undertaken by the individual by the local market price for home help ($AUD 36 per hour in 2009). All costs were adjusted by the Australian mean quarterly consumer price index to convert cost data to a 2006 base year in $AUD (Australian currency). These costs were compared between groups using the Wilcoxon rank-sum test to account for the skewed distribution of these data. Uncertainty in the precision of point estimates for the primary utility-based and value-based cost-effectiveness ratios were examined using cost-effectiveness acceptability curve analysis where 2000 bootstrap replications of the dataset were undertaken and the resultant cost (Y axis) and effect (X axis) estimate pairs plotted on the cost-effectiveness plane. Confidence ellipses (95%) were plotted and amounts that stakeholders were willing to pay to gain one QALY for the intervention to become preferable with 95% probability, given the data, were identified. Sensitivity analyses were undertaken excluding data from seven extreme outlier cases (inter-quartile range greater than upper quartile or below lower quartile) for the total costs (per participant) data. The cost-effectiveness analyses were then re-run. These outliers were primarily driven by extreme hospitalization costs (2 patients $33,000 in hospitalisation costs alone), extreme pharmaceutical costs (3 patients $25,000 in pharmaceutical costs alone) and extreme productivity costs (2 patients increased productivity by $22,000 over 6 months from baseline assessment levels). Removal of these outliers favoured the intervention group in each case in terms of total costs. All the analyses were undertaken using Stata I/C version 9.0
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Intervention (N = 46)

Control (N = 43)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 46)	Control (N = 43)
Mean age (SD) Mean (SD)	55.9 (10.5)	54.2 (11.5)
Chemotherapy No of events	n = 15 ; % = 33	n = 17 ; % = 40

Characteristic	Intervention (N = 46)	Control (N = 43)
Radiotherapy No of events	n = 43 ; % = 93	n = 39 ; % = 91
Hormonal therapy No of events	n = 16 ; % = 35	n = 19 ; % = 44

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Harder, 2015

Bibliographic Reference	Harder, H.; Langridge, C.; Solis-Trapala, I.; Zammit, C.; Grant, M.; Rees, D.; Burkinshaw, L.; Jenkins, V.; Post-operative exercises after breast cancer surgery: Results of a RCT evaluating standard care versus standard care plus additional yoga exercise; European Journal of Integrative Medicine; 2015; vol. 7 (no. 3); 202-210

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated	Not applicable

with this study included in review	
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	United Kingdom
Study setting	In hospital and outpatient settings
Study dates	Between April 2011 and May 2013
Sources of funding	Not reported
Inclusion criteria	Women aged 18-80 Women with early breast cancer, scheduled for stage I-III axillary surgery
Exclusion criteria	Not reported
Intervention(s)	Participants were given a self-practise yoga DVD, that incorporated 16 postures that were used in a 10-week course of general yoga. Participants were shown how to use the DVD and follow the poses by the yoga teacher prior to participation. They were asked to use the DVD at least once per week for 10 weeks at level 1 and were given yoga materials to use during the intervention period.
Comparator	Standard care which comprised of post-operative exercise materials distributed by the hospital prior to surgery. The materials included written instructions for arm and shoulder mobilisation, leaflet, poster or DVD. Women allocated to this group were offered the yoga DVD after the last follow-up assessment.
Outcome measures	Upper limb function (QuickDASH) Pain intensity Quality of life Patient adherence
Number of participants	90 participants
Duration of follow-up	6 months
Loss to follow-up	6 from intervention group 6 from control group
Methods of analysis	Changes in scores were assessed using random effects regression models which extend standard regression analyses to account for the correlation

	amongst responses for each individual to yield valid inferences on the size of the regression coefficients. Changes in the single items of the FACT B+4 arm subscale were assessed using logistic regression models for the probability of reporting symptoms (i.e. the proportion of participants who reported 'somewhat', 'quite a bit' and 'very much' for the items) using a generalised estimating equations approach to account for the correlation amongst repeated observations. Standard linear regression models for the differences at 10 weeks in the secondary outcomes were used. In all the analysis, difference in response by participants characteristics were explored by adding age, adjuvant chemo (yes/no), previous yoga experience (yes/no), mastectomy (yes/no) and axillary surgery (axillary lymph node dissection or axillary clearance) as explanatory variables in the regression models. All analyses were conducted using the statistical software R.
Additional comments	Baseline characteristics between both groups were balanced.

Study arms

Yoga (N = 46)

Standard care (N = 46)

Characteristics

Arm-level characteristics

Characteristic	Yoga (N = 46)	Standard care (N = 46)
Mean age (SD) Mean (SD)	54.6 (10.9)	55.8 (11.6)
Wide local excision No of events	n = 32 ; % = 69.6	n = 29 ; % = 63
Mastectomy No of events	n = 14 ; % = 30.4	n = 17 ; % = 37
Sentinel lymph node biopsy No of events	n = 36 ; % = 78.3	n = 35 ; % = 76.1
Axillary lymph node clearance No of events	n = 10 ; % = 21.7	n = 11 ; % = 23.9
Chemotherapy	n = 24 ; % = 54.5	n = 19 ; % = 43.2

Characteristic	Yoga (N = 46)	Standard care (N = 46)
No of events		
Radiotherapy No of events	n = 29 ; % = 67.4	n = 29 ; % = 65.9
Hormone therapy No of events	n = 17 ; % = 53.1	n = 17 ; % = 51.5
No chemo/radiotherapy No of events	n = 6 ; % = 13	n = 7 ; % = 15.2
Unknown No of events	n = 2 ; % = 4.3	n = 2 ; % = 4.3

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study reported details of randomisation and blinding. Participants were aware of their allocation but were asked to not inform physiotherapists. The study did not assess baseline shoulder function and as such, there may have been group differences and they may not have been balanced. The measurement of the outcome may have been impacted by baseline exercise levels of participants as well as patient adherence to the yoga exercise programme.)*
Overall Directness	Directly applicable

Hayes, 2013

Bibliographic Reference	Hayes, Sandra C; Rye, Sheree; Disipio, Tracey; Yates, Patsy; Bashford, John; Pyke, Chris; Saunders, Christobel; Battistutta, Diana; Eakin, Elizabeth; Exercise for health: a randomized, controlled trial evaluating the impact of a pragmatic, translational exercise intervention on the quality of life, function and treatment-related side effects following breast cancer.; Breast cancer research and treatment; 2013; vol. 137 (no. 1); 175-86

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Exercise for Health trial (EfH): Registration number: 012606000233527
Study type	Randomised controlled trial (RCT)
Study location	Australia
Study setting	In hospital and outpatient settings
Study dates	Between October 2006 and June 2008
Sources of funding	National Breast Cancer Foundation
Inclusion criteria	Women aged 20-69 years Residing within 30 kilometre radius of Brisbane central business district
Exclusion criteria	Elective reconstructive surgery at the same time as the initial breast cancer surgery Women who were lactating Women with poor English
Intervention(s)	Women in the face-to-face and telephone groups began the 8-month exercise intervention at 6 weeks post-surgery. The intervention involved 16 scheduled sessions with a designated exercise physiologist, starting weekly and tapering to monthly contacts after 4 months.
Comparator	Women in the usual care group were given no advice outside that provided through usual care, which may have varied depending on the treating clinician and/or hospital and may have included encouragement for participating in physical activity during and beyond breast cancer. These women did not receive formal or regular advice about what to do and how to do it.

Outcome measures	Upper limb function (DASH) Upper limb muscle strength Neuropathic pain Incidence of lymphoedema Quality of life Patient adherence
Number of participants	194 participants
Duration of follow-up	12 months
Loss to follow-up	14 participants were lost to follow-up
Methods of analysis	Summary descriptive statistics for baseline characteristics included counts and percentages for categorical variables or means (standard deviations), alternatively medians (ranges), for continuously-scaled variables. Continuous outcomes were modelled using generalised estimating equations (GEE) to determine time (baseline, mid- and post-intervention) and 12 intervention group (FtF, Tel, UC) effects and the interaction between time and group. Means and 95% confidence intervals (CI) are reported for each estimate. GEEs were considered the most appropriate multivariate modelling technique, as unlike conventional repeated measures approaches, it is able to incorporate baseline data as well as all available data including those from participants with missing data over time. Intention-to-treat principles were applied to the analysis of data. No imputation was generated. All analysis was undertaken using SPSS version 18 software (SPSS inc, Chicago, IL).
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Face-to-face (N = 67)

Telephone (N = 67)

Usual care (N = 60)

Characteristics

Arm-level characteristics

Characteristic	Face-to-face (N = 67)	Telephone (N = 67)	Usual care (N = 60)
Mean age (SD) Mean (SD)	51.2 (8.8)	52.2 (8.6)	53.9 (7.7)
Lumpectomy No of events	n = 41 ; % = 31.2	n = 52 ; % = 77.6	n = 34 ; % = 56.7
Mastectomy No of events	n = 26 ; % = 38.8	n = 15 ; % = 22.4	n = 26 ; % = 43.3
Chemotherapy No of events	n = 41 ; % = 61.2	n = 52 ; % = 77.6	n = 34 ; % = 56.7
Hormone therapy No of events	n = 42 ; % = 62.7	n = 38 ; % = 56.7	n = 34 ; % = 56.7
Radiotherapy No of events	n = 26 ; % = 38.8	n = 26 ; % = 38.8	n = 23 ; % = 38.3

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details of randomisation, blinding and allocation concealment. Some participants withdrew after randomisation, however adjusted analyses were undertaken to account for any differences/imbalance.)*
Overall Directness	Directly applicable

Hwang, 2008

Bibliographic Reference	Hwang, J.H.; Chang, H.J.; Shim, Y.H.; Park, W.H.; Park, W.; Huh, S.J.; Yang, J.-H.; Effects of supervised exercise therapy in patients receiving radiotherapy for breast cancer; Yonsei Medical Journal; 2008; vol. 49 (no. 3); 443-450

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	South Korea
Study setting	Outpatient settings
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Women waiting for radiotherapy for breast cancer
Exclusion criteria	Women with concurrent major health problems that could affect their participation in an exercise program
Intervention(s)	Participants attended a supervised exercise program 3 times per week for 5 weeks. The 50-min program consisted of a 10-min warm-up, 30 min of exercise (including stretching exercises focused on the shoulders, aerobic exercise such as treadmill walking and bicycling, and strengthening exercise), and a 10-min cool-down (relaxation period). Heart rates were monitored throughout the class to ensure that patients were exercising at the target heart rate of 50 - 70% of the age-adjusted heart rate maximum.
Comparator	Participants were shown how to perform shoulder range of motion exercises and were encouraged to continue with normal activities.
Outcome measures	Range of movement (shoulder external rotation, internal rotation not reported in an extractable format) Pain intensity Quality of life

Number of participants	37 participants
Duration of follow-up	After completion of radiotherapy
Loss to follow-up	3 participants were lost to follow-up
Methods of analysis	Data were analysed using SPSS version 10.0 software (SPSS Inc., Chicago, IL, USA). The baseline characteristics of the 2 groups were compared using independent-samples t-tests. Data were analysed using analyses of covariance in which groups were compared according to follow-up data with baseline data as the covariate. P value < 0.05 was taken as significant

Study arms

Exercise (N = 17)

Control (N = 20)

Characteristics

Arm-level characteristics

Characteristic	Exercise (N = 17)	Control (N = 20)
Mean age (SD) Mean (SE)	46.3 (7.5)	46.3 (9.5)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details of randomisation, blinding and allocation concealment.)*
Overall Directness	Directly applicable

Ibrahim, 2017

Bibliographic Reference	Ibrahim, M.; Muanza, T.; Smirnow, N.; Sateren, W.; Fournier, B.; Kavan, P.; Palumbo, M.; Dalfen, R.; Dalzell, M.-A.; Time course of upper limb function and return-to-work post-radiotherapy in young adults with breast cancer: a pilot randomized control trial on effects of targeted exercise program; Journal of cancer survivorship : research and practice; 2017; vol. 11 (no. 6); 791-799

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Canada
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Hope & Cope The CURE Foundation The Jewish General Hospital Foundation & Weekend to End Breast Cancer
Inclusion criteria	Women with breast cancer Scheduled for post-operative adjuvant treatment
Exclusion criteria	Previous contralateral breast surgery Detectable metastatic disease Significant cardiac, pulmonary or metabolic co-morbidities Post-surgical capsulitis, tendonitis, or other shoulder inflammatory complications Post-surgical lymphoedema on the affected side

Intervention(s)	The intervention arm received a progressive program for developing and maintaining mobility, strength, and endurance of the upper limb for a total of 12 weeks. Each participant was provided with a one-on-one teaching session supervised by an exercise physiologist. Participants unable to train at the centre were provided with equipment and instructed on how to execute the program at home. Resistance intensity was individually tailored to personal fitness levels, but included an initial program for 6 weeks and progressed to a more advanced set of exercises for the remaining 6 weeks. The program included a minimum of 10-min cardiovascular exercise as a warm-up (e.g., NuStep, walking or stairs), followed by an upper body strength training and gentle endurance program, an upper limb stretching program, and light cool-down. Weight training resistance levels were determined for an 8–10 repetitions maximum for strength and 20 repetitions maximum for endurance training exercises. Participants were encouraged to perform the program 2–3 times/week, progressing gradually over the duration of the 12 weeks. Exercise intensity, attendance, and compliance were recorded weekly in a self-report log completed by the participants.
Comparator	The control group received standard care, which included advice on the benefits of an active lifestyle including exercise without a specific intervention. The patients were encouraged to maintain a healthy lifestyle, without restricting their physical activity and/or sport participation levels. Their exercise levels were recorded at the six time points.
Outcome measures	Upper limb function (DASH) Range of motion (shoulder flexion, abduction, external rotation, internal rotation not reported in an extractable format) Pain intensity
Number of participants	59 participants
Duration of follow-up	18 months
Loss to follow-up	Not reported
Methods of analysis	Data were analysed using JMP Software version 11.2. The chi-square test, ANOVA, and the non-parametric Wilcoxon tests were employed to test for statistical significance. A p value of <0.05 was considered significant. Missing data were not included in the analysis.
Additional comments	Baseline characteristics were balanced between the groups.

Study arms

Exercise (N = 29)

Control (N = 30)

Characteristics

Study-level characteristics

Characteristic	Study (N = 59)
Mean age (SD) Mean (SD)	39.2 (5)

Arm-level characteristics

Characteristic	Exercise (N = 29)	Control (N = 30)
Lumpectomy No of events	n = 24 ; % = 82.8	n = 27 ; % = 90
Mastectomy No of events	n = 7 ; % = 24.1	n = 4 ; % = 13.3
Chemotherapy No of events	n = 19 ; % = 65.52	n = 23 ; % = 76.67

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation, blinding and allocation concealment. There were some concerns regarding the participants in the control group who may have continued with regular physical activity and that may have impacted the outcomes as well as patient adherence to reporting in the logs. This was not adjusted for in the analysis.)*
Overall Directness	Directly applicable

Ibrahim, 2018

Bibliographic Reference	Ibrahim, M.; Muanza, T.; Smirnow, N.; Sateren, W.; Fournier, B.; Kavan, P.; Palumbo, M.; Dalfen, R.; Dalzell, M.-A.; A Pilot Randomized Controlled Trial on the Effects of a Progressive Exercise Program on the Range of Motion and Upper Extremity Grip Strength in Young Adults With Breast Cancer; Clinical Breast Cancer; 2018; vol. 18 (no. 1); e55-e64

Study details

Secondary publication of another included study- see primary study for details	Ibrahim 2017
Other publications associated with this study included in review	Ibrahim 2017
Sources of funding	

Study arms

Intervention (N = 29)

Control (N = 30)

Characteristics

Study-level characteristics

Characteristic	**Study (N =)**
Mean age (SD) Mean (SD)	39.2 (5)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation, blinding and allocation concealment. There were some concerns regarding the participants in the control group who may have continued with regular physical activity and that may have impacted the outcomes as well as patient adherence to reporting in the logs. This was not adjusted for in the analysis.)*
Overall Directness	Directly applicable

Jansen, 1990

Bibliographic Reference	Jansen, R.F.M.; Van Geel, A.N.; De Groot, H.G.W.; Rottier, A.B.; Olthuis, G.A.A.; Van Putten, W.L.J.; Immediate versus delayed shoulder exercises after axillary lymph node dissection; American Journal of Surgery; 1990; vol. 160 (no. 5); 481-484

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number	Not reported

and/or trial name	
Study type	Randomised controlled trial (RCT)
Study location	The Netherlands
Study setting	In hospital and outpatient settings
Study dates	Between March 1987 and April 1988
Sources of funding	Not reported
Inclusion criteria	Women undergoing primary surgical treatment of breast carcinoma
Exclusion criteria	Previous diseases or operations influencing ipsilateral axillary operations or radiotherapy Immediate postoperative iridium implantation and simultaneous bilateral axillary lymph node dissection
Intervention(s)	Participants were prescribed active shoulder exercises 1 day after the operation. Movements of the shoulder were performed actively once a day under the supervision of a physiotherapist. All spontaneous movements and use of the arm during the remaining part of the day were allowed, provided pain did not occur. Physiotherapeutic supervision was discontinued when shoulder function had returned to its preoperative level or when the patient was discharged. Physiotherapy at home was prescribed when anteflexion was restricted more than 20 degrees or exo-rotation was restricted more than 10 degrees.
Comparator	Participants were prescribed active shoulder exercises on the 8th day after the operation. Movements of the shoulder were performed actively once a day under the supervision of a physiotherapist. All spontaneous movements and use of the arm during the remaining part of the day were allowed, provided pain did not occur. Physiotherapeutic supervision was discontinued when shoulder function had returned to its preoperative level or when the patient was discharged. Physiotherapy at home was prescribed when anteflexion was restricted by more than 20 degrees or exo-rotation was restricted by more than 10 degrees.
Outcome measures	Range of movement Incidence of lymphoedema
Number of participants	144 participants
Duration of follow-up	6 months
Loss to follow-up	Not reported
Methods of analysis	For a graphical description, the means of the measurements at all time points were used, but these values were not used for testing purposes. The Wilcoxon signed-rank test was used to assess differences between both groups in the total volume of seroma and in the 6-month measurements of shoulder function.

Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Immediate shoulder exercises (N = 78)

Delayed shoulder exercises (N = 66)

Characteristics

Study-level characteristics

Characteristic	**Study (N =)**
Mean age (SD) Mean (SD)	59.2 (13.3)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	**Answer**
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding was reported.)*
Overall Directness	Directly applicable

Kilbreath, 2006

Bibliographic Reference	Kilbreath, S; Refshauge, K; Beith, J; Lee, MJ; Resistance and stretching shoulder exercises early following axillary surgery for breast cancer; Rehabilitation oncology; 2006; vol. 24 (no. 2); 9-14

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study location	Australia
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Impedimed
Inclusion criteria	Women who underwent surgery to the axilla for early breast cancer
Exclusion criteria	Infection or any comorbidity which may interfere with the test procedures
Intervention(s)	Participants received the same usual care as the control group as well as exercises aimed at increasing the range of motion at the shoulder and strengthening the shoulder muscles. Exercises were performed daily and supervised by a physiotherapist once a week.
Comparator	Participants received no additional care to that provided by the hospital. They were admitted on the day of surgery and discharged 2 to 7 days later. Women were not followed-up after discharge from hospital.
Outcome measures	Range of movement (Data not reported in an extractable format) Upper limb muscle strength (Data not reported in an extractable format) Pain (Data not reported in an extractable format) Incidence of lymphoedema Quality of life (Data not reported in an extractable format)
Number of participants	22 participants

Duration of follow-up	8 weeks
Loss to follow-up	Not reported
Methods of analysis	Descriptive statistics summarised the outcomes for each group. Data from the available assessment was substituted for the missing data. The results are presented as median and interquartile ranges unless otherwise indicated. Statistical analyses were performed using SPSS version 12.0 statistical software. Chi-square was used to compare the number of participants with >2cm interlimb difference. Between-group comparisons of quality of life, range, and strength measures were performed with Mann-Whitney U tests.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Exercise (N = 14)

Control (N = 8)

Characteristics

Arm-level characteristics

Characteristic	Exercise (N = 14)	Control (N = 8)
Mean age (SD) Mean (SD)	52.7 (14)	51.5 (10.2)
Mastectomy No of events	n = 8 ; % = 57.1	n = 4 ; % = 50
Wide local excision No of events	n = 6 ; % = 42.9	n = 4 ; % = 50
Axillary node dissection No of events	n = 7 ; % = 50	n = 3 ; % = 37.5
Sentinel node biopsy No of events	n = 7 ; % = 50	n = 5 ; % = 62.5
Radiotherapy No of events	n = 9 ; % = 64.3	n = 7 ; % = 87.5
Chemotherapy No of events	n = 7 ; % = 50	n = 6 ; % = 75

Characteristic	Exercise (N = 14)	Control (N = 8)
Hormone therapy No of events	n = 8 ; % = 57.1	n = 6 ; % = 75
Other planned therapy No of events	n = 1 ; % = 7.1	n = 0 ; % = 0

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported some detail on randomisation but non on allocation concealment and blinding.)*
Overall Directness	Directly applicable

Kilbreath, 2012

Bibliographic Reference	Kilbreath, S.L.; Refshauge, K.M.; Beith, J.M.; Ward, L.C.; Lee, M.; Simpson, J.M.; Hansen, R.; Upper limb progressive resistance training and stretching exercises following surgery for early breast cancer: A randomized controlled trial; Breast Cancer Research and Treatment; 2012; vol. 133 (no. 2); 667-676

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications	Not applicable

associated with this study included in review	
Trial registration number and/or trial name	Australian Clinical Trials Registry: ACTRN012606000050550
Study type	Randomised controlled trial (RCT)
Study location	Australia
Study setting	In hospital and outpatient settings.
Study dates	Not reported
Sources of funding	NSW Cancer Council National Breast Cancer Foundation
Exclusion criteria	Detectable metastatic disease Bilateral breast cancer History of lymphoedema Pre-existing arm impairments that would interfere with testing for exercises for the arm
Intervention(s)	Women attended a weekly supervised exercise session of resistance training and passive stretching for the shoulder muscles. They also were instructed in a home program of resistance training and stretching.
Comparator	Women in the control group were seen fortnightly to assess their arms for the presence of lymphedema. No exercise or advice was provided at these sessions. Women were referred to the breast nurse if lymphedema was identified who would then organize for the patient to be seen by an occupational therapist for, at minimum, fitting of a compression garment.
Outcome measures	Range of movement Upper limb muscle strength Incidence of lymphoedema Quality of life
Number of participants	160 participants
Duration of follow-up	6 months
Loss to follow-up	Not reported
Methods of analysis	Treatment group was coded to enable blinded analysis, which was by intention-to-treat for participants with complete data for each variable. The

	unadjusted mean change from baseline in arm and breast symptom scores as well as shoulder range of motion and strength on the affected side were compared between the two groups using the student's two-sample t test. Chi-square analysis was used to determine the effect of exercise on lymphoedema immediately following the intervention and at 6 months post-intervention. Mean and standard deviation are reported unless otherwise stated. IBM SPSS version 19 for Windows (IBM Corp. Somers, NY) was used and significance was set at P<0.05.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Exercise (N = 81)

Control (N = 79)

Characteristics

Arm-level characteristics

Characteristic	Exercise (N = 81)	Control (N = 79)
Mean age (SD) Mean (SD)	53.5 (12.1)	51.6 (11)
BMI Mean (SD)	26.2 (5.1)	26.5 (4.6)
Mastectomy No of events	n = 39 ; % = 48	n = 37 ; % = 47
Axillary node dissection No of events	n = 50 ; % = 62	n = 46 ; % = 58
Chemotherapy No of events	n = 55 ; % = 68	n = 59 ; % = 74
Radiotherapy No of events	n = 64 ; % = 79	n = 60 ; % = 76

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported some detail on randomisation but non on allocation concealment and blinding.)*
Overall Directness	Directly applicable

Kilgour, 2008

Bibliographic Reference	Kilgour, Robert D; Jones, David H; Keyserlingk, John R; Effectiveness of a self-administered, home-based exercise rehabilitation program for women following a modified radical mastectomy and axillary node dissection: a preliminary study.; Breast cancer research and treatment; 2008; vol. 109 (no. 2); 285-95

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)

Study location	Canada
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Ville Marie Oncology Foundation General Research Fund of Concordia University
Exclusion criteria	Sever heart disease Severe mental disorders History or presence of shoulder dysfunction Age >65 years
Intervention(s)	Participants assigned to the home-based exercise intervention followed their video home exercise programme and brochure. They followed an 11-day programme.
Comparator	Participants received all the usual standard information (written and verbal) that the typical patient would receive from medical centres.
Outcome measures	Range of movement (shoulder external rotation not reported in an extractable format) Upper limb muscle strength (Date not reported in an extractable format)
Number of participants	27 participants
Duration of follow-up	11 days post intervention
Loss to follow-up	4 participants from the home based exercise group 9 participants from the usual care group
Methods of analysis	Simple t-tests were used to describe group differences in age, weight, height, number of surgical incisions, the number of lymph nodes removed as well as the levels of perceived pain. Separate 2x2 general linear models with repeated measures were conducted for each outcome measure. The pre-surgical, baseline measures were used as a control variable so that each specific outcome measure was included as a covariate to adjust for individual variations. All analyses were conducted using SAS Version 9.1.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Home-based exercise (N = 16)

Usual care (N = 11)

Characteristics

Arm-level characteristics

Characteristic	Home-based exercise (N = 16)	Usual care (N = 11)
Mean age (SD) Mean (SD)	50.6 (9.3)	49.1 (5.7)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation, allocation concealment and blinding. There may have been differences in patient adherence as this data was not collected and may have impacted outcome measures in the intervention group.)*
Overall Directness	Directly applicable

Klein, 2021

Bibliographic Reference	Klein, I.; Kalichman, L.; Chen, N.; Susmallian, S.; A pilot study evaluating the effect of early physical therapy on pain and disabilities after breast cancer surgery: Prospective randomized control trail; Breast; 2021; vol. 59; 286-293

Study details

Secondary publication of another included study- see	Not applicable

primary study for details	
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	NCT03389204
Study type	Randomised controlled trial (RCT)
Study location	Israel
Study setting	In hospital and outpatient settings
Study dates	Between October 1 2018 and April 30 2019
Sources of funding	Not reported
Inclusion criteria	Women aged 18-85 Women who were diagnosed with breast cancer and referred to oncology surgery
Exclusion criteria	Breast reconstruction with flaps Presence of lymphoedema Previous diagnosis of fibromyalgia Cognitive disorders Chronic pain disorders Neurological disorders causing permanent disability Previous shoulder surgery or injuries causing limited range of motion, back and spinal morbidity Renal failure Ischaemic heart disease Radical mastectomies
Intervention(s)	Participants received physical therapy treatment that included therapeutic exercises and instructions for home exercise in the form of a booklet. Exercises were performed three times a day, with five repetitions of each exercise until maximum function and range of motion are restored without pain.

Comparator	The control group did not receive orientation to perform exercises and physical therapy. Participants received the guidance of a breast cancer nurse during hospitalisation, regarding pain, wound care, and instructions.
Outcome measures	Upper limb function (QuickDASH) Range of movement Pain intensity Incidence of lymphoedema
Number of participants	157 participants
Duration of follow-up	6 months
Loss to follow-up	1 participant from the intervention group 2 participants from the control group
Methods of analysis	Statistical analysis was performed using the SPSS statistical package, Version 21 (SPSS Inc, Chicago, IL, USA). The significance level was set at $p < 0.05$. The T-test was used to compare normally distributed parameters. The non-parametric Mann-Whitney rank-sum test for independent samples and Kruskal Wallis for several independent variables were applied for the testing difference between continuous parameters. Nominal variables were evaluated by the chi-squared test.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Intervention (N = 72)

Control (N = 85)

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 72)	Control (N = 85)
Mean age (SD) Mean (SD)	53.3 (12.7)	51.2 (13.1)
BMI	25 (4.7)	25 (4.7)

Characteristic	Intervention (N = 72)	Control (N = 85)
Mean (SD)		
Lumpectomy No of events	n = 4 ; % = 5.6	n = 15 ; % = 17.6
Lumpectomy and SLNB No of events	n = 23 ; % = 31.9	n = 16 ; % = 18.8
Lumpectomy and ALND No of events	n = 7 ; % = 9.7	n = 0 ; % = 0
Partial/modified mastectomy and SLNB No of events	n = 14 ; % = 19.4	n = 21 ; % = 24.7
Partial/modified mastectomy and ALND No of events	n = 1 ; % = 1.4	n = 4 ; % = 4.7
Partial/modified/bilateral mastectomy + reconstruction No of events	n = 23 ; % = 31.9	n = 29 ; % = 34.1
Neoadjuvant No of events	n = 17 ; % = 23.6	n = 18 ; % = 21.1
Adjuvant No of events	n = 33 ; % = 45.8	n = 27 ; % = 31.8
Radiation No of events	n = 51 ; % = 70.8	n = 45 ; % = 52.9
Intraoperative radiation therapy No of events	n = 8	*empty data*

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer

Risk of bias judgement	Moderate *(The study reported details on randomisation, allocation concealment and blinding. There are some concerns around adherence to study protocol as this data was not collected.)*
Overall Directness	Directly applicable

Lauridsen, 2005

Bibliographic Reference	Lauridsen, M.C.; Christiansen, P.; Hessov, I.; The effect of physiotherapy on shoulder function in patients surgically treated for breast cancer: A randomized study; Acta Oncologica; 2005; vol. 44 (no. 5); 449-457

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Denmark
Study setting	In hospital and outpatient settings
Study dates	August 1998 to April 2000
Sources of funding	Not reported
Inclusion criteria	Unilateral surgery planned

Exclusion criteria	Reported illnesses affecting the upper extremities preoperatively Unable to give written or oral consent
Intervention(s)	Participants were offered the standard treatment of the ward and in addition, team instructed physiotherapy consisting of 12 sessions of 60 minutes, 2 sessions a week. Treatment was initiated during the sixth to eighth postoperative weeks.
Comparator	Participants were offered standard ward treatment and team-instructed physiotherapy.
Outcome measures	Patient adherence
Number of participants	125 participants
Duration of follow-up	56 weeks
Loss to follow-up	8 participants from intervention group 6 participants from the control group
Methods of analysis	The statistical analyses were completed on an intention-to-treat basis. Preoperative Constant Shoulder Score (CSS) values on both the operated and non-operated side were adequately approximated by a normal distribution whereas postoperative CSS and DCSS values on the operated side were not. Therefore, non-parametric statistics were used for all analyses. The results are expressed as median values and quartiles. A Mann-Withney U-test with a 95% level of significance was used for comparing the DCSS values. For analysing the difference in proportions the chi-squared tests with a 95% level of significance were used. All analyses were performed by the computer program SPSS/WINDOWS (9.0).
Additional comments	Baseline characteristics were balanced between both groups

Study arms

Early physiotherapy (N = 72)

Delayed physiotherapy (N = 67)

Characteristics

Arm-level characteristics

Characteristic	Early physiotherapy (N = 72)	Delayed physiotherapy (N = 67)
Modified radical mastectomy + radiotherapy Median (IQR)	49 (40 to 70)	51 (29 to 70)
Modified radical mastectomy Median (IQR)	60 (37 to 74)	63 (32 to 77)
Breast conserving surgery Median (IQR)	54 (31 to 79)	54 (42 to 69)
Modified radical mastectomy + radiotherapy No of events	n = 13 ; % = 70	n = 11 ; % = 48
Modified radical mastectomy No of events	n = 3 ; % = 14	n = 4 ; % = 31
Breast conserving surgery No of events	n = 10 ; % = 32	n = 6 ; % = 21
Modified radical mastectomy + radiotherapy No of events	n = 7 ; % = 40	n = 8 ; % = 35
Modified radical mastectomy No of events	n = 6 ; % = 29	n = 2 ; % = 15
Breast conserving surgery No of events	n = 12 ; % = 39	n = 7 ; % = 24

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer

Risk of bias judgement	Moderate *(The study reported some information on randomisation, but no detail on allocation concealment and blinding.)*
Overall Directness	Directly applicable

Leal, 2016

Bibliographic Reference	Leal, N.F.; Oliveira, H.F.; Carrara, H.H.; Supervised physical therapy in women treated with radiotherapy for breast cancer; Revista latino-americana de enfermagem; 2016; vol. 24; e2755

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Trial registration number and/or trial name	NCT02198118
Study type	Randomised controlled trial (RCT)
Study location	Brazil
Study setting	In hospital and outpatient settings
Study dates	Between November 2009 and March 2012
Sources of funding	Not reported
Inclusion criteria	Diagnosed with primary unilateral breast cancer Undergoing surgery and radiotherapy for breast cancer
Exclusion criteria	Detectable metastatic disease Bilateral breast cancer Orthopaedic and/or neurological disorders that limited the movement of the upper limbs

	Prior thoracic radiotherapy
Intervention(s)	Participants were offered supervised kinesiotherapy of the upper limb
Comparator	Participants were not offered any kinesiotherapy, and only had measurements taken throughout study period
Outcome measures	Range of movement
Number of participants	35 participants
Duration of follow-up	Not reported
Loss to follow-up	5 participants in intervention group 6 participants in control group
Methods of analysis	Considering an α of 0.05, a test power of 80%, differences in the mean perimetry values of 3.0 cm before and after radiotherapy, and a standard deviation of 4.5, a required sample size of 16 was calculated using Power and Sample Size Calculation version software 2.1.31. The analysis involved the assessment of the intention to treat (ITT) and included all participants in the study group who were originally allocated by randomisation, irrespective of the period of initiation of treatment, discontinuation of therapy, nonadherence to the protocol received, or the use of treatment protocols that differed from the original. For the intragroup analysis, an unpaired t-test was used to compare the goniometry results between the ipsilateral and contralateral limbs within the same evaluation. One-way analysis of variance (ANOVA) was used to assess differences in perimetry among the three evaluations. For intergroup analysis, unpaired t-tests were used to evaluate the goniometry results in the ipsilateral limb and differences in perimetry. P-values lower than 5% were considered statistically significant.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Kinesiotherapy (N = 17)

Control (N = 18)

Characteristics

Arm-level characteristics

Characteristic	Kinesiotherapy (N = 17)	Control (N = 18)
Mean age (SD) Mean (SD)	55.2 (7.14)	54.8 (11.56)
Conservative No of events	n = 13 ; % = 76.5	n = 13 ; % = 72
Radical No of events	n = 4 ; % = 20	n = 4 ; % = 23.5
Axillary lymphadenectomy No of events	n = 11 ; % = 61	n = 11 ; % = 64.7
SLNB No of events	n = 7 ; % = 38	n = 4 ; % = 23.5
Plastic surgery No of events	n = 0 ; % = 0	n = 2 ; % = 10
Chemotherapy No of events	n = 12 ; % = 70.6	n = 15 ; % = 83
Hormone therapy No of events	n = 11 ; % = 64.7	n = 13 ; % = 72

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details on randomisation, allocation concealment but stated it was non-blinded. There were some concerns around patient adherence to trial interventions as this data was not collected.)*
Overall Directness	Directly applicable

Lee, 2007

Bibliographic Reference	Lee, T.S.; Kilbreath, S.L.; Refshauge, K.M.; Pendlebury, S.C.; Beith, J.M.; Lee, M.J.; Pectoral stretching program for women undergoing radiotherapy for breast cancer; Breast Cancer Research and Treatment; 2007; vol. 102 (no. 3); 313-321

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number	Not reported

and/or trial name	
Study type	Randomised controlled trial (RCT)
Study location	Australia
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Preparing to undergo surgery Receiving radiotherapy to the breast or chest wall in either two field or three fields (including a supraclavicular field)
Exclusion criteria	Receiving radiotherapy to the axilla
Intervention(s)	Participants followed an independent exercise program, outlined in a pamphlet given to them after breast cancer surgery. The exercise program consisted of gentler shoulder range of motion exercises in addition to usual care, and weekly physical therapist appointments.
Comparator	Participants did not receive any exercise advice during their weekly physical therapist appointments. Skin care and lymphedema information were reviewed with patients by their therapist.
Outcome measures	Range of movement (shoulder external rotation not reported in an extractable format) Upper limb muscle strength (shoulder flexion, abduction, external rotation not reported in an extractable format) Incidence of lymphoedema Quality of life
Number of participants	61 participants
Duration of follow-up	7 months
Loss to follow-up	Not reported.
Methods of analysis	Statistical analysis was carried out using ‘‘intention-to-treat’’ analysis. To determine whether there was an increase in range of motion at 7 months following the completion of radiotherapy, two-way repeated measures analysis of variance (ANOVA) was used. The within-group factor was arm (affected, unaffected) and the between-group factor was group allocation (control, stretch). In addition, two-way repeated measures ANOVAs were used on each outcome of range, strength, and factors related to quality of life to identify any changes over time. The dependant variables were group allocation and time (baseline, post-radiotherapy, and 7 months after radiotherapy). Planned contrasts were performed if significant differences were obtained. Stepwise linear regression was used to determine whether patient characteristics and treatment factors explained the range obtained at 7 months. Variables included age, BMI, cancer staging (DCIS, Stage I,

	II, III), type of breast surgery (mastectomy or conservative surgery), axillary surgery, affected side (dominant or non-dominant), the time between surgery and radiotherapy, boost treatment, radiotherapy dose (42.5Gy or 50Gy), machine (4 or 6MV), pain at baseline, lymphedema at baseline, and skin desquamation (requiring treatment or not requiring treatment). One participant's data from the stretch group were not included in the between-limb analysis because she had a frozen shoulder on the unaffected side. Mean scores replaced missing data for outcome measures except questionnaire data. Cases with missing data from questionnaires were excluded from the repeated measures tests, hence there were 29 complete data sets from the control group and 28 from the stretch group. Means and standard deviations are reported in the results unless otherwise stated. Statistical significance was set at $P < 0.05$. Statistical analyses were performed using SPSS Version 12.0 software (SPSS Inc. Chicago, USA).
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Stretch (N = 31)

Control (N = 30)

Characteristics

Arm-level characteristics

Characteristic	Stretch (N = 31)	Control (N = 30)
% Female No of events	n = 31 ; % = 100	n = 30 ; % = 100
Mean age (SD) Mean (SD)	55 (13)	53 (12)
BMI Mean (SD)	25.9 (4)	27.3 (5.5)
Mastectomy No of events	n = 6 ; % = 19.4	n = 7
Conservative No of events	n = 25 ; % = 80.7	n = 23 ; % = 76
Sentinel node biopsy	n = 8 ; % = 25.9	n = 13 ; % = 43

Characteristic	Stretch (N = 31)	Control (N = 30)
No of events		
Axillary dissection No of events	n = 11 ; % = 35.5	n = 13 ; % = 43
Chemotherapy No of events	n = 16 ; % = 51.6	n = 18 ; % = 60
Tamoxifen or Arimidex No of events	n = 17 ; % = 54.9	n = 23 ; % = 76

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details of randomisation, allocation concealment and blinding but there are some concerns around confounding that may have arisen by the control group continuing physical exercise which was not standardised/logged appropriately.)*
Overall Directness	Directly applicable

Majed, 2022

Bibliographic Reference	Majed, M.; Neimi, C.A.; Youssef, S.M.; Takey, K.A.; Badr, L.K.; The Impact of Therapeutic Exercises on the Quality of Life and Shoulder Range of Motion in Women After a Mastectomy, an RCT; Journal of cancer education : the official journal of the American Association for Cancer Education; 2022; vol. 37 (no. 3); 843-851

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	NCT04184102
Study location	Lebanon
Study setting	In hospital and outpatient settings
Study dates	Between March 2017 and November 2017
Sources of funding	Not reported
Inclusion criteria	Undergoing modified radical mastectomy Women between 35-55 years old
Exclusion criteria	Pregnancy Women who had comorbidities that affected their quality of life Women not able to communicate
Intervention(s)	Participants received pre-surgery education and training on therapeutic exercises by the principal investigator in addition to routine hospital care.
Comparator	Usual care: routine hospital care that did not include any exercise training or education. It also includes explanation by the surgeon on the surgical procedure with follow-up at two and four weeks after discharge.
Outcome measures	Range of movement Quality of life (global score/breast cancer specific functions were not reported)
Number of participants	69 participants
Duration of follow-up	4 weeks after discharge

Loss to follow-up	5 participants from the intervention group 4 participants from the control group
Methods of analysis	Data analysis was conducted using SPSS version 24. Descriptive statistics were conducted using means, standard deviations for continuous variables, and frequencies or percentages for categorical variables. Significant differences in the range of motion and quality of life scores between the study and control groups were compared using an independent two-sample t-test. A p-value of less than 0.05 was considered significant
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Pre-surgery education (N = 35)

Usual care (N = 34)

Characteristics

Arm-level characteristics

Characteristic	Pre-surgery education (N = 35)	Usual care (N = 34)
35-42 years No of events	n = 14 ; % = 46.7	n = 14 ; % = 46.7
43-48 years No of events	n = 10 ; % = 33.3	n = 10 ; % = 33.3
49-55 years No of events	n = 6 ; % = 20	n = 6 ; % = 20

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer

Risk of bias judgement	Moderate *(The study did not report on details of allocation concealment and blinding. There were some concerns around confounding bias introduced by regular follow-up in the intervention group as well as patient adherence to exercise programmes as they were performed at home.)*
Overall Directness	Directly applicable

Marshall-Mckenna, 2014

Bibliographic Reference	Marshall-Mckenna, R.; Paul, L.; McFadyen, A.K.; Gilmartin, A.; Armstrong, A.; Rice, A.M.; McIlroy, P.; Myofascial release for women undergoing radiotherapy for breast cancer: A pilot study; European Journal of Physiotherapy; 2014; vol. 16 (no. 1); 58-64

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Study type	Randomised controlled trial (RCT)
Study location	United Kingdom
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Breast Cancer Campaign
Inclusion criteria	Undergoing breast conserving surgery with complete local excision and axillary dissection Women who received mastectomy

Exclusion criteria	Detectable metastatic disease Only had a sentinel node biopsy Participants with recent musculoskeletal injuries Condition associated with pain or reduced upper limb mobility Unable to read or speak English fluently
Intervention(s)	Participants received myofascial release massage. The participants
Comparator	Participants received usual care which included a form for participants to record any treatment they received to improve their arm mobility and did not include routine physiotherapy.
Outcome measures	Upper limb function (DASH score) Range of movement
Number of participants	14 participants
Duration of follow-up	3 months
Loss to follow-up	Not reported
Methods of analysis	Mean (standard deviation) values are presented for all outcome variables for each group at Baseline, Week 4 and Follow-up. Demographic comparisons (parametric t-tests and a Fishers test) were used to assess any significant group differences at Baseline. Frequency values were used to illustrate clinical significance for range of movement. The main outcome measures were analysed using a two-factor repeated-measures analysis of variance (ANOVA) model with main factors of Group (MFR group, Control group) and Time (Baseline, Week 4, Follow-up). The significance of the intervention effect was assessed using the Group/Time interaction within the ANOVA models. A 5% level of significance was set and where appropriate Tukey's post hoc tests were used. Where multiple comparisons took place, a Bonferroni correction factor was employed, and the significance level was reduced to $p < 0.017$. All analysis was performed on SPSS (version 15).
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Myofascial release (N = 14)

Control (N = 10)

Characteristics

Arm-level characteristics

Characteristic	Myofascial release (N = 14)	Control (N = 10)
Mean age (SD) Mean (SD)	63.5 (11.1)	51.4 (11.9)
BMI Mean (SD)	27.6 (5.5)	29.1 (4.9)
Mastectomy and axillary node clearance No of events	n = 11 ; % = 78.6	n = 7 ; % = 70
Wide local excision and axillary node sample No of events	n = 3 ; % = 21.4	n = 3 ; % = 30

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation and allocation concealment but no information on blinding was reported.)*
Overall Directness	Directly applicable

Mutrie, 2007

Bibliographic Reference	Mutrie, N.; Campbell, A.M.; Whyte, F.; McConnachie, A.; Emslie, C.; Lee, L.; Kearney, N.; Walker, A.; Ritchie, D.; Benefits of supervised group exercise programme for women being treated for early stage breast cancer: Pragmatic randomised controlled trial; British Medical Journal; 2007; vol. 334 (no. 7592); 517-520

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Mutrie 2012 - secondary publication
Trial registration number and/or trial name	ISRCTN12587864.
Study type	Randomised controlled trial (RCT)
Study location	United Kingdom
Study setting	In hospital and outpatient settings
Study dates	From January 2004 to January 2005
Sources of funding	Cancer Research UK.
Inclusion criteria	Women with stage 0 - III breast cancer
Exclusion criteria	Concurrent unstable cardiac, hypertensive, or respiratory disease Cognitive dysfunction Regular exercise
Intervention(s)	Participants received usual care and supervised group exercise programme for 12 weeks
Comparator	Participants received usual care which included a two-page leaflet entitled "exercise after cancer diagnosis" with safe guidelines from the healthcare team
Outcome measures	Quality of life (Data on FACT-B at 18 months and 5 years [Mutrie 2012] was not reported in an extractable format)
Number of participants	201 participants
Duration of follow-up	6 months
Loss to follow-up	7 participants from the supervised exercise programme

	4 participants from the usual care group
Methods of analysis	Statistical power and analyses were conducted with 91 participants in each group. The study was designed to have 90% power at a 5% level of significance to detect an intervention effect of approximately 7.5 units on the change in FACT-G score after 12 weeks, assuming a standard deviation of this outcome of 15 units. The primary analysis, and the main analysis applied to each secondary outcome, was to test whether significant differences existed between the exercise group and control group in outcomes at the end of the 12 week intervention period and at six months post-intervention, adjusting for the stratification variables (study site and treatment at baseline), age, and baseline value of the outcome. The analysis was done on an intention-to-treat basis, and did not take into account adherence to the intervention.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Usual care and supervised group exercise programme (N = 101)

Usual care (N = 102)

Characteristics

Arm-level characteristics

Characteristic	Usual care and supervised group exercise programme (N = 101)	Usual care (N = 102)
Chemotherapy No of events	n = 8 ; % = 8.1	n = 7 ; % = 6.9
Radiotherapy No of events	n = 28 ; % = 28.3	n = 29 ; % = 28.4
Combination No of events	n = 63 ; % = 63.6	n = 66 ; % = 64.7
Mastectomy No of events	n = 39 ; % = 39.4	n = 42 ; % = 41.2
Lumpectomy No of events	n = 59 ; % = 59.6	n = 60 ; % = 58.8

Characteristic	Usual care and supervised group exercise programme (N = 101)	Usual care (N = 102)
Reconstructive surgery No of events	n = 13 ; % = 13.1	n = 10 ; % = 9.8

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation and was an open label trial.)*
Overall Directness	Directly applicable

Odynets, 2018a

Bibliographic Reference	Odynets, T.; Briskin, Y.; Perederiy, A.; Pityn, M.; Svistelnyk, I.; Effect of water physical therapy on quality of life in breast cancer survivors; Physiotherapy Quarterly; 2018; vol. 26 (no. 4); 11-16

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study	Odynets 2019a - The effectiveness of two individualized physical interventions on the upper limb condition after radical mastectomy

included in review	
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Ukraine
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	None
Inclusion criteria	Age between 50 and 60 years Average time after breast cancer surgery between 5 and 6 months Tumour stage I-II Poor quality of life
Exclusion criteria	Bilateral surgery Detectable metastatic disease Stage III tumour Women with contraindications limiting activity Time after surgery more than 6 months Congestive heart failure
Intervention(s)	Water exercise individualised programme for 3 months
Comparator	Pilates individualised programme for 3 months
Outcome measures	Range of movement Upper limb muscle strength Quality of life
Number of participants	68 participants
Duration of follow-up	12 weeks
Loss to follow-up	Not reported
Methods of analysis	Data (mean and standard error of the mean) were analysed with the use of the Statistica for Windows (version 8.00) software. Before the statistical analysis, the Shapiro-Wilk test was applied to test for the normal

	distribution of data. Dependent sample t-test was used to analyse life quality changes in one group from baseline to post-intervention. Independent sample t-test served to compare life quality between the women of the experimental group and active control group.
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Water physical therapy program (N = 34)

Pilates physical therapy program (N = 34)

Characteristics

Arm-level characteristics

Characteristic	Water physical therapy program (N = 34)	Pilates physical therapy program (N = 34)
Mean age (SD) Mean (SD)	57.44 (2.16)	57.99 (2.24)
BMI Mean (SD)	25.92 (0.42)	26.01 (0.81)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(Details on randomisation, allocation concealment and blinding were not reported. There were some differences between baseline characteristics of patients which may have impacted outcomes.)*
Overall Directness	Partially applicable

	(The study included participants with shoulder joint limitation.)

Odynets, 2019b

Bibliographic Reference	Odynets T; Briskin Y; Todorova V; Effects of Different Exercise Interventions on Quality of Life in Breast Cancer Patients: A Randomized Controlled Trial.; Integrative cancer therapies; 2019; vol. 18

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Odynets 2018b - Effectiveness of individualised physical rehabilitation programs on post-mastectomy pain in breast cancer survivors
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Ukraine
Study setting	In hospital and outpatient settings
Study dates	Between December 2017 and March 2019
Sources of funding	Not reported
Inclusion criteria	Age between 50 and 60 years Average time after breast cancer surgery between 5 and 6 months Women who completed adjuvant chemotherapy and radiotherapy
Exclusion criteria	Bilateral surgery

	Detectable metastatic disease Stage III tumour Women with contraindications limiting activity
Intervention(s)	• One group received water exercise interventions that were implemented 3 times per week for 12 months. Water exercises consisted of a wide range of breathing exercises and physical exercises that helped solve current tasks. They were built on a rational combination of swimming, combined developing exercises, and exercises of local impact on different muscle groups using various initial positions. • One group received Pilates exercises 3 times per week for 12 months. They were performed on the floor and included warmup, the main part using a resistance band, and a cool-down. The total duration of the session was 60 minutes
Comparator	Participants received yoga exercises based on the Hatha yoga approach, with 3 sessions per week for 12 months. The yoga exercise session was performed as follows: warmup, exercising and cooling down.
Outcome measures	Pain intensity (Data was not reported in an extractable format [Odynets 2018b]) Quality of life
Number of participants	124 participants
Duration of follow-up	12 months
Loss to follow-up	• 5 participants from the water exercise group • 4 participants from the Pilates exercise group
Methods of analysis	Data recorded (mean and standard error of the mean) were analysed using Statistica for Windows (version 8.00). Before concluding analysis, data were evaluated for normality assumption, homogeneity, and occurrence of extreme scores. The distribution of the data recorded was tested using the Shapiro-Wilk test. This analysis was performed as a preliminary measure before parametric calculations of the analysis of difference. Dependent t-test samples were used to analyse life quality changes in one group between baseline and postintervention. Independent sample t-tests were used to compare postintervention life quality parameters between the women of the 3 groups. Sample size was based on detection of meaningful differences in primary end points with 80% power and a 2-sided 5% significance level.
Additional comments	Baseline characteristics were balanced between all intervention groups

Study arms

Water-exercise group (N = 45)

Pilates group (N = 40)

Yoga group (N = 30)

Characteristics

Arm-level characteristics

Characteristic	Water-exercise group (N = 45)	Pilates group (N = 40)	Yoga group (N = 30)
Mean age (SD) Mean (SD)	58.84 (1.36)	59.4 (1.24)	59.1 (1.37)
Radiotherapy No of events	n = 42 ; % = 94	n = 38 ; % = 95	n = 27 ; % = 90
Chemotherapy No of events	n = 3 ; % = 6	n = 2 ; % = 5	n = 3 ; % = 10
Mastectomy No of events	n = 45 ; % = 100	n = 40 ; % = 100	n = 30 ; % = 100

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(Details on randomisation, allocation concealment and blinding were not reported. There were some differences between baseline characteristics of patients which may have impacted outcomes.)*

Overall Directness	Partially applicable *(The study included participants with shoulder joint limitation.)*

Oliveira, 2009

Bibliographic Reference	Oliveira, MMF; Gurgel, MSC; Miranda, MS; Okubo, MA; Feijo, LFA; Souza, GA; Efficacy of shoulder exercises on locoregional complications in women undergoing radiotherapy for breast cancer: clinical trial; Brazilian journal of physical therapy / revista brasileira de fisioterapia; 2009; vol. 13 (no. 2); 136-143

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	UMIN Clinical Trials Registry: R000001387.
Study location	Brazil
Study setting	In hospital and outpatient settings
Study dates	Between May 2005 and September 2006
Sources of funding	Not reported
Inclusion criteria	Women who underwent breast surgery for breast cancer Functional degree of range of motion of the shoulder
Exclusion criteria	Receiving chemotherapy or radiotherapy at the time of the study

	History of lymphoedema History or presence of shoulder dysfunction Women who physical exercise was medically contraindicated for Women with local recurrence
Intervention(s)	Participants started physical therapy sessions concomitantly with radiotherapy. A total of 18 sessions (45 minutes for each session, 3 times a week) were performed during the treatment period. Kinesiotherapy was used as the physical therapy technique.
Comparator	Participants did not undergo any physical therapy during radiotherapy treatment
Outcome measures	Range of movement (shoulder external rotation not reported in an extractable format)
Number of participants	6 participants
Duration of follow-up	6 months
Loss to follow-up	3 participants from the physical therapy group 3 participants from the control group
Methods of analysis	The chi-square test and Fisher's exact test were used to investigate the homogeneity of categorical variables between the groups. The t-test was used to compare ages and the Mann-Whitney test was used to compare the BMI between groups. The measurements of flexion, rotation and abduction were evaluated with the means for both shoulders (ipsilateral and contralateral) and with the difference between them. The data were tested for normal distribution using the Kolmogorov-Smirnov test and, if normality was detected, the three evaluations were compared by means of multivariate analysis of variance (MANOVA), using Wilk's test, to evaluate group and time effects between groups. Friedman's test was used for this in cases of non-normally distributed data. The significance level was set at $p<0.05$. The software used for the analysis was SAS 9.1.3.><0.05. The software used for analysis was SAS (version 9.1.3).
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Physical therapy (N = 35)

Control (N = 34)

Characteristics

Arm-level characteristics

Characteristic	Physical therapy (N = 35)	Control (N = 34)
Mean age (SD) Mean (SD)	52.7 (10.2)	48 (10.1)
Radical mastectomy No of events	n = 23 ; % = 65.5	n = 24 ; % = 70.6
Quadrantectomy + ALND No of events	n = 12	n = 10 ; % = 29.4
Chemotherapy No of events	n = 33 ; % = 94.3	n = 32 ; % = 94.1
Hormone therapy No of events	n = 15 ; % = 42.9	n = 18 ; % = 52.9

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The assessors and participants were aware of the intervention which may have impacted outcomes.)*
Overall Directness	Directly applicable

Pace do Amaral, 2012

Bibliographic Reference	Pace do Amaral, M.T.; Freire de Oliveira, M.M.; Ferreira, N.O.; Guimaraes, R.V.; Sarian, L.O.; Gurgel, M.S.; Manual therapy associated with upper limb exercises vs. exercises alone for shoulder rehabilitation in postoperative breast cancer; Physiotherapy theory and practice; 2012; vol. 28 (no. 4); 299-306

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Brazil
Study setting	In hospital and outpatient settings
Study dates	From August 2006 roto September 2009
Sources of funding	Not reported
Inclusion criteria	Had surgery including ALND Women who had flexion and/or abduction range of motion <=100 degrees of the ipsilateral shoulder on the 1st day postoperatively
Exclusion criteria	Bilateral surgery Elective reconstructive surgery at the same time as the initial breast cancer surgery Detectable metastatic disease Previous axillary operation or radiotherapy History or presence of shoulder dysfunction Only had a sentinel node biopsy Total or partial lesion of the long thoracic nerve Under palliative care
Intervention(s)	Participants received upper limb exercises on the 1st postoperative day, with one set with 10 repetitions of three active upper limb exercises and

	were advised to attend the physical therapy outpatient facility for upper limb exercises. After the upper limb exercise sessions, the manual therapy consisted of mobilisation and therapeutic massage. Each session lasted approximately 20 minutes, twice a week and took place after the upper limb exercises group. The total duration of manual therapy sessions was 1 month (with 8 sessions in total).
Comparator	Participants received upper limb exercises on the 1st postoperative day, with one set with 10 repetitions of three active upper limb exercises and were advised to attend the physical therapy outpatient facility for upper limb exercises. The total duration of the program was 1 month.
Outcome measures	Range of movement
Number of participants	131 participants
Duration of follow-up	18 months
Loss to follow-up	40 participants from the manual therapy group 36 participants from the control group
Methods of analysis	Data were stored in Microsoft Excel spreadsheets and analysed in the R environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria). Confidence intervals were set to 95% (95% CI; p = 0.05). The chi-square tests were used to compare the clinical and pathological features of the patients between the manual therapy associated with upper limb exercises and upper limb exercises isolated groups (alternatively, Fisher's exact test was used when one of the cross-tabulation cells contained five or less subjects). Means and standard deviations were calculated for the goniometry scores for flexion, abduction, and for the functionality score. Then, multivariate analysis of variance models was fit to compare the scores obtained at each of the assessment rounds. Analysis of variance (ANOVA) for repeated measures was used to determine the time and group effects on the abduction and flexion scores. An interaction graph was then produced to depict the outcomes of the flexion and abduction shoulder capacities during the 18-month follow-up..
Additional comments	Baseline characteristics were balanced between both groups.

Study arms

Manual therapy and upper limb exercise (N = 65)

Upper limb exercise (N = 66)

Characteristics

Arm-level characteristics

Characteristic	Manual therapy and upper limb exercise (N = 65)	Upper limb exercise (N = 66)
Mean age (SD) Mean (SD)	55 (11.4)	56.7 (11.7)
BMI Mean (SD)	27.1 (4.9)	28.9 (5.2)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study did not report details of randomisation but stated that it was partially blinded. Details on the standardisation of outcome measures and patient adherence to intervention were not reported and differences were not adjusted for which may have impacted outcome data.)*
Overall Directness	Directly applicable

Rafn, 2018

Bibliographic Reference	Rafn, B.S.; Hung, S.; Hoens, A.M.; McNeely, M.L.; Singh, C.A.; Kwan, W.; Dingee, C.; McKevitt, E.C.; Kuusk, U.; Pao, J.; Van Laeken, N.; Goldsmith, C.H.; Campbell, K.L.; Prospective surveillance and targeted physiotherapy for arm morbidity after breast cancer surgery: a pilot randomized controlled trial; Clinical rehabilitation; 2018; vol. 32 (no. 6); 811-826

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	NCT02754427
Study location	Canada
Study setting	In hospital and outpatient settings
Study dates	Between February 2013 and August 2014
Sources of funding	The University of British Columbia
Inclusion criteria	Undergoing breast conserving surgery with complete local excision and axillary dissection Women aged 30-75 years
Exclusion criteria	History of lymphoedema Pre-existing shoulder pathology that limited shoulder range of motion by >25% Previous breast cancer surgery
Intervention(s)	Participants received prospective surveillance and targeted physiotherapy as well as usual care. Initially, participants received standardised physiotherapy assessment at three sessions by a physiotherapist; if arm morbidity was identified at any of these visits, the participant was referred to the outpatient physiotherapy clinic for individual treatment u
Comparator	Participants received education and usual care which comprised of preoperative education by clinic staff and the provision of an educational booklet for breast cancer survivors following surgery; the education booklet contains a protocol for postsurgical arm exercises education The participants also received three in-person education sessions delivered by study staff; the sessions included nutrition, stress management, and fatigue management using information based on patient materials available.

Outcome measures	Range of motion Lymphoedema Quality of life Patient adherence Upper limb muscle strength
Number of participants	41
Duration of follow-up	12 months
Loss to follow-up	2 participants in the intervention group 2 participants in the comparator group
Methods of analysis	Presurgical patient characteristics data were summarised using descriptive statistics and presented as mean and standard deviation (SD) for continuous variables and frequency counts and percentages for categorical variables. An intention-to-treat analysis with multiple imputations was employed for all analyses except for the categorical outcome of the prevalence of arm morbidity. In each group, 10% of the data were missing randomly and subsequently imputed. No imputation was performed for one participant who died during the study period. Paired t-tests were applied to outcome measures to compare changes from pre-surgery to 12 months post-surgery within groups. Repeated-measure split-plot analysis of variance tested whether the means of the dependent variables were significantly different over time for the prospective surveillance and targeted physiotherapy group compared with the education group. The total number of surgical arms was considered in the pre-surgery and 12 months post-surgery analysis. The number of participants with arm morbidity, presented as percentages for each group, was compared using chi-square tests. The total number of arm morbidity domains at 12 months post-surgery were summarised as frequency counts, and categorised as resolved (identified at 3, 6, or 9 months post-surgery and not present at 12 months post-surgery), persistent (identified at 3, 6, or 9 months post-surgery and remained present at 12months post-surgery), and newly identified (identified at 12months post-surgery only). For the cost description analysis, the total number of surveillance assessments, physiotherapy treatment sessions, and physiotherapy referrals for the prospective surveillance group was summarised as mean, SD, minimum, and maximum. Descriptive statistics showing cost distributions (mean, SD, and 95% confidence intervals) and sums are presented. Cost data were summarised for Prospective Surveillance Program costs and Targeted physiotherapy treatment costs and presented separately for Patient Out-of-Pocket Travel and Health Care Provider costs. Costs are calculated in 2017 Canadian dollars. The IBM SPSS statistics v. 23 software package was applied as a statistical tool. The significance level was set at 0.05
Additional comments	All participants were women

	Baseline characteristics were balanced between both groups

Study arms

Targeted physio therapy (N = 21)

Education (N = 20)

Characteristics

Arm-level characteristics

Characteristic	Targeted physio therapy (N = 21)	Education (N = 20)
Mean age (SD) Mean (SD)	55.05 (6.4)	53.25 (10)
BMI Mean (SD)	28.4 (6.9)	26 (6.6)
Mastectomy No of events	n = 9 ; % = 43	n = 9 ; % = 45
Breast conserving surgery No of events	n = 12 ; % = 57	n = 11 ; % = 55
Axillary lymph node dissection No of events	n = 7 ; % = 33	n = 5 ; % = 25
Sentinel lymph node dissection No of events	n = 11 ; % = 52	n = 14 ; % = 70
Radiotherapy No of events	n = 16 ; % = 76	n = 12 ; % = 60
Chemotherapy No of events	n = 13 ; % = 62	n = 10 ; % = 50

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Low *(The study reported details of randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Reis, 2013

Bibliographic Reference	Reis, D.; Walsh, M.E.; Young-McCaughan, S.; Jones, T.; Effects of nia exercise in women receiving radiation therapy for breast cancer; Oncology Nursing Forum; 2013; vol. 40 (no. 5); e374-e382

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported

Study location	United States
Study setting	Outpatient settings
Study dates	November 2008 to January 2010
Sources of funding	Not reported
Inclusion criteria	Age 18 years or older Women receiving radiation therapy for stage I, II, III breast cancer
Exclusion criteria	Not reported
Intervention(s)	Participants in the Nia group (Nia exercise) met individually with the principal investigator and received instructions and a demonstration about the Nia techniques and a Nia DVD for home use; for 12 weeks
Comparator	Participants in teh control group met individually with the principal investigator and were instructed to maintain their current exercise regimen for 12 weeks following the 12-week assessment. participants were then given the opportunity to participate in Nia group exercise
Outcome measures	Range of movement Quality of life Resource costs Patient adherence
Number of participants	41 participants
Duration of follow-up	12 weeks
Loss to follow-up	Not reported
Methods of analysis	Descriptive statistics were used to summarise participant characteristics. Chi-square tests were used with categorical data to evaluate differences between groups. Repeated-measures analysis of variance (ANOVA) and repeated-measured analysis of covariance were used to assess change over time between the groups.
Additional comments	All participants were women Baseline characteristics were balanced between both groups

Study arms

Nia exercise (N = 22)

Control (N = 19)

Characteristics

Arm-level characteristics

Characteristic	Nia exercise (N = 22)	Control (N = 19)
Mean age (SD) Mean (SD)	54 (11.1)	59 (10.7)
Lumpectomy No of events	n = 12 ; % = 54.5	n = 11 ; % = 57.9
Mastectomy No of events	n = 5 ; % = 22.7	n = 2 ; % = 10.5
Partial mastectomy No of events	n = 4 ; % = 18	n = 4 ; % = 21
Reconstruction No of events	n = 1 ; % = 4.5	n = 2 ; % = 10.5
Bilateral mastectomy No of events	n = 8 ; % = 36.4	n = 9 ; % = 40.9
Hormone therapy No of events	n = 10 ; % = 45.5	n = 9 ; % = 47.4
Chemotherapy No of events	n = 13 ; % = 59.9	n = 13 ; % = 68.4

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study did not report details on randomisation, allocation concealment and blinding. However, there were differences between baseline characteristics of the groups which may*

	have impacted the results of the study. No adjustments were made to account for these differences.)
Overall Directness	Directly applicable

Schultz, 1997

Bibliographic Reference	Schultz, I.; Barholm, M.; Grondal, S.; Delayed shoulder exercises in reducing seroma frequency after modified radical mastectomy: a prospective randomized study; Annals of surgical oncology : the official journal of the Society of Surgical Oncology; 1997; vol. 4 (no. 4); 293-297

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Sweden
Study setting	In-patient and out-patient settings
Study dates	February 1992 to June 1994
Sources of funding	Karolinska Institute Danderyd Hospital

Intervention(s)	Patients were instructed to do active shoulder exercises to regain full range of motion, especially in directions that may be difficult post-operatively (for example, ante-flexion, abduction and rotation) three times daily. Pain was the limiting factor for the extent of motion.
Comparator	Patients were instructed to start the full exercise program of the intervention group, one week post-operatively.
Outcome measures	Impaired shoulder mobility
Number of participants	163
Duration of follow-up	3 to 6 months
Loss to follow-up	Not reported
Methods of analysis	Logistic regression analyses were performed to determine the most powerful predictive factors with respect to the outcome variables postoperative seroma and postoperative shoulder mobility. The results are presented as odds ratios with a 95% confidence interval. The interpretation of an odds ratio is the odds of seroma for a patient in the early group relative to the odds of seroma for a patient in the delayed group. Fisher's exact test was used for the analysis of shoulder mobility. A p-value less than 0.05 was considered significant.
Additional comments	Not applicable

Study arms

Early post-operative shoulder exercises (N = 89)
Began exercises on the first postoperative day, under the guidance of a physiotherapist.

Delayed post-operative shoulder exercises (N = 74)
Started full-exercise program, one week postoperatively, after instructions from a physiotherapist.

Characteristics

Arm-level characteristics

Characteristic	Early post-operative shoulder exercises (N = 89)	Delayed post-operative shoulder exercises (N = 74)
Mean age (SD) Median (IQR)	59 (35 to 83)	62 (41 to 84)

Characteristic	Early post-operative shoulder exercises (N = 89)	Delayed post-operative shoulder exercises (N = 74)
BMI (kg/m2) Median (IQR)	23.5 (16 to 35)	23.1 (19 to 42)
Lymphnodes Nominal	0	0
Lymphnodes Median (IQR)	9 (0 to 24)	8 (1 to 16)
Positive nodes Nominal	38	39
Positive nodes Median (IQR)	0 (0 to 0)	0 (0 to 0)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported some detail on randomisation and no details on allocation concealment and blinding.)*
Overall Directness	Directly applicable

Simoncini, 2017

Bibliographic Reference	Simoncini, M.C.; Santoro, L.; Baggi, F.; Nevola Teixeira, L.F.; Sciotto Marotta, M.; Sandrin, F.; Bonacossa, E.; Lanni, G.; Massaro, M.A.; Intra,

M.; Berrocal, C.; Can group education improve adherence and enhance breast cancer rehabilitation after axillary dissection? A randomized clinical trial; Journal of Evidence-Based Psychotherapies; 2017; vol. 17 (no. 2); 1-22

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Italy
Study setting	Hospital and outpatient settings
Study dates	April 2009 to April 2010
Sources of funding	Not reported
Inclusion criteria	Women with breast cancer Undergoing radical mastectomy or quadrantectomy with complete unilateral ALND
Exclusion criteria	Previous axillary surgery Severe mental disorders Breast reconstruction with flaps
Intervention(s)	Group rehabilitation supported by visual information: one education session was conducted in small groups of 3-4 patients. Discussions were supported by images related to the different ALND topics described in the booklet. Images relating to the topics were designed to help patients better understand the different mechanisms of possible complications, how to recognise signs and symptoms and know what to do to prevent or deal with them once they have occurred. The advice relating to exercises, quality of

	life and post-surgical sequel prevention was encouraged to be continued into the future and to be incorporated into each patient's lifestyle. The physiotherapist used interactive methods and cognitive-behavioural strategies to enhance both knowledge gain on ALND side effects and self-strategies to enhance both knowledge gain on ALND side effects and self-management skills.
Comparator	Usual rehabilitation program: involved the standard protocol after ALND which involves a single educational session conducted on a one-to-one basis by a physiotherapist. It covers the same topics presented in the group-based program and in the patient booklets. This program does not involve images, active learning or cognitive-behavioural techniques.
Outcome measures	Upper limb function (Data not reported in an extractable format) Range of movement (Data not reported in an extractable format) Pain intensity Quality of life (Data not reported in an extractable format) Patient adherence
Number of participants	186 patients were randomised; of which 168 received relevant treatment group education
Loss to follow-up	7 dropped out after receipt of the education program. 2 in usual rehabilitation program and 5 in group-based program.
Methods of analysis	Frequencies and percentages were used to describe categorical variables. Medians, inter-quartile ranges, and minimum and maximum values were used for continuous variables. Parametric tests were performed for continuous variables showing a normal distribution, otherwise, nonparametric tests were applied. The Analysis of Covariance test was applied if adjustment for baseline values was required. Between-group differences on categorical variables were tested by Pearson’s chi-square test. The statistical analyses were performed using SAS for Windows, version 8.2. All comparisons were tested at the 0.05 p–value level.
Additional comments	On the first day following surgery, range of motion exercises were limited to 90 degrees of abduction and flexion, and on the second day, they were performed without restrictions. Following this, all patients followed a home-based seld-administered exercise program over 6 weeks. Participants were instructed to perform exercises once a day if they still had the drainage and three times a day, once the drains were removed. All participants received a booklet containing information on the pathogenesis, prevention and treatment of ALND side effects, and details of the exercise program to be implemented at home.

Study arms

Group-based educational program and visual material (N = 93)

Usual rehabilitation (N = 93)

Characteristics

Arm-level characteristics

Characteristic	Group-based educational program and visual material (N = 93)	Usual rehabilitation (N = 93)
Mean age (SD) Mean (SD)	50.6 (10.9)	49 (12)
Total mastectomy and ALND No of events	n = 29 ; % = 34.5	*empty data*
Nipple sparing mastectomy and ALND No of events	n = 16	n = 15 ; % = 17.9
Quadrantectomy and ALND No of events	n = 38 ; % = 45.2	n = 39 ; % = 46.4
Intraoperative radiation therapy No of events	n = 16 ; % = 19.1	n = 15 ; % = 17.9

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(The study reported details on randomisation but not blinding and allocation concealment. The interventions and the scales used were not standardised so there may have been differences which contributed to differences in outcome measures between both groups.)*
Overall Directness	Directly applicable

Testa, 2014

Bibliographic Reference	Testa, A.; Iannace, C.; Di Libero, L.; Strengths of early physical rehabilitation programs in surgical breast cancer patients: results of a randomized controlled study; European journal of physical and rehabilitation medicine; 2014; vol. 50 (no. 3); 275-284

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration	Not reported

number and/or trial name	
Study location	Italy
Study setting	In hospital and outpatient settings
Study dates	March 2010 - February 2011
Sources of funding	Not applicable
Inclusion criteria	Women scheduled for a modified radical mastectomy or for segmental mastectomy with axillary dissection
Exclusion criteria	Only had a sentinel node biopsy
Intervention(s)	Participants received early physical rehabilitation by a physiotherapist on the 2nd postoperative day for 1 month
Comparator	Participants received no intervention and did not undergo early physical rehabilitation or receive instructions from a physiotherapist
Outcome measures	Range of movement Pain intensity Quality of life
Number of participants	70 participants
Duration of follow-up	12 months
Loss to follow-up	Not reported
Methods of analysis	IBM SPSS software v20.0 was used for statistical tests. Data regarding demographics, complications, adjuvant therapies, glenohumeral joint mobility, pain perceived and quality of life were compared. Both groups were statistically analysed through the use of two-tailed t-tests and chi-squared tests. Considering the randomisation of the groups and structure of the study, ANCOVA test was used to compare the outcomes between the groups regarding joint mobility and pain perceived, baseline data were used as covariates. Two-tailed t-tests were used for the statistical analysis within groups.
Additional comments	All participants were female Baseline characteristics were balanced between both groups

Study arms

Treatment Group (N = 35)

Control group (N = 35)

Characteristics

Arm-level characteristics

Characteristic	Treatment Group (N = 35)	Control group (N = 35)
Mean age (SD) Mean (SD)	54.3 (8.02)	55.3 (8.5)
BMI (kg/m2) Median (IQR)	25.06 (19 to 31)	25.57 (20 to 35)
Modified radical mastectomy No of events	n = 19 ; % = 54.3	n = 21 ; % = 60
Segmental mastectomy+ axillary dissection No of events	n = 16 ; % = 45.7	n = 14 ; % = 40
Chemotherapy No of events	n = 24 ; % = 68.6	n = 25 ; % = 71.4
Radiotherapy No of events	n = 90 ; % = 85.7	n = 27 ; % = 77.1

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding was reported.)*
Overall Directness	Directly applicable

Todd, 2008

Bibliographic Reference	Todd, J.; Scally, A.; Dodwell, D.; Horgan, K.; Topping, A.; A randomised controlled trial of two programmes of shoulder exercise following axillary node dissection for invasive breast cancer; Physiotherapy; 2008; vol. 94 (no. 4); 265-273

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study location	United Kingdom
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Had surgery including ALND Women with breast cancer
Exclusion criteria	Presence of lymphoedema Women under 18 years Women with an existing history of breast cancer/axillary surgery/previous irradiation of the breast or truncal quadrant
Intervention(s)	Participants had full shoulder mobilisation introduced immediately on the 1st postoperative day with vigorous arm and shoulder exercises also started within the first 2 postoperative days

Comparator	Participants followed a programme of exercises that limited movement of the arm below 90 degrees in all planes of movement over the first week followed by the introduction of a full range of shoulder movement in the second week
Outcome measures	Range of movement (Data not reported in an extractable format) Incidence of lymphoedema
Number of participants	116 participants
Duration of follow-up	12 months
Loss to follow-up	3 participants in intervention group 3 participants in comparator group
Methods of analysis	Statistical analysis was performed using Statistical Package for the Social Sciences Version 13.0 for Windows (SPSS Inc. UK Ltd, Woking). A relative risk of lymphoedema was calculated to test for equality between groups. Volume differences were calculated as the treated (ipsilateral) arm minus the untreated (contralateral) arm. Percentage differences in arm volumes were expressed as limb volume difference divided by the contralateral volume multiplied by 100 (difference/contralateral arm volume × 100). Comparison between groups was undertaken using the Mann-Whitney U-test (the Kolmogorov-Smirnov test identified that data were not normally distributed). The Mann-Whitney U-test was also used in the analysis of change scores in postoperative drainage volume and percentage difference, range of movement and self-evaluated outcomes. Parametric methods (t-test, paired t-test) were used for univariate analysis of normally distributed data (hand grip strength). Confidence intervals (CI) were obtained for results using parametric methods of statistical analysis (relative risk of incidence of lymphoedema and hand grip strength). Where non-parametric methods of statistical analysis were used, P-values were obtained (limb volume differences, range of movement, quality-of-life scores).
Additional comments	All participants were women Baseline characteristics were balanced between both groups

Study arms

Delayed mobilisation (N = 58)

Early mobilisation (N = 58)

Characteristics

Arm-level characteristics

Characteristic	Delayed mobilisation (N = 58)	Early mobilisation (N = 58)
Mean age (SD) Mean (SD)	56.5 (12.4)	57.2 (14)
BMI Mean (SD)	27.5 (5.6)	28.4 (5.7)
Wide local excision No of events	n = 36 ; % = 57	n = 29 ; % = 50
Mastectomy No of events	n = 24 ; % = 43	n = 29 ; % = 50
Radiotherapy No of events	n = 39 ; % = 67	n = 41 ; % = 71
Chemotherapy No of events	n = 30 ; % = 52	n = 26 ; % = 45
Hormonal therapy No of events	n = 34 ; % = 59	n = 41 ; % = 71

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Low *(The study reported details of randomisation, allocation concealment and blinding.)*
Overall Directness	Directly applicable

Van Der Horst Ch., 1985

Bibliographic Reference	Van Der Horst Ch., M.A.M.; Kenter, J.A.L.; De Jong, M.T.; Keeman, J.N.; Shoulder function following early mobilization of the shoulder after mastectomy and axillary dissection; Netherlands Journal of Surgery; 1985; vol. 37 (no. 4); 105-108

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	The Netherlands
Study setting	In hospital and outpatient settings
Sources of funding	Not reported
Inclusion criteria	Had surgery including ALND
Intervention(s)	Participants had early active mobilisation (physiotherapy) on the 1st postoperative day with guidance from a physiotherapist
Comparator	Participants had late active mobilisation (physiotherapy) on the 7th postoperative day with guidance from a physiotherapist
Outcome measures	Shoulder function Incidence of lymphoedema
Number of participants	57 participants
Duration of follow-up	6 months

Loss to follow-up	Not reported
Methods of analysis	Not reported

Study arms

Early exercise (N = 25)

Late exercise (N = 22)

Characteristics

Study-level characteristics

Characteristic	**Study (N =)**
Mean age (SD) Mean (SD)	62.1 (16)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	**Answer**
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding of participant as well as analysis plan.)*
Overall Directness	Directly applicable

Wiskemann, 2017

Bibliographic Reference	Wiskemann, J.; Schmidt, M.E.; Klassen, O.; Debus, J.; Ulrich, C.M.; Potthoff, K.; Steindorf, K.; Effects of 12-week resistance training during radiotherapy in breast cancer patients; Scandinavian journal of medicine & science in sports; 2017; vol. 27 (no. 11); 1500-1510

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	NCT01468766 - BEST study
Study type	Randomised controlled trial (RCT)
Study location	Germany
Study setting	In hospital and outpatient settings
Study dates	February 2011 to March 2013
Sources of funding	Interdisciplinary Research Funding program Stifung Leben mit Krebs Manfred-Lautenschlaeger-Stifung
Inclusion criteria	Women with stage 0 - III breast cancer BMI =>18 kg/m2
Exclusion criteria	Participants with contraindications for resistance training Women with concomitant malignant disease
Intervention(s)	Progressive resistance training for 12 weeks
Comparator	Progressive muscle relaxation (Jacobsen method) without any aerobic or muscle-strengthening components in small groups
Outcome measures	Upper limb muscle strength Patient adherence (Data not reported in an extractable format)
Number of participants	160 participants
Duration of follow-up	12 weeks

Loss to follow-up	1 participant from the intervention group 2 participants from the control group
Methods of analysis	Analyses of covariance (ANCOVA) based on the intent-to-treat-principle were conducted with change in fitness from pre- to post-intervention as dependent variables, intervention group as independent variable, and the baseline measure as covariate. There was no evidence of a deviation from normality assumptions. As the number of missing values was low (<9%), we performed complete-case analyses. Due to randomization the final models were not adjusted for further covariates. However, in sensitivity analyses we explored potential confounding by age, height, baseline BMI or weight, previous treatment, depressive symptoms, education, or experience with resistance training. There were no substantial changes in the results. In subgroup analyses considering the EX group only, ANCOVA were performed to describe adjusted mean strength gain by training adherence (><50%, 50–75%, >75%) and by previous chemotherapy (yes/no), respectively. Differences in strength gain between the operated and non-operated side were investigated using paired t-tests. The primary endpoint of the BEST study was cancer-related fatigue, hence all analyses presented here were explorative in nature, and therefore no adjustment for multiple testing was performed. SAS Version 9.3 was used. Statistical significance was set at $P < 0.05$ and all tests were two-sided.
Additional comments	All participants were women Baseline characteristics were balanced between groups

Study arms

Resistance exercise (N = 80)

Control group (N = 80)

Characteristics

Arm-level characteristics

Characteristic	Resistance exercise (N = 80)	Control group (N = 80)
Mean age (SD) Mean (SD)	54.5 (9.6)	55.9 (8.7)
BMI Mean (SD)	*empty data*	27.4 (5.1)
Hormone therapy No of events	n = 41 ; % = 56.2	*empty data*

Characteristic	Resistance exercise (N = 80)	Control group (N = 80)
Radiotherapy No of events	n = 57 ; % = 78.1	n = 53 ; % = 72.6

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation, allocation concealment and blinding (assessors were not blinded). There was concern over the standardisation of 1-RM and any differences were not adjusted for in analysis.)*
Overall Directness	Directly applicable

Xie, 2010

Bibliographic Reference	Xie, X.; Liu, Z.; Qu, S.; Guo, F.; Zheng, Z.; Liu, Y.; Song, M.; Bai, X.; 169 patients with postoperative breast cancer on exercising the function of limbs and investigating quality of life: A clinical study; Chinese-German Journal of Clinical Oncology; 2010; vol. 9 (no. 10); 590-593

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications associated with this	Not applicable

study included in review	
Trial registration number and/or trial name	Not reported
Study location	China
Study setting	In hospital and outpatient settings
Study dates	Between February 2007 and December 2008
Sources of funding	Not reported
Inclusion criteria	Women with breast cancer Undergoing modified radical mastectomy
Exclusion criteria	Detectable metastatic disease
Intervention(s)	Rehabilitative training by a rehabilitation gymnastics t combine the methods of exercising upper limbs and yoga
Comparator	Participants performed rehabilitative training by themselves
Outcome measures	Range of movement
Number of participants	179 participants
Duration of follow-up	28 days
Loss to follow-up	Not reported
Methods of analysis	All data were analysed using SPSS v10.0. The chi-square test was used to test for correlation and a p-value <0.05 was defined as statistically significant.
Additional comments	All participants were women

Study arms

Treatment (N = 80)

Control (N = 89)

Characteristics

Study-level characteristics

Characteristic	Study (N =)
Mean age (SD) Median (IQR)	49 (23 to 71)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(The study reported details on randomisation and allocation but no information on allocation concealment and blinding. The reporting of some outcomes may have been influenced by personal attitudes and misrepresentation; the study did not report any adjustment for these differences.)*
Overall Directness	Directly applicable

Zengin Alpozgen, 2017

Bibliographic Reference	Zengin Alpozgen, A.; Razak Ozdincler, A.; Karanlik, H.; Yaman Agaoglu, F.; Narin, A.N.; Effectiveness of Pilates-based exercises on upper extremity disorders related with breast cancer treatment; European journal of cancer care; 2017; vol. 26 (no. 6)

Study details

Secondary publication of another included study- see primary study for details	Not applicable

Other publications associated with this study included in review	Not applicable
Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	In hospital and outpatient settings
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Between 25 - 65 years Stage I-II breast cancer and development of a shoulder range of movement limitation >20 degrees
Exclusion criteria	Sever heart disease Presence of lymphoedema Women not able to communicate Neurological deficits and complications Significant shoulder problems before the intervention for breast cancer Rheumatological disease
Intervention(s)	All participants received usual, standard verbal and written information (including causes of UE problems, arm care, prosthetic breast, situations that require attention in the arm movements, movements should be avoided, the benefits of exercise, exercise types and training) in the first interview Intervention 1: Pilates-based exercise supervised by a physiotherapist Intervention 2: Combined exercises supervised by a physiotherapist
Comparator	Home exercises: the appropriate exercise programme for patients were arranged and each exercise was taught by a physiotherapist as practical in the clinic until the exercise was performed properly
Outcome measures	Upper limb function (DASH score) Range of movement

	Upper limb muscle strength Pain intensity
Number of participants	55 participants
Duration of follow-up	8 weeks
Loss to follow-up	2 participants
Methods of analysis	Data analyses were performed using SPSS v.21 (SPSS Inc., Chicago, IL, USA) . One-way ANOVA was used for the quantitative measurement of the normal distribution of groups to compare subjects' onset characteristics in different groups. Kruskal–Wallis test was used to compare abnormal score-type parameters. To determine the difference between the two groups post hoc Tukey's HSD test (highly significant difference) was used. Before and after intervention, values were compared using paired samples t-test in each group, and group comparisons regarding the differences in the parameters evaluated were made using Kruskal–Wallis test with Bonferroni adjusted significance. In all analyses, $p \leq .05$ (two-sided) was considered statistically significant.
Additional comments	All participants were women Baseline characteristics were balanced between groups

Study arms

Physical exercise (N = 19)

Combined exercise (N = 19)

Home exercise (N = 19)

Characteristics

Arm-level characteristics

Characteristic	Physical exercise (N = 19)	Combined exercise (N = 19)	Home exercise (N = 19)
Mean age (SD) Mean (SD)	46.22 (11.19)	51.94 (8.05)	51.53 (13.81)

Characteristic	Physical exercise (N = 19)	Combined exercise (N = 19)	Home exercise (N = 19)
BMI Mean (SD)	30.68 (5.28)	28.73 (5.49)	28.27 (3.99)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Question	Answer
Risk of bias judgement	Moderate *(Assessors were blinded but participants were aware of their allocation, unclear how this may have affected patient adherence and study did not make any adjustments to account for its effects.)*
Overall Directness	Directly applicable

Zhou, 2019

Bibliographic Reference	Zhou, K.; Wang, W.; An, J.; Li, M.; Li, J.; Li, X.; Effects of Progressive Upper Limb Exercises and Muscle Relaxation Training on Upper Limb Function and Health-Related Quality of Life Following Surgery in Women with Breast Cancer: A Clinical Randomized Controlled Trial; Annals of Surgical Oncology; 2019; vol. 26 (no. 7); 2156-2165

Study details

Secondary publication of another included study- see primary study for details	Not applicable
Other publications	Not applicable

associated with this study included in review	
Trial registration number and/or trial name	ChiCTR-IOR-16008253
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Hospital and out-patient settings
Study dates	01/01/2016 to 31/12/2018
Sources of funding	National Natural Science Foundation of China.
Inclusion criteria	Age 18 years or older Preparing to undergo surgery Can speak Chinese
Exclusion criteria	Mastitis Active or severe potential infection Psychiatric or cognitive disorders
Intervention(s)	Progressive upper limb exercises and muscle relaxation training (PULE-MRT) and nursing care
Comparator	Routine nursing care for 6 months
Outcome measures	Upper limb muscle strength Pain Quality of life
Number of participants	102
Duration of follow-up	6 months
Loss to follow-up	Not reported
Methods of analysis	All data analyses were performed using SPSS version 23.0 (IBM Corporation) and on an intention-to-treat basis. The primary endpoint was the FACT-Bv4.0 score change at 6 months, while the secondary endpoints were FACT-Bv4.0 score changes at 1 and 3 months and CMS changes at 1, 3, and 6 months. A linear mixed-effect model with repeated measurements was used to analyze the score changes in FACT-Bv4.0 and CMS. In the model, the FACT-Bv4.0 or CMS baseline measurement was

	considered as a covariate. Group, time, and group-by-time interaction were considered as fixed effects, and the patient was considered as a random effect. The missing data caused by loss-to-follow-up across the study were assumed to be missing at random in the model analysis. The estimated within- and between-group differences with their 95% confidence intervals (CIs) are reported. A two-sided p-value <0.05 was considered statistically significant, and a difference of more than 2 standard deviations was considered to be clinically relevant.
Additional comments	Not applicable

Study arms

Intervention (N = 51)
Progressive upper limb exercises and muscle relaxation training (PULE-MRT) and nursing care

Control (N = 51)
Routine nursing care for 6 months

Characteristics

Arm-level characteristics

Characteristic	Intervention (N = 51)	Control (N = 51)
Mean age (SD) Mean (SD)	49.94 (8.88)	49.4 (9.88)
Yes No of events	n = 10 ; % = 19.6	n = 10 ; % = 19.6
No No of events	n = 41 ; % = 76.5	n = 37 ; % = 72.5
Mastectomy and SLNB No of events	n = 24 ; % = 47.1	n = 25 ; % = 49
Mastectomy and ALND No of events	n = 15 ; % = 29.4	n = 17 ; % = 33.3
Breast conserving surgery and SLNB No of events	n = 10 ; % = 19.6	n = 6 ; % = 11.8

Characteristic	Intervention (N = 51)	Control (N = 51)
Breast conserving surgery and ALND No of events	n = 2	n = 3 ; % = 5.9
Yes No of events	n = 41 ; % = 80.4	n = 43 ; % = 84.3
No No of events	n = 10 ; % = 19.6	n = 8 ; % = 15.7

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

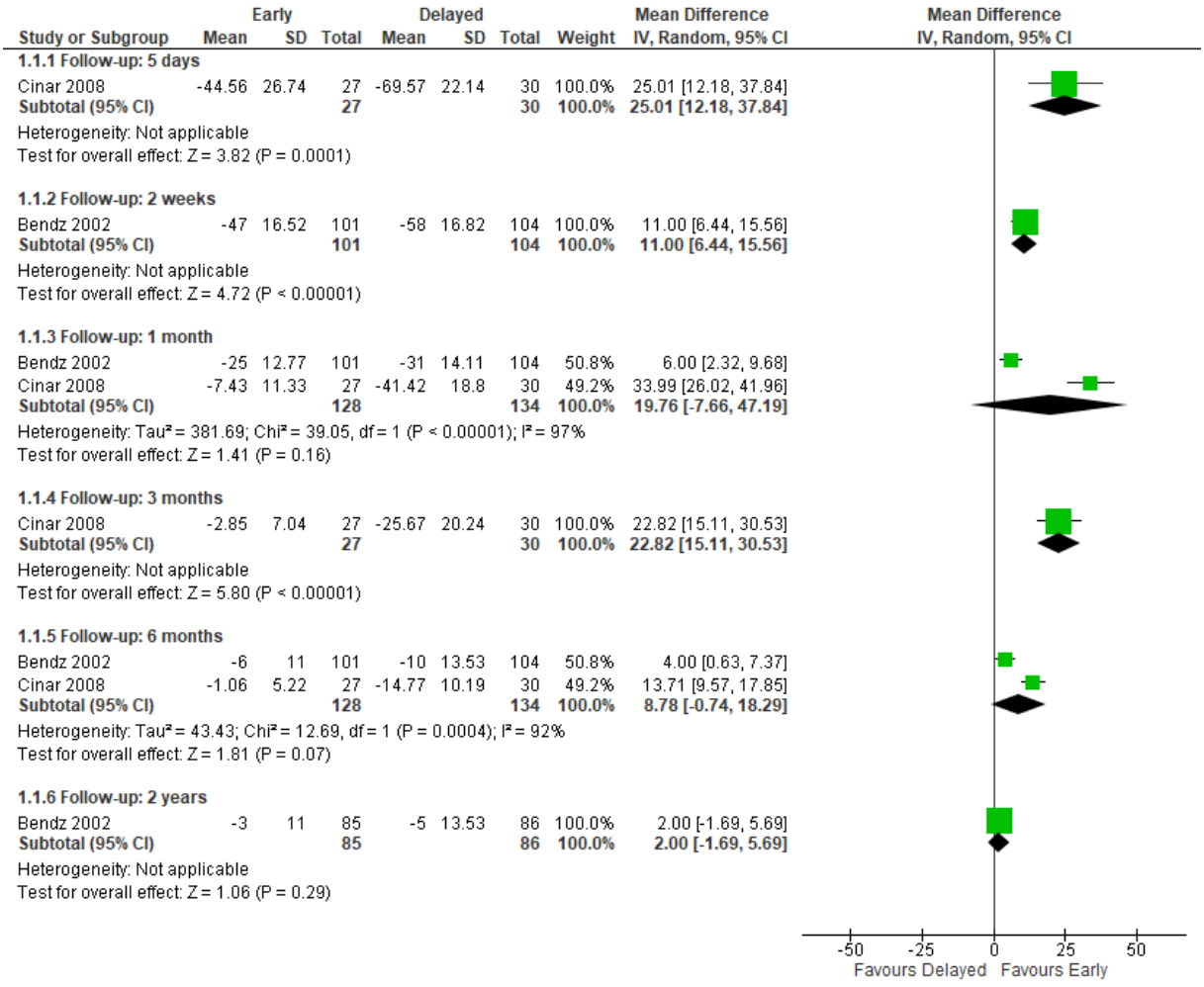
Question	Answer
Risk of bias judgement	High *(No information on randomisation, allocation concealment and blinding of participants. As some of the outcomes were self-reported, they were not adjusted for and this may have impacted outcome measures.)*
Overall Directness	Directly applicable

Appendix E – Forest plots

Forest plots are shown when there is either a meta-analysis or multiple time points reported within a comparison.

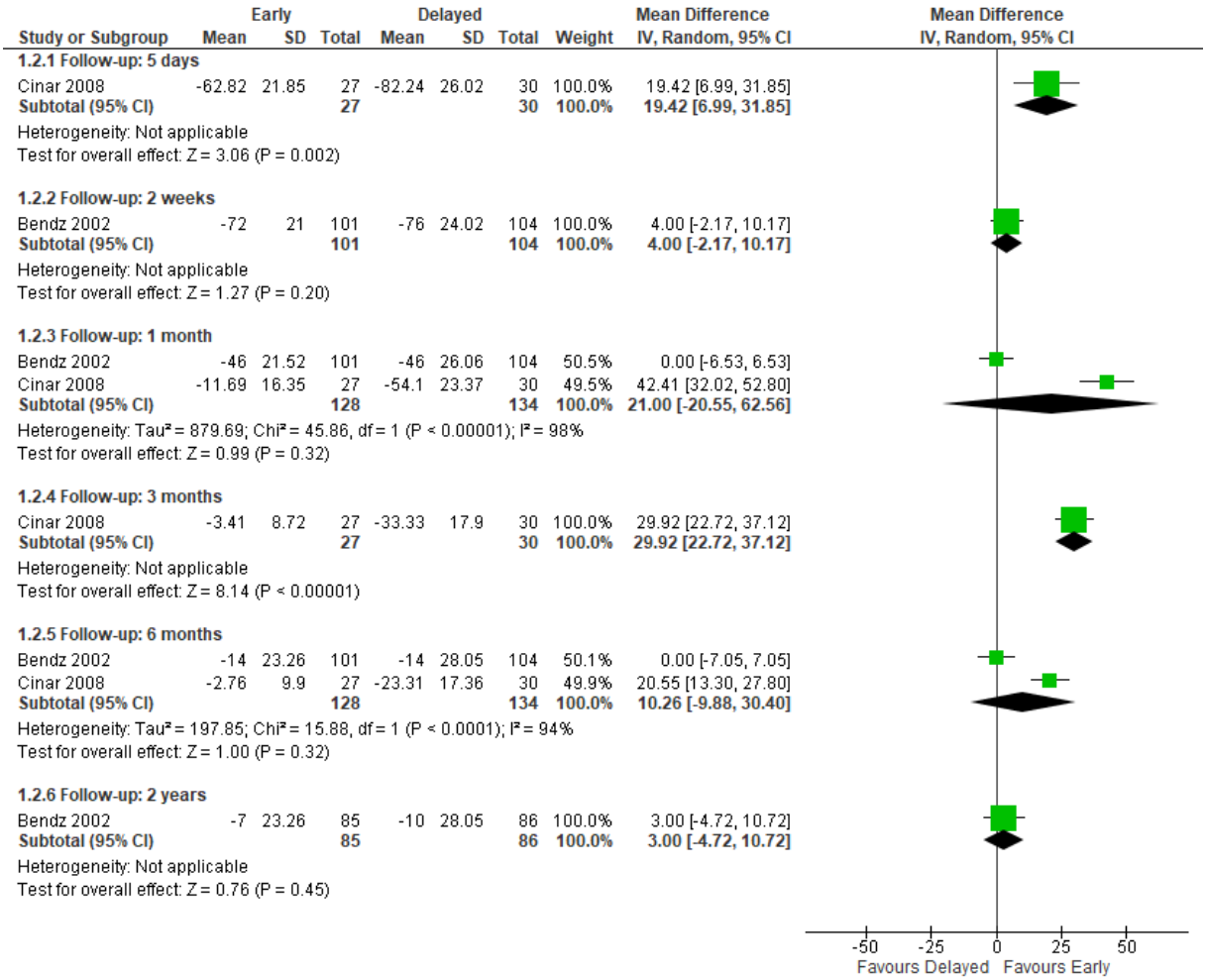
Physiotherapy: early compared to delayed

Figure 1 Range of movement: shoulder flexion in degrees



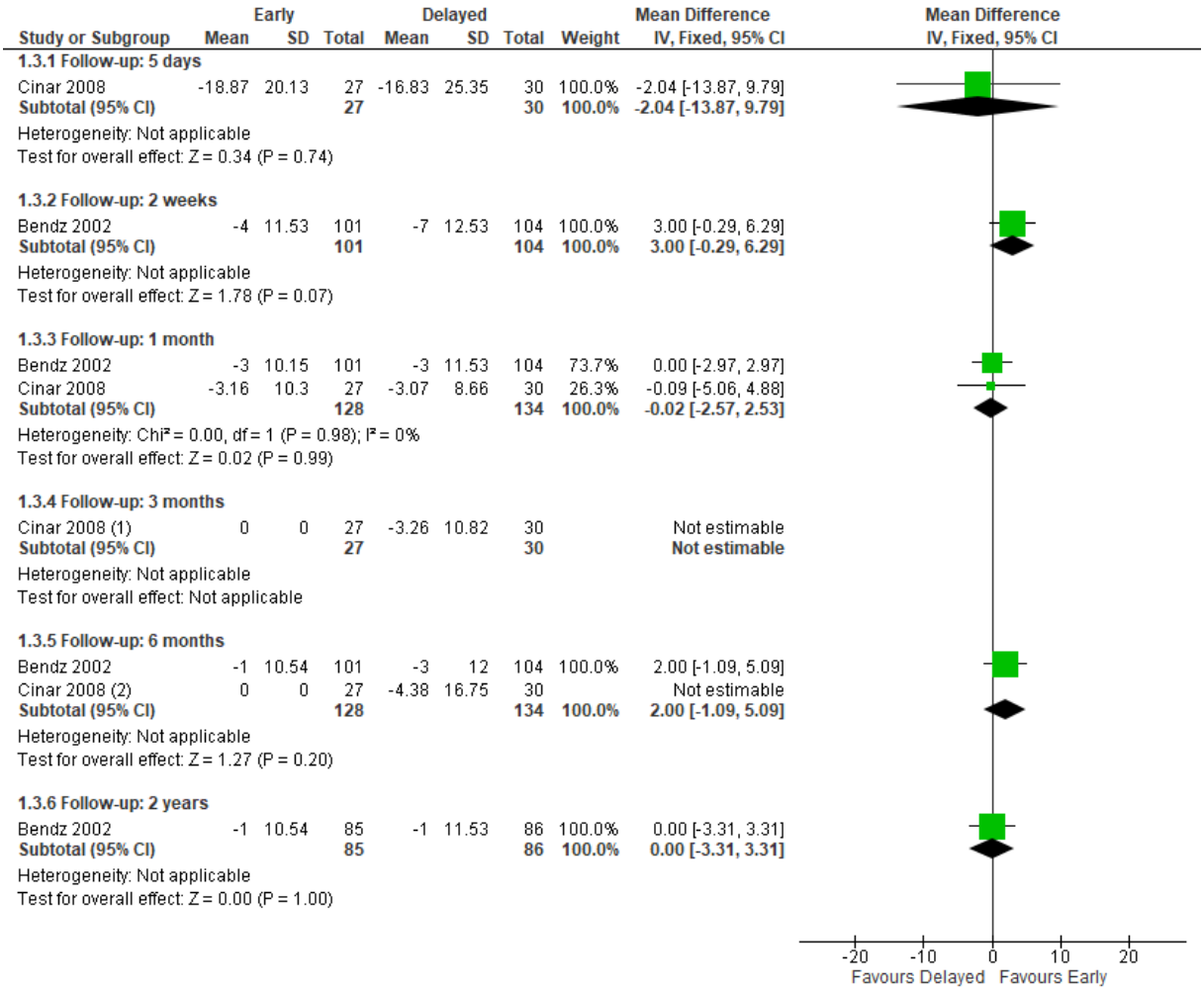
Change from baseline calculated by reviewer

Figure 2 Range of movement: shoulder abduction in degrees



Change from baseline calculated by reviewer

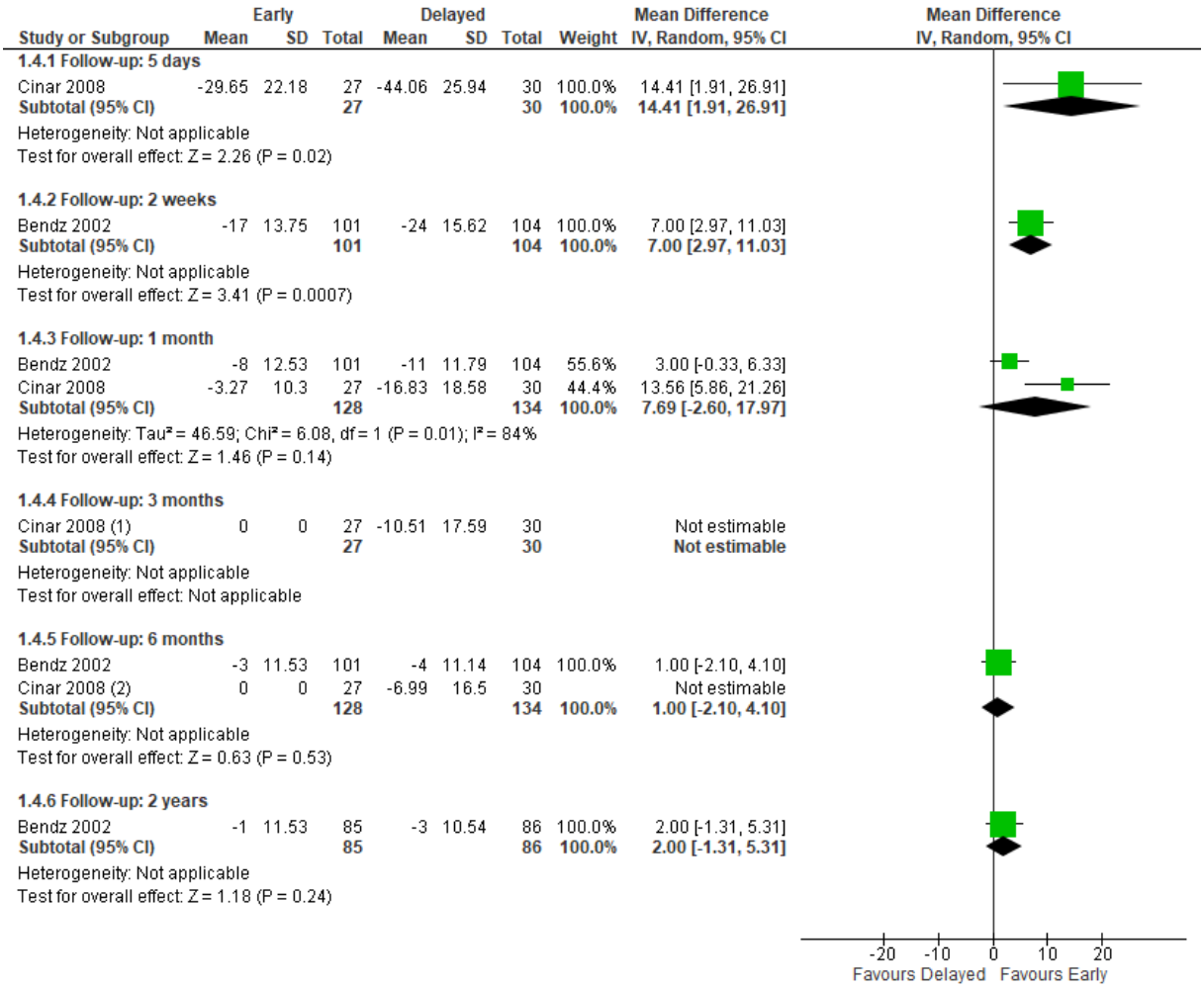
Figure 3 Range of movement: shoulder internal rotation in degrees



Footnotes
(1) Study reported SD as 0.00. There was no variability. Mean difference could not be estimated
(2) Study reported SD as 0.00. There was no variability. Mean difference could not be estimated

Change from baseline calculated by reviewer

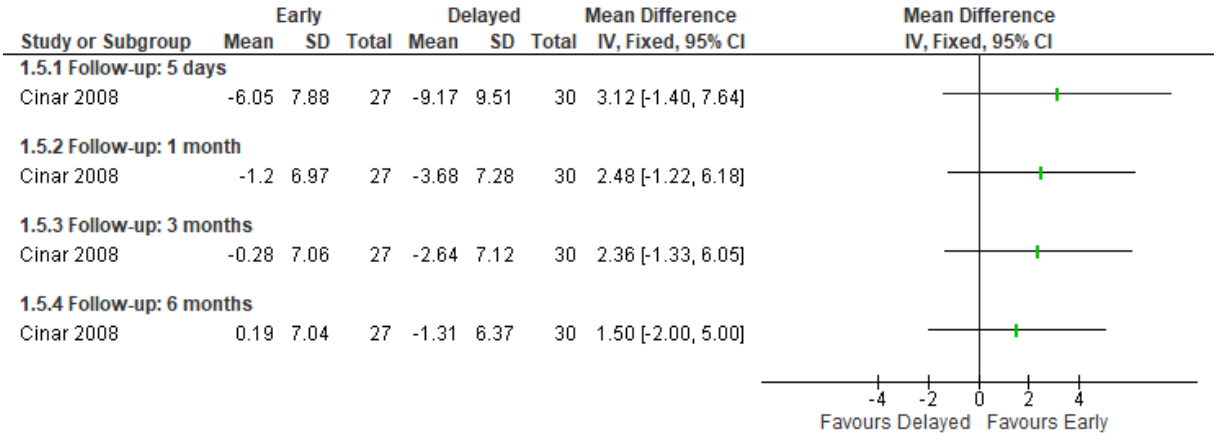
Figure 4 Range of movement: shoulder external rotation in degrees



Footnotes
(1) Study reported SD as 0.00. There was no variability. Mean difference could not be estimated
(2) Study reported SD as 0.00. There was no variability. Mean difference could not be estimated

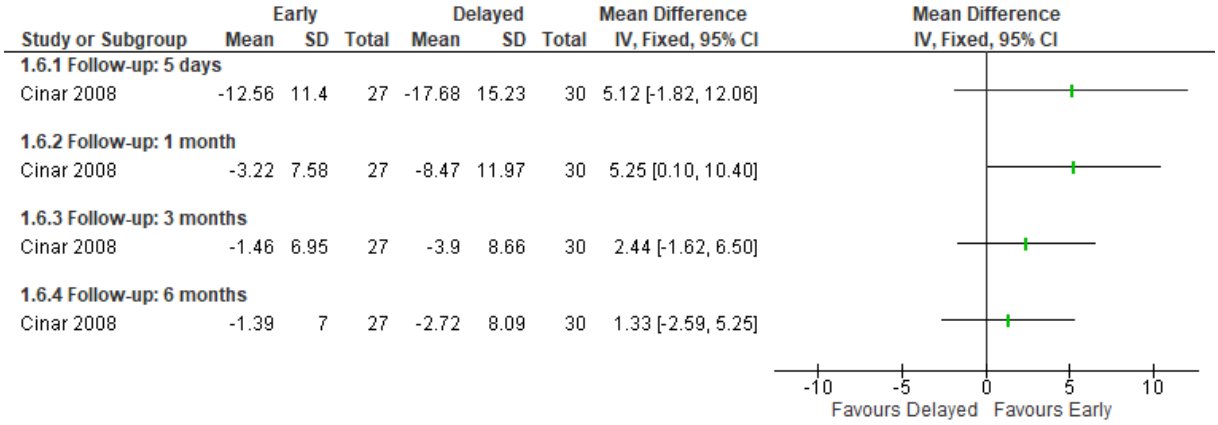
Change from baseline calculated by reviewer

Figure 5 Range of movement: shoulder adduction in degrees



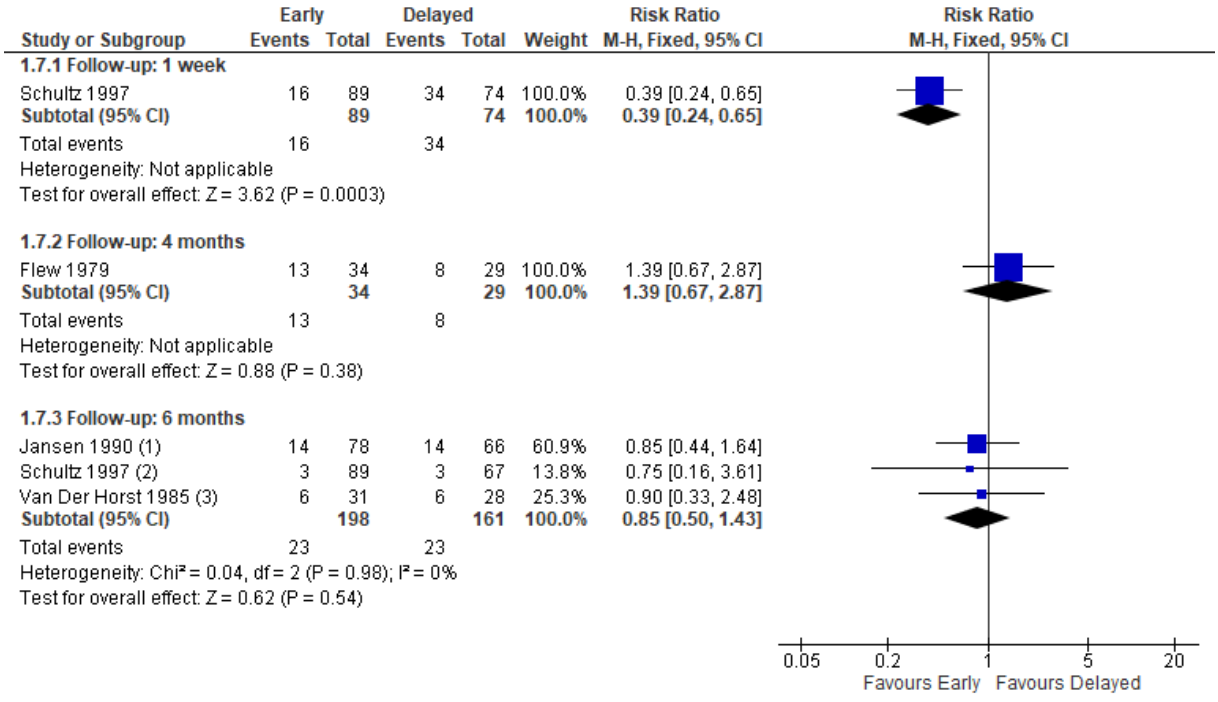
Change from baseline calculated by reviewer

Figure 6 Range of movement: shoulder extension in degrees



Change from baseline calculated by reviewer

Figure 7 Impaired shoulder mobility



Footnotes
(1) reported as percentages by Jansen 1990
(2) Data taken from McNeely 2010
(3) Data taken from McNeely 2010

Figure 8 Pain (mild or moderate)

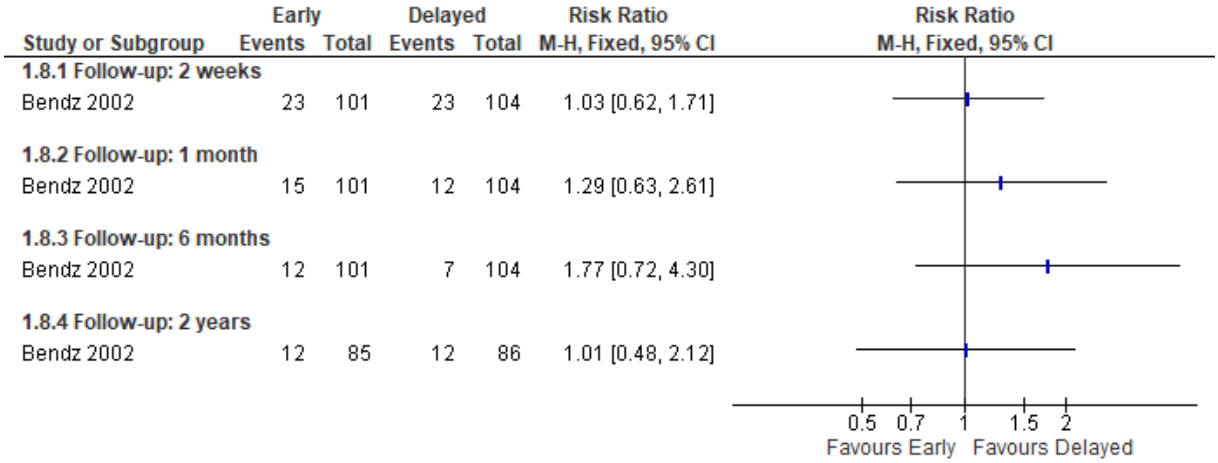
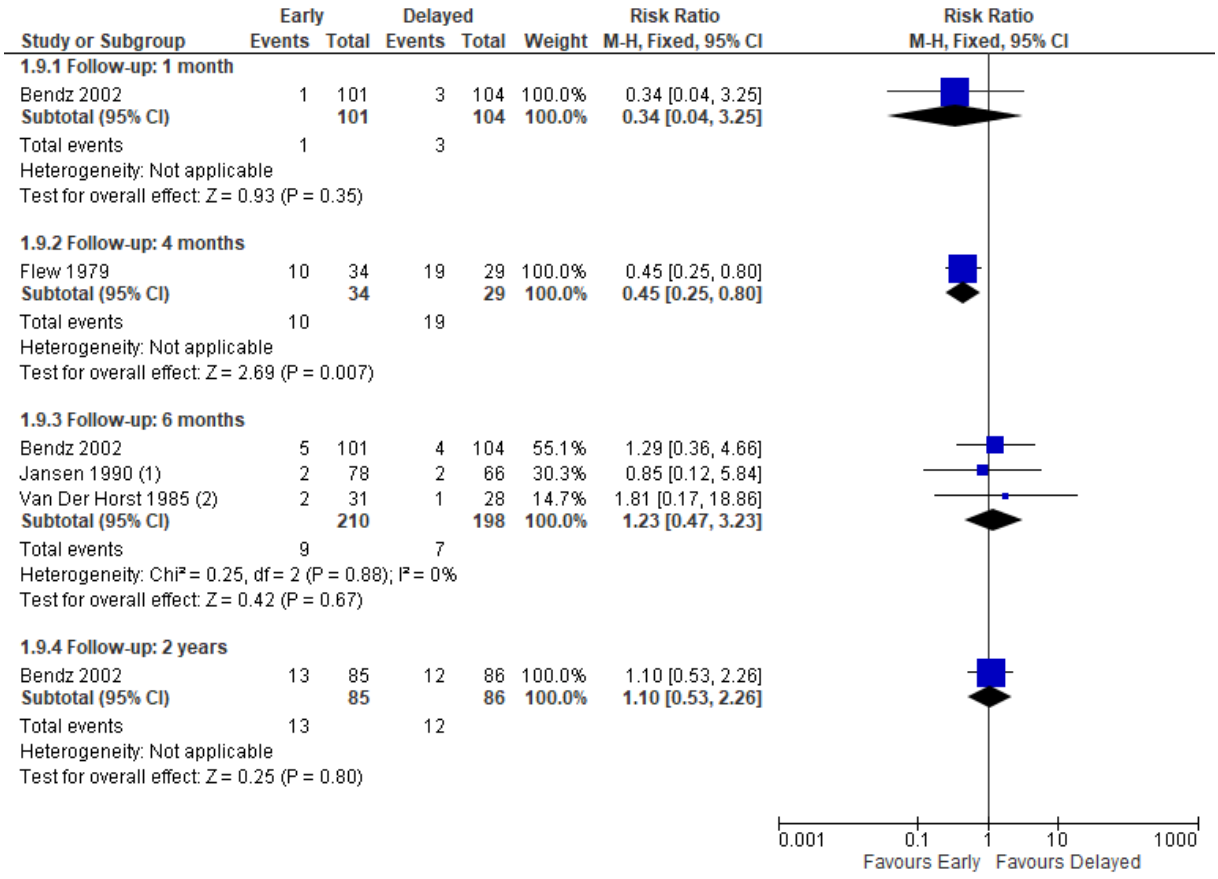


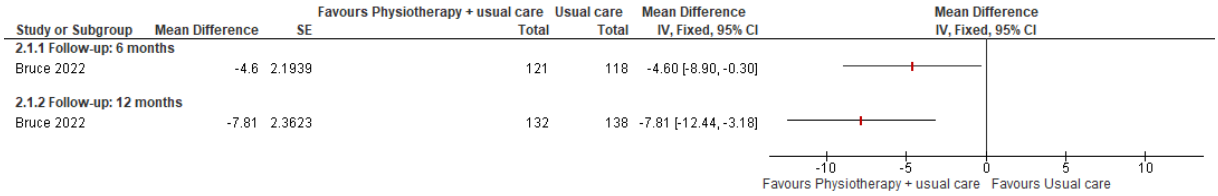
Figure 9 Incidence of lymphoedema



Footnotes
(1) reported as percentages by Jansen 1990
(2) Data taken from McNeely 2010

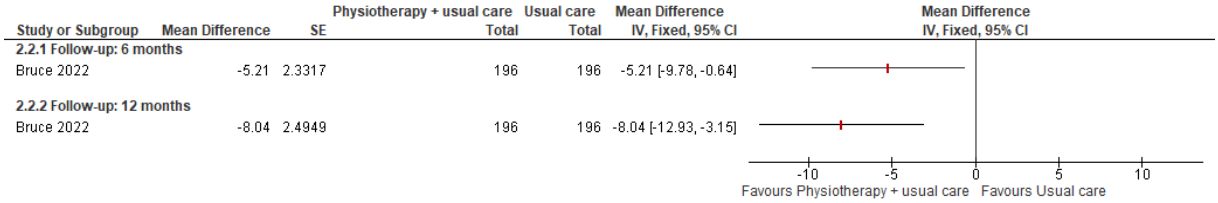
Physiotherapy and usual care compared to usual care

Figure 10 Upper limb function: DASH overall score



Change from baseline calculated by reviewer

Figure 11 Upper limb function: DASH activity limitation score



Change from baseline calculated by reviewer

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

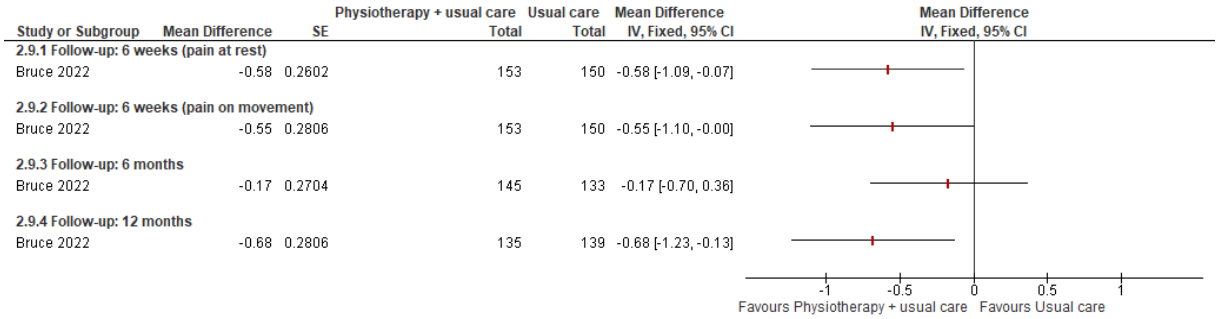
Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Upper limb muscle strength: shoulder flexion in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder abduction in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder external rotation in kg (1 RCT without multiple time points)

Figure 12 Pain numerical rating scale (0 to 10)



Change from baseline calculated by reviewer

Figure 13 Neuropathic pain: DN4 (≥ 4 indicative of neuropathic pain)

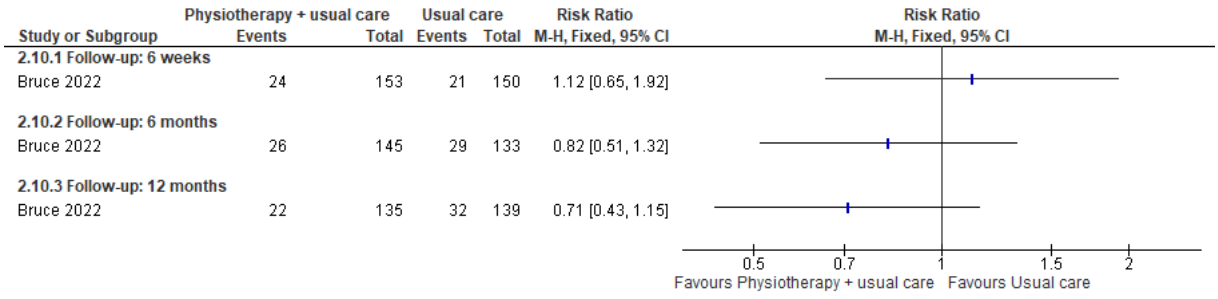
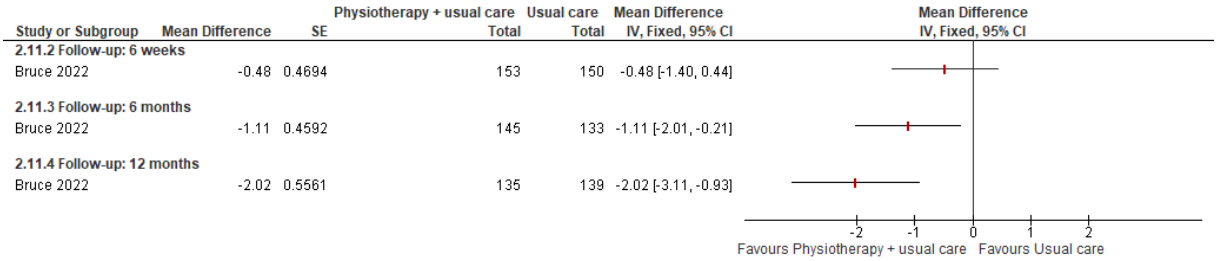


Figure 14 Pain: FACT-B4 (arm symptom scale, 0 to 4)



Change from baseline calculated by reviewer

Figure 15 Incidence of lymphoedema

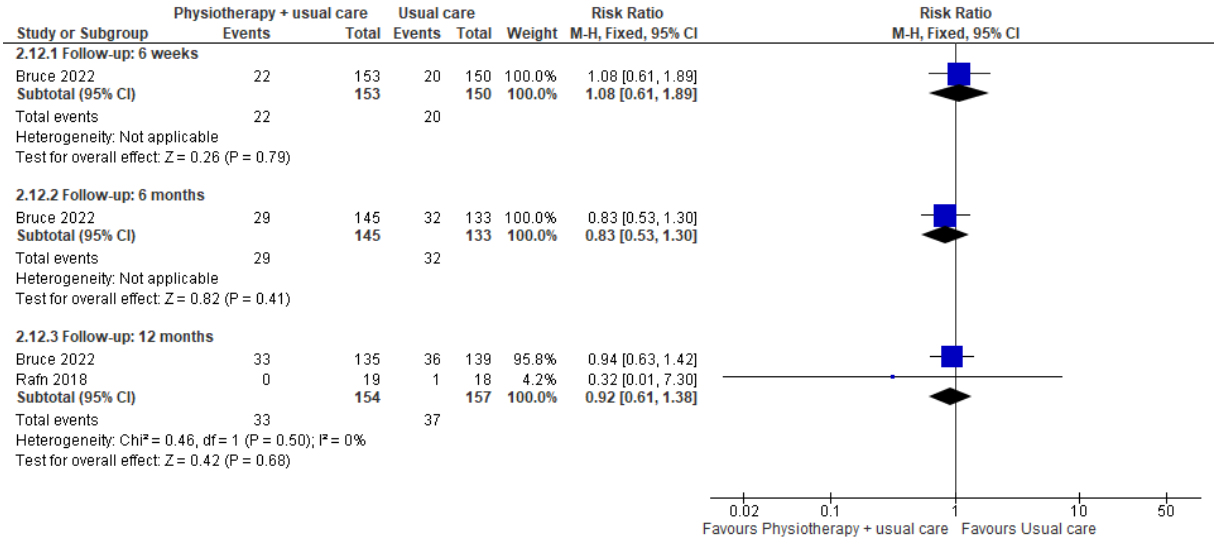
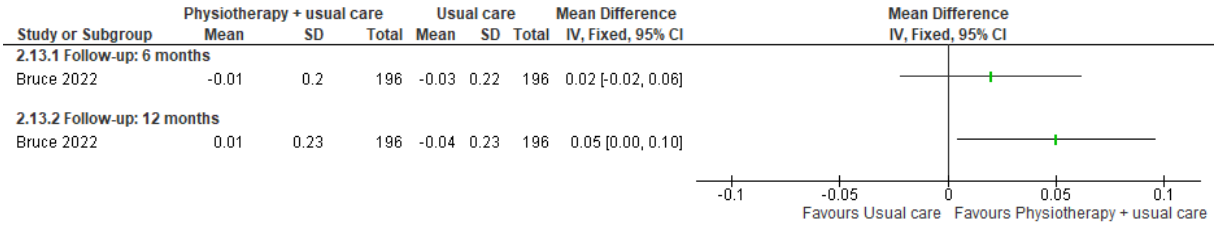
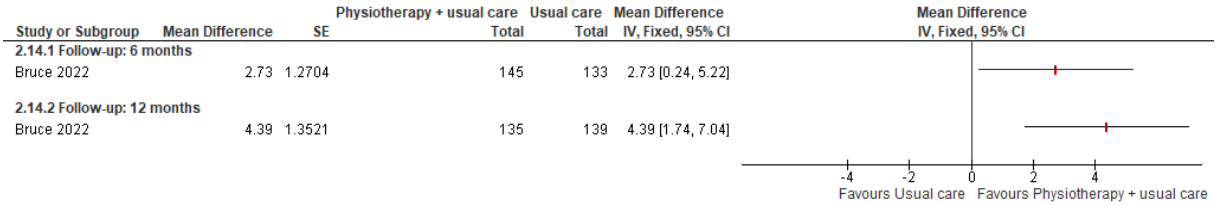


Figure 16 Quality of life: EQ-5D-5L



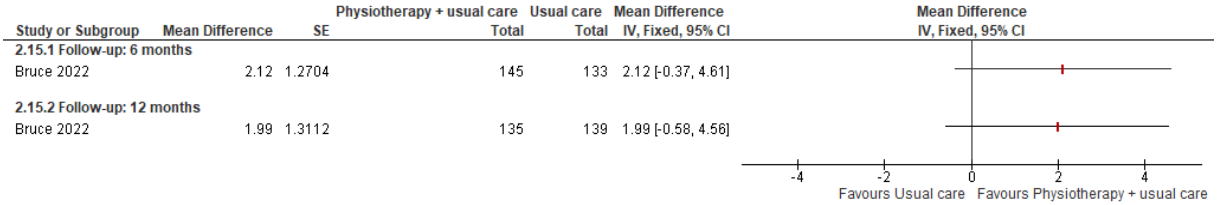
Change from baseline calculated by reviewer

Figure 17 Quality of life: SF-12 physical health composite scale



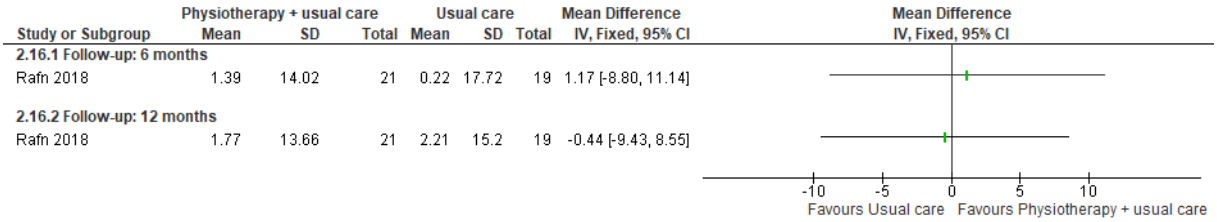
Change from baseline calculated by reviewer

Figure 18 Quality of life: SF-12 mental health composite scale



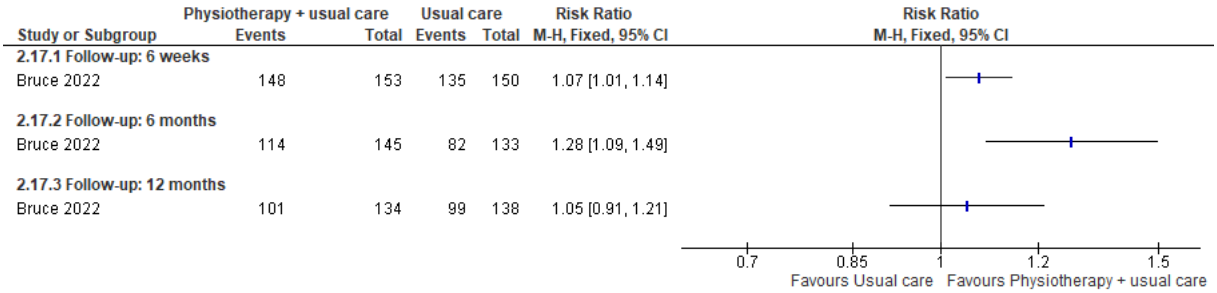
Change from baseline calculated by reviewer

Figure 19 Quality of life: FACT-B+4 overall score



Change from baseline calculated by reviewer

Figure 20 Adherence: number of participants doing arm or shoulder exercises

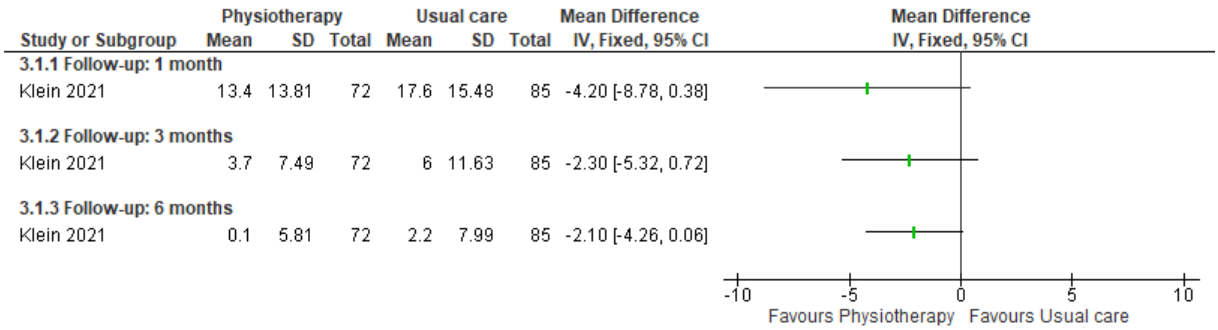


Change from baseline calculated by reviewer

Adherence: number of participants attending physiotherapy sessions (1 RCT without multiple time points)

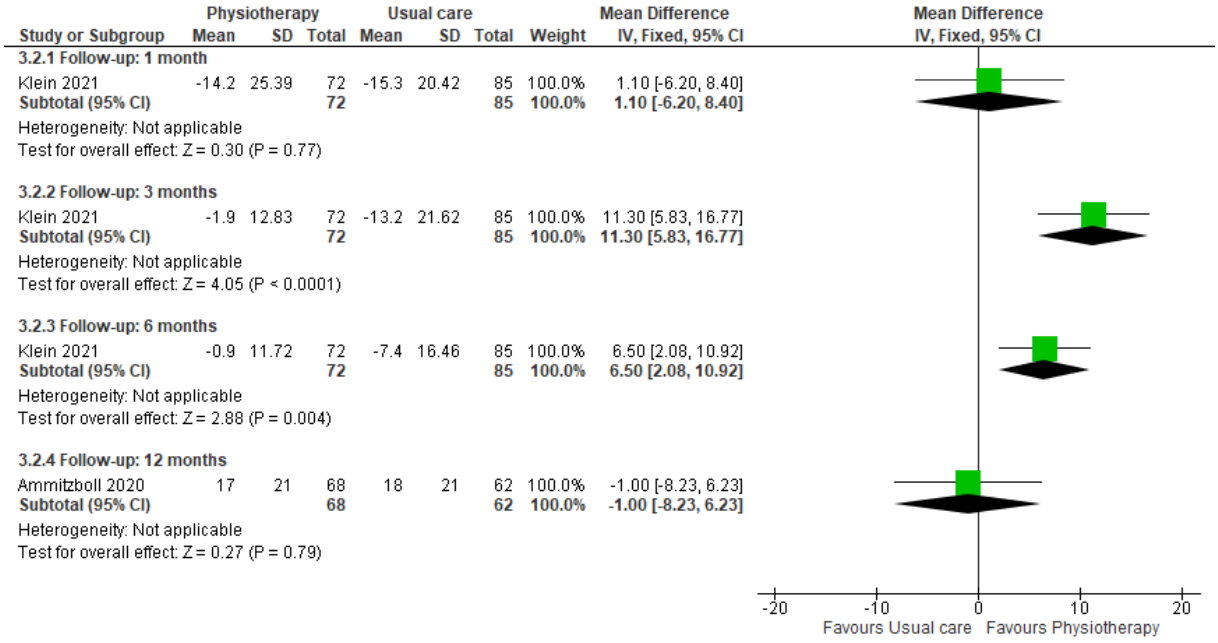
Physiotherapy (exercise programme) compared to usual care

Figure 21 Upper limb function: QuickDASH overall score



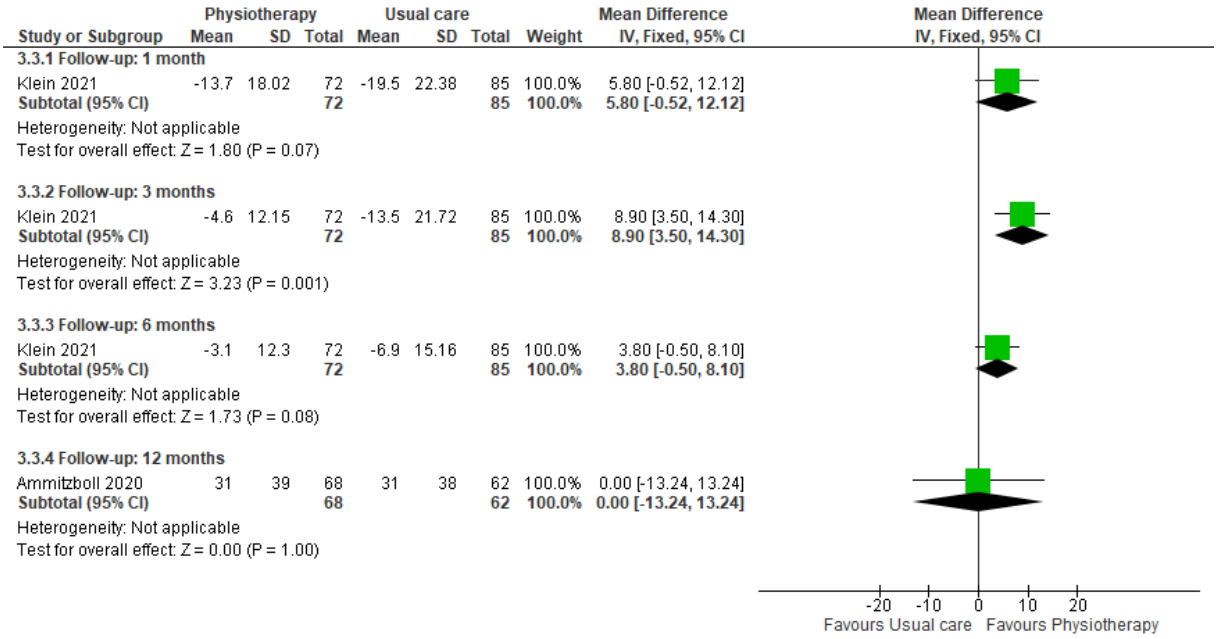
Change from baseline calculated by reviewer

Figure 22 Range of movement: shoulder flexion in degrees



Change from baseline calculated by reviewer

Figure 23 Range of movement: shoulder abduction in degrees

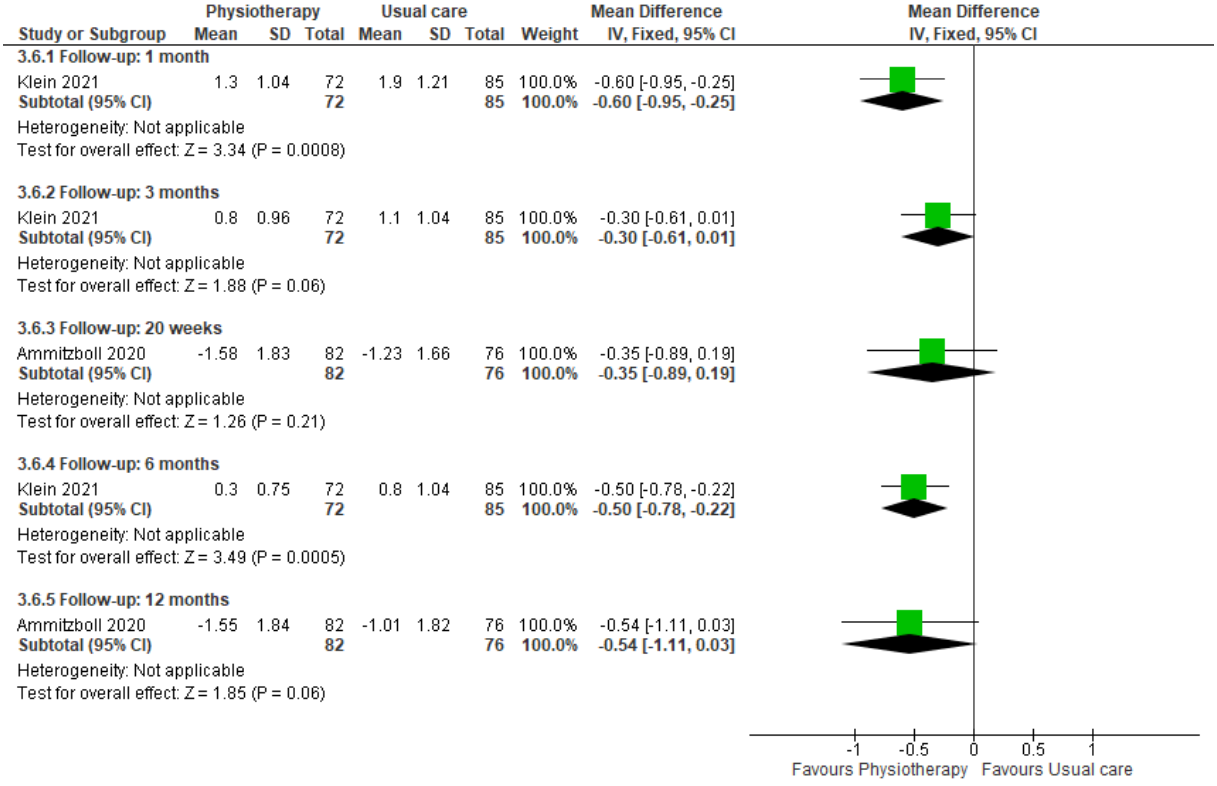


Change from baseline calculated by reviewer

Range of movement: shoulder external rotation (ipsilateral) in degrees (1 RCT without multiple time points)

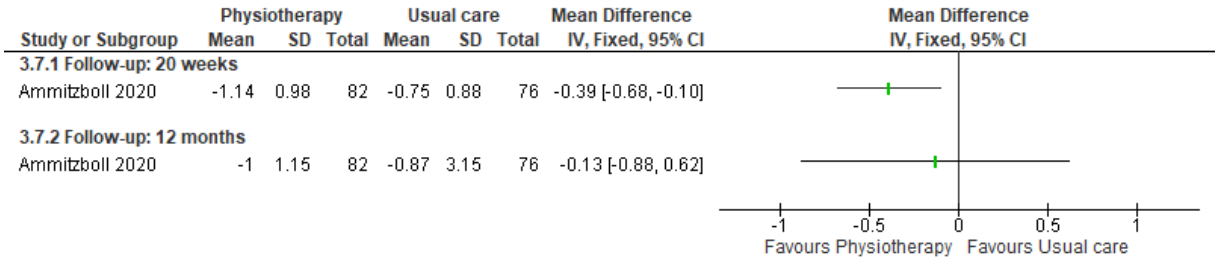
Upper limb muscle strength (dynamic muscle strength): shoulder abduction (ipsilateral) in kg (1 RCT without multiple time points)

Figure 24 Pain: numerical rating scale (0 to 10)



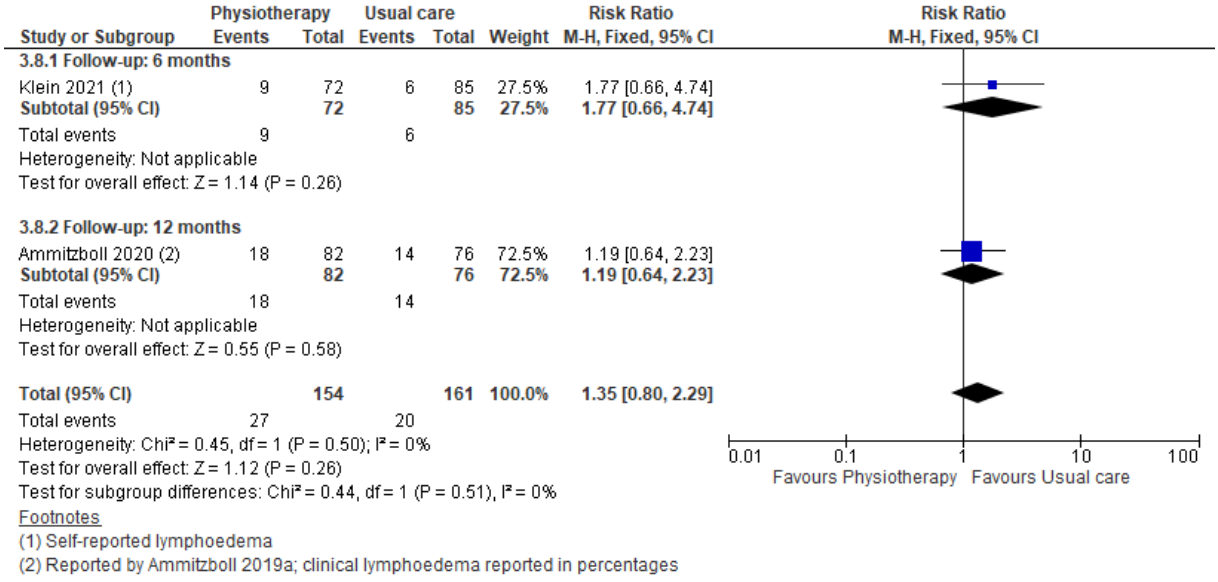
Change from baseline calculated by reviewer

Figure 25 Neuropathic pain: NeuPPS (0 to 5)



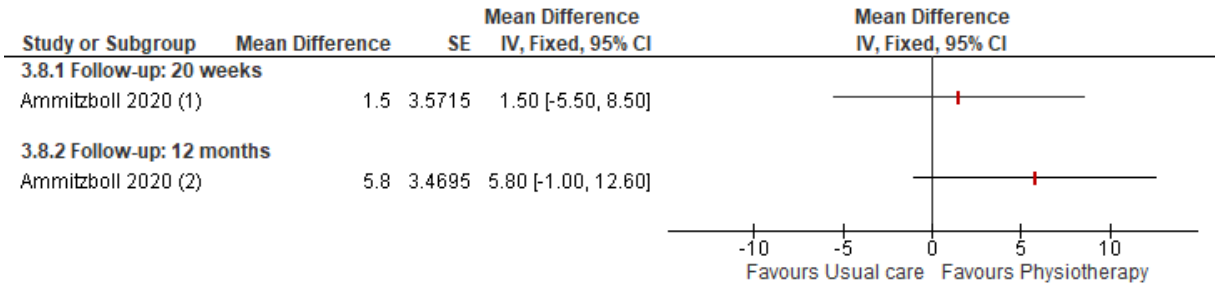
Change from baseline calculated by reviewer

Figure 26 Incidence of lymphoedema



Footnotes
(1) Self-reported lymphoedema
(2) Reported by Ammitzboll 2019a; clinical lymphoedema reported in percentages

Figure 27 Quality of life: EORTC-C30 (global health scale)



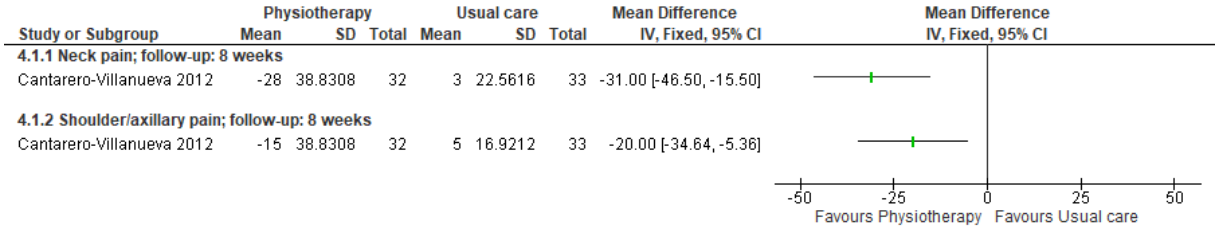
Footnotes
(1) Reported by Ammitzboll 2019b
(2) Reported by Ammitzboll 2019b

Change from baseline calculated by reviewer

Adherence: any regular exercise (on a weekly basis) in the study period (1 RCT without multiple time points)

Physiotherapy (water exercise programme) compared to usual care

Figure 28 Pain: visual analogue scale (0 to 100)



Change from baseline calculated by reviewer

Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) compared to usual care

Upper limb function: DASH overall score (1 RCT without multiple time points)

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Upper limb muscle strength: shoulder flexion in kg (1 RCT without multiple time points)

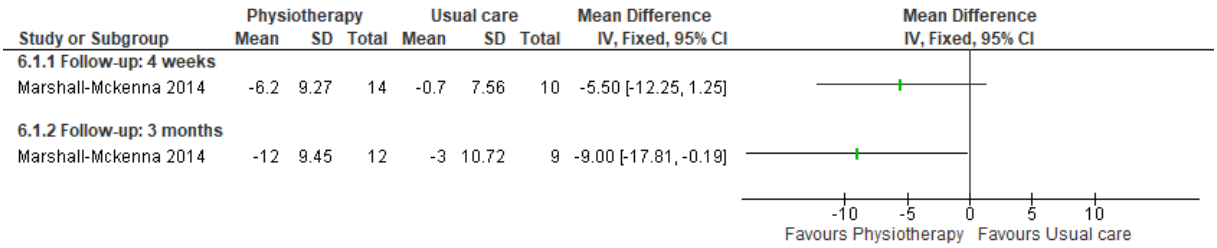
Upper limb muscle strength: shoulder abduction in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder external rotation in kg (1 RCT without multiple time points)

Pain: visual analogue scale (0 to 10) (1 RCT without multiple time points)

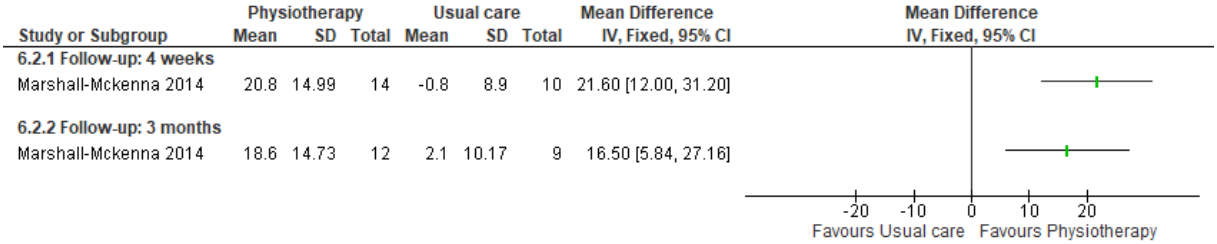
Physiotherapy (myofascial release massage) compared to usual care

Figure 29 Upper limb function: DASH overall score



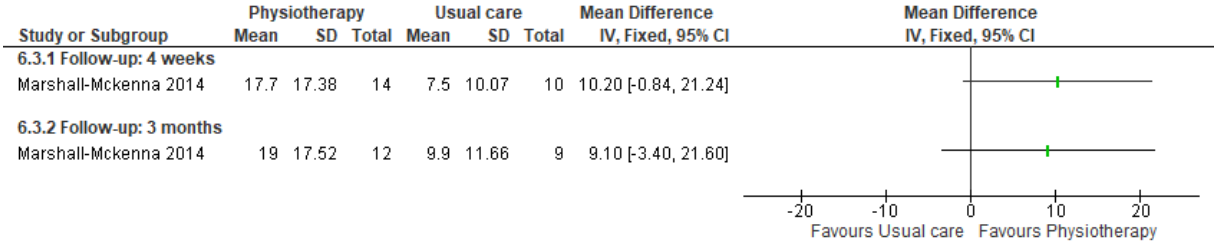
Change from baseline calculated by reviewer

Figure 30 Range of movement: shoulder abduction in degrees



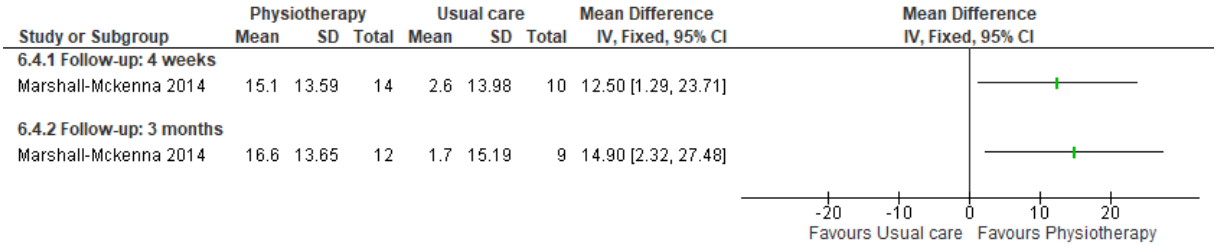
Change from baseline calculated by reviewer

Figure 31 Range of movement: shoulder flexion in degrees



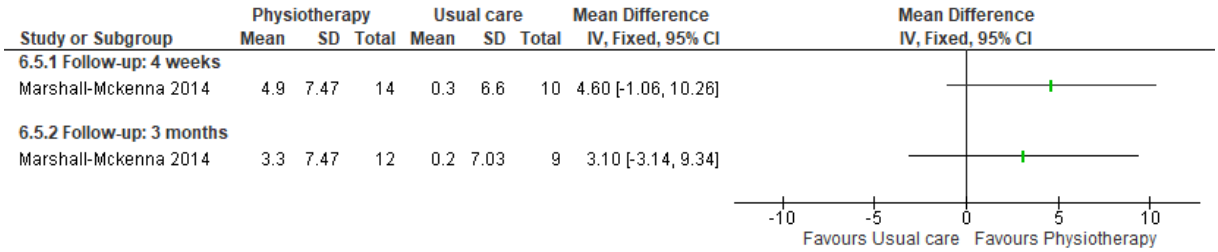
Change from baseline calculated by reviewer

Figure 32 Range of movement: shoulder external rotation in degrees



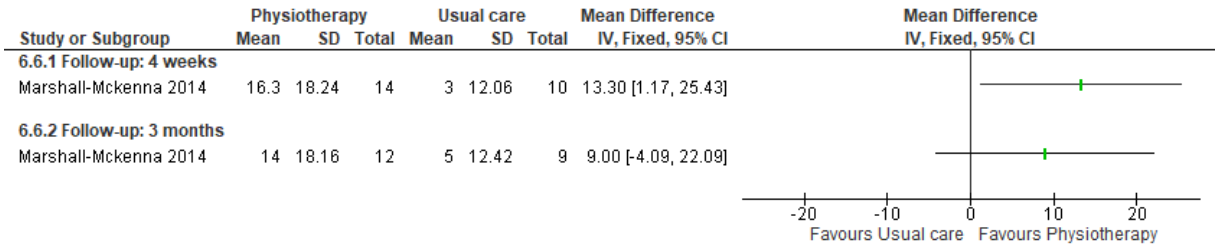
Change from baseline calculated by reviewer

Figure 33 Range of movement: shoulder internal rotation in degrees



Change from baseline calculated by reviewer

Figure 34 Range of movement: combination movement of abduction/flexion/external rotation in degrees



Change from baseline calculated by reviewer

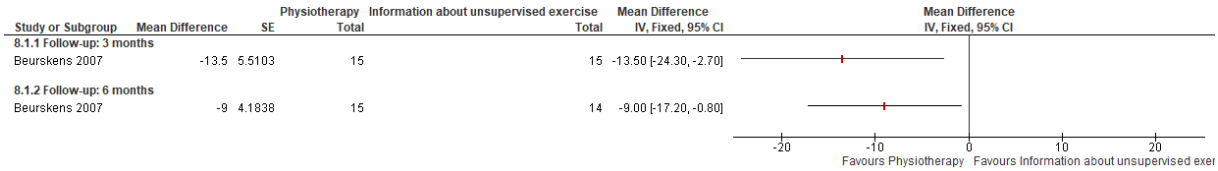
Physiotherapy (group-based educational program and visual material) compared to usual care

Pain: visual analogue scale (0 to 10) (1 RCT without multiple time points)

Adherence to advice provided during interventions: ≥80% (1 RCT without multiple time points)

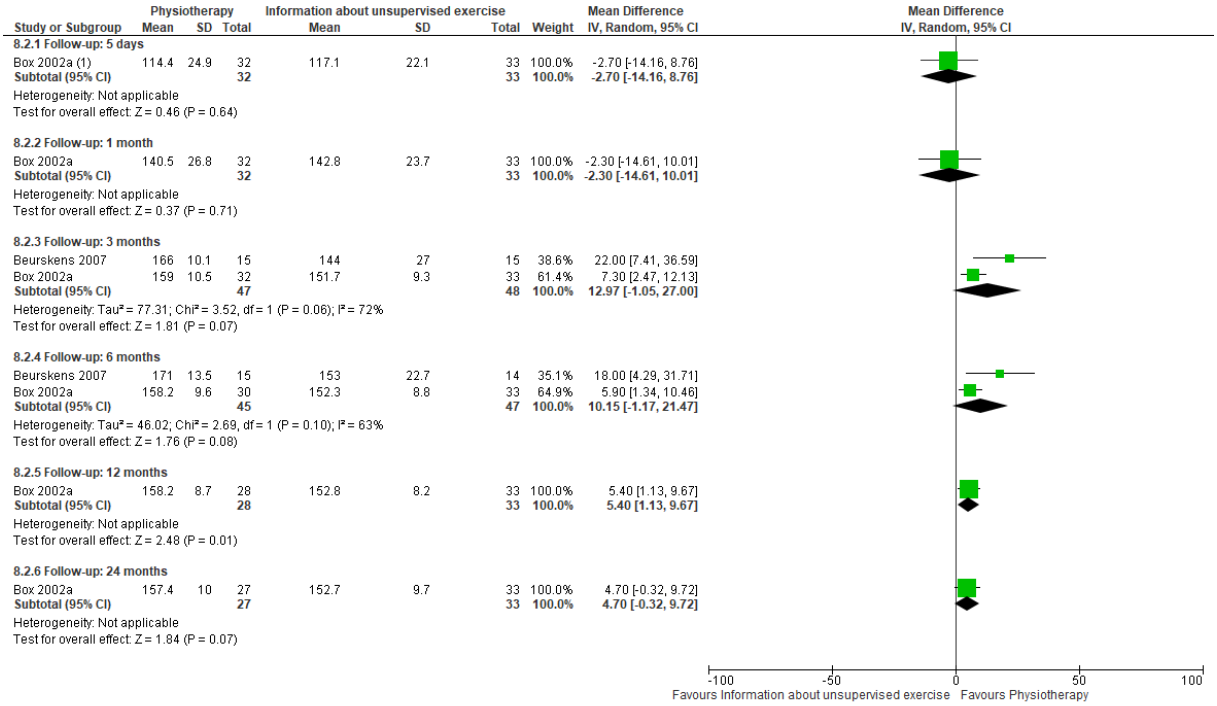
Physiotherapy compared to information about unsupervised exercise

Figure 35 Upper limb function: DASH overall score



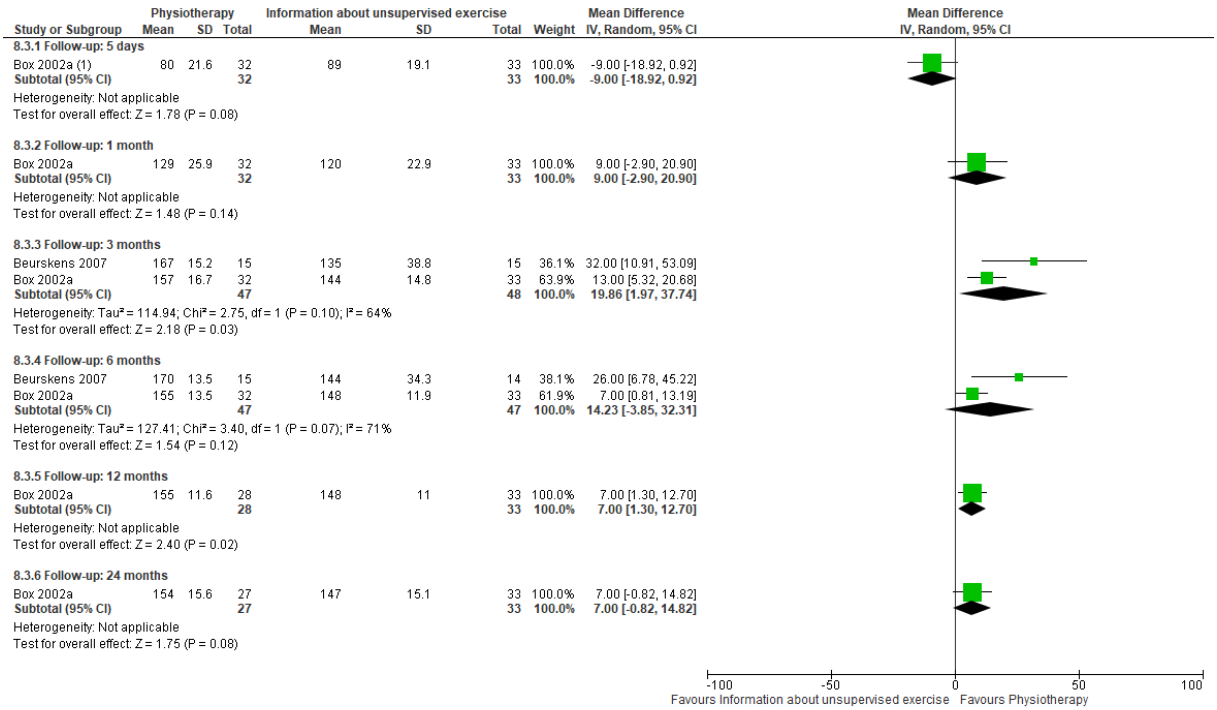
Change from baseline calculated by reviewer

Figure 36 Range of movement: shoulder flexion in degrees at follow-up



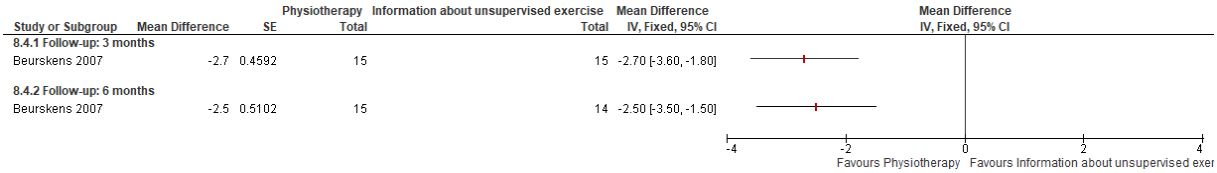
Footnotes
(1) Data for all time points for Box 2002a was taken from McNeely 2010

Figure 37 Range of movement: shoulder abduction in degrees at follow-up



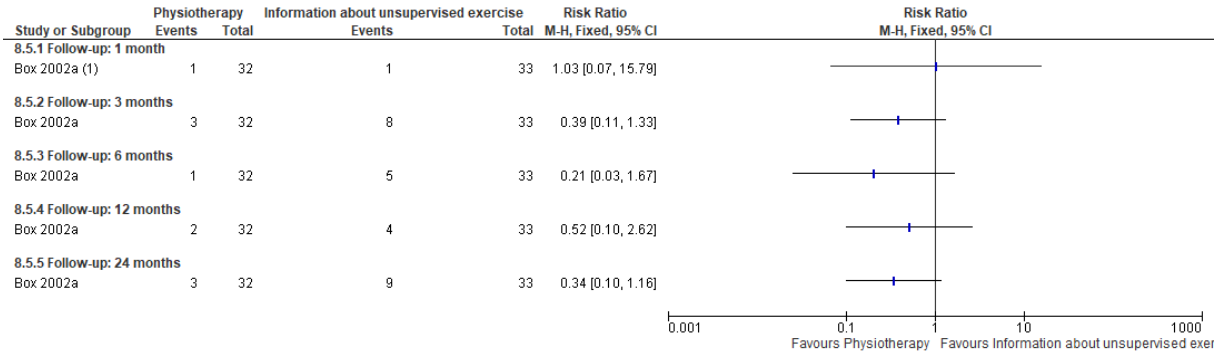
Footnotes
(1) Data for all time points for Box 2002a was taken from McNeely 2010

Figure 38 Pain: visual analogue scale (0 to 10)



Change from baseline calculated by reviewer

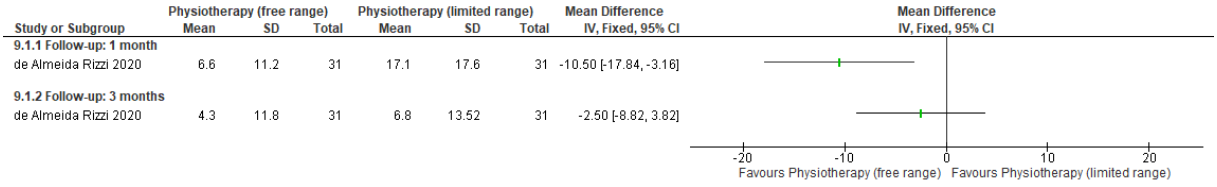
Figure 39 Incidence of lymphoedema: increase of >200ml



Footnotes
(1) Data for all time points for Box 2002a was taken from McNeely 2010

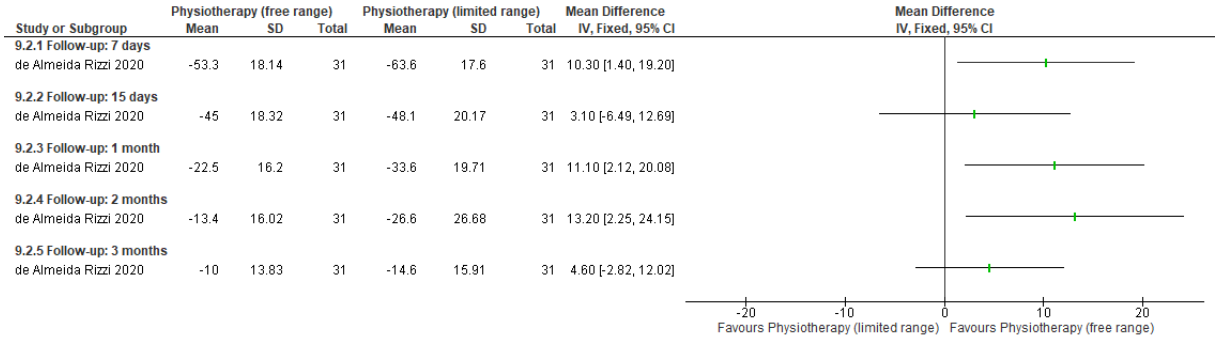
Physiotherapy (free-range exercises) compared to physiotherapy (limited-range exercises)

Figure 40 Upper limb function: DASH overall score



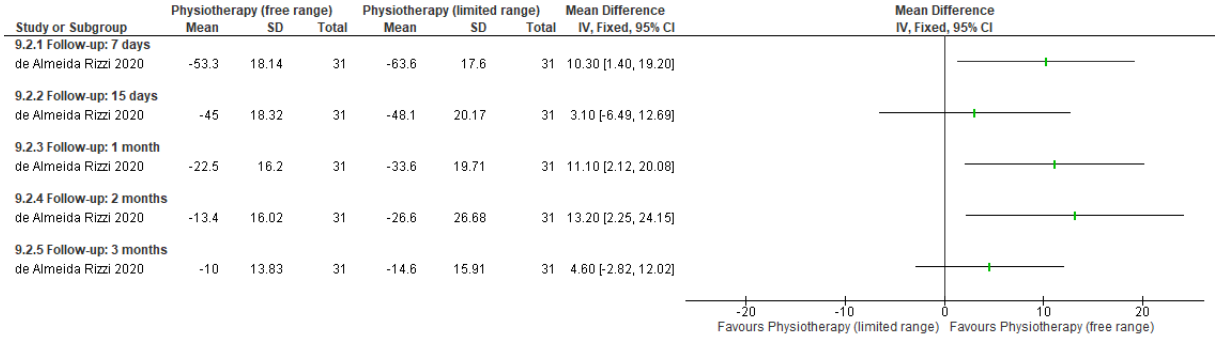
Change from baseline calculated by reviewer

Figure 41 Range of movement: shoulder flexion in degrees



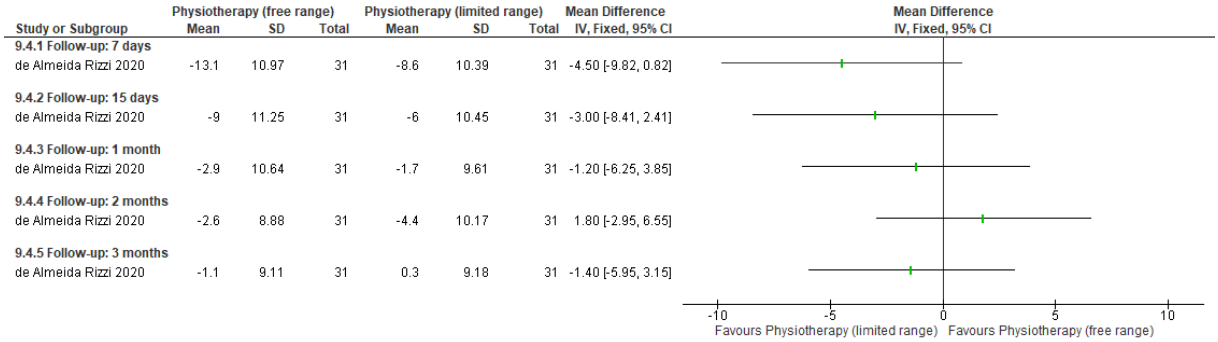
Change from baseline calculated by reviewer

Figure 42 Range of movement: shoulder abduction in degrees



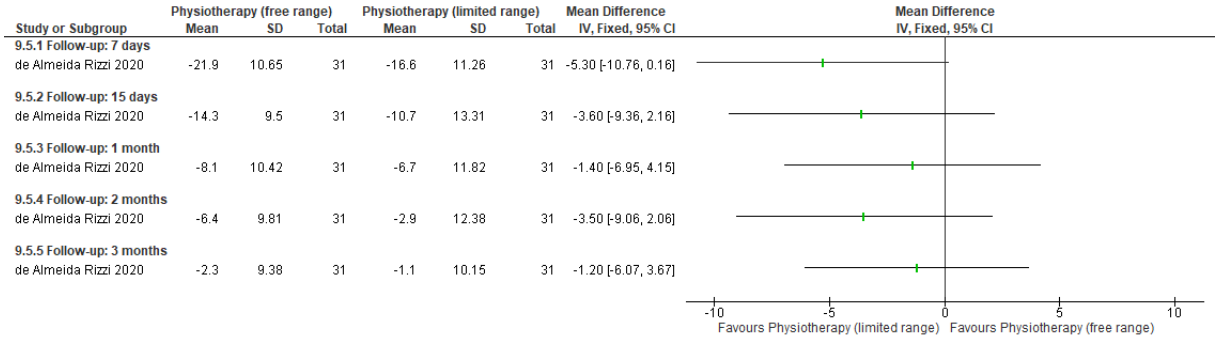
Change from baseline calculated by reviewer

Figure 43 Range of movement: shoulder extension in degrees



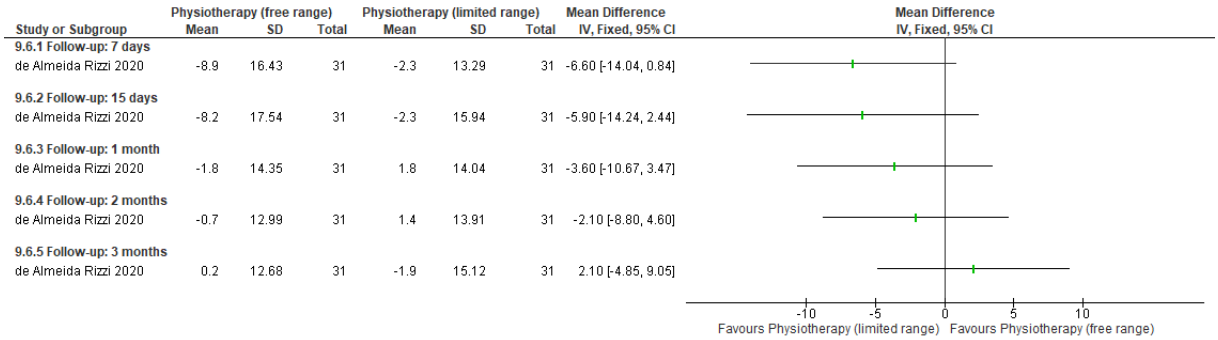
Change from baseline calculated by reviewer

Figure 44 Range of movement: shoulder adduction in degrees



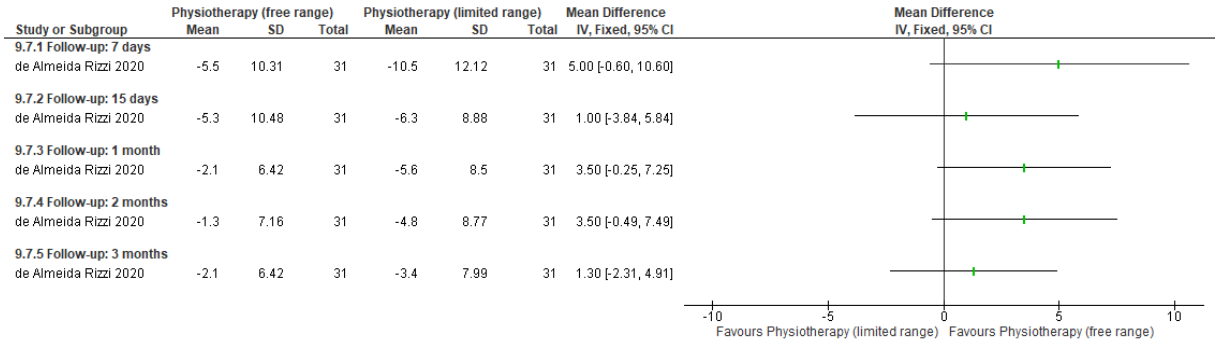
Change from baseline calculated by reviewer

Figure 45 Range of movement: shoulder internal rotation in degrees



Change from baseline calculated by reviewer

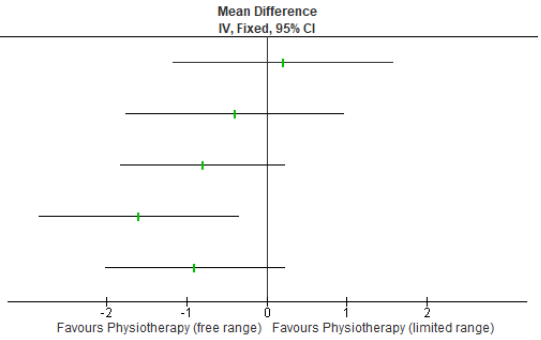
Figure 46 Range of movement: shoulder external rotation in degrees



Change from baseline calculated by reviewer

Figure 47 Pain: visual analogue scale (0 to 10)

Study or Subgroup	Physiotherapy (free range) Mean	SD	Total	Physiotherapy (limited range) Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
9.8.1 Follow-up: 7 days							
de Almeida Rizzi 2020	2.4	2.51	31	2.2	2.99	31	0.20 [-1.17, 1.57]
9.8.2 Follow-up: 15 days							
de Almeida Rizzi 2020	1.8	2.6	31	2.2	2.84	31	-0.40 [-1.76, 0.96]
9.8.3 Follow-up: 1 month							
de Almeida Rizzi 2020	0.3	1.71	31	1.1	2.36	31	-0.80 [-1.83, 0.23]
9.8.4 Follow-up: 2 months							
de Almeida Rizzi 2020	0.6	1.45	31	2.2	3.22	31	-1.60 [-2.84, -0.36]
9.8.5 Follow-up: 3 months							
de Almeida Rizzi 2020	0.2	1.78	31	1.1	2.62	31	-0.90 [-2.02, 0.22]

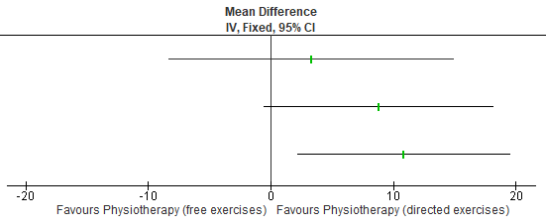


Change from baseline calculated by reviewer

Physiotherapy (directed exercises) compared to physiotherapy (free exercises)

Figure 48 Range of movement: shoulder flexion in degrees

Study or Subgroup	Physiotherapy (directed exercises) Mean	SD	Total	Physiotherapy (free exercises) Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
10.1.1 Follow-up: 14 days							
De Rezende 2006	-50.9	25.08	30	-54.2	20.55	30	3.30 [-8.30, 14.90]
10.1.2 Follow-up: 28 days							
De Rezende 2006	-30.9	20.01	30	-39.7	16.82	30	8.80 [-0.55, 18.15]
10.1.3 Follow-up: 42 days							
De Rezende 2006	-19	18.7	30	-29.8	15.33	30	10.80 [2.15, 19.45]



Change from baseline calculated by reviewer

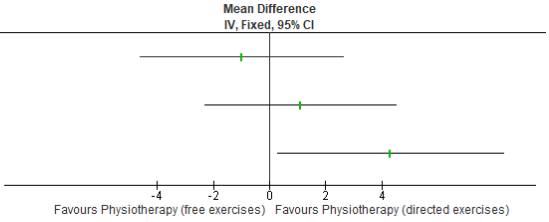
Figure 49 Range of movement: shoulder abduction in degrees

Study or Subgroup	Physiotherapy (directed exercises) Mean	SD	Total	Physiotherapy (free exercises) Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
10.2.1 Follow-up: 14 days							
De Rezende 2006	-73.1	18.39	30	-76.3	19.02	30	3.20 [-6.27, 12.67]
10.2.2 Follow-up: 28 days							
De Rezende 2006	-52	22.44	30	-62.7	20.29	30	10.70 [-0.13, 21.53]
10.2.3 Follow-up: 42 days							
De Rezende 2006	-34.7	23.4	30	-49.7	20.38	30	15.00 [3.90, 26.10]

Change from baseline calculated by reviewer

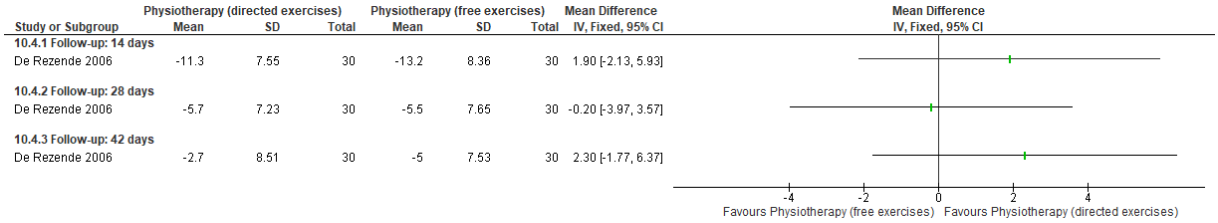
Figure 50 Range of movement: shoulder extension in degrees

Study or Subgroup	Physiotherapy (directed exercises) Mean	SD	Total	Physiotherapy (free exercises) Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
10.3.1 Follow-up: 14 days							
De Rezende 2006	-4.5	7.87	30	-3.5	6.34	30	-1.00 [-4.62, 2.62]
10.3.2 Follow-up: 28 days							
De Rezende 2006	-0.6	6.84	30	-1.7	6.56	30	1.10 [-2.29, 4.49]
10.3.3 Follow-up: 42 days							
De Rezende 2006	3.9	7.09	30	-0.4	8.75	30	4.30 [0.27, 8.33]



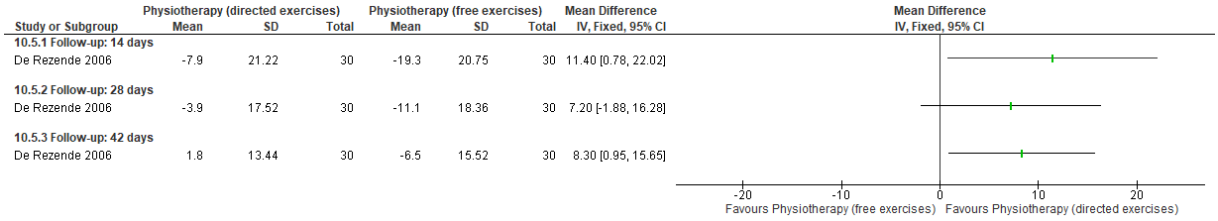
Change from baseline calculated by reviewer

Figure 51 Range of movement: shoulder adduction in degrees



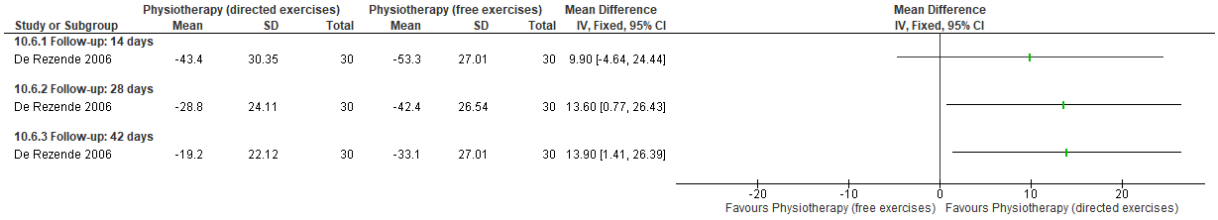
Change from baseline calculated by reviewer

Figure 52 Range of movement: shoulder internal rotation in degrees



Change from baseline calculated by reviewer

Figure 53 Range of movement: shoulder external rotation in degrees

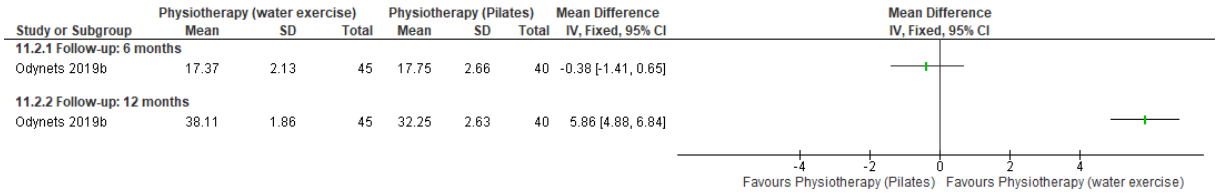


Change from baseline calculated by reviewer

Adherence: number of physiotherapy sessions (1 RCT without multiple time points)

Physiotherapy (water exercise) compared to physiotherapy (Pilates)

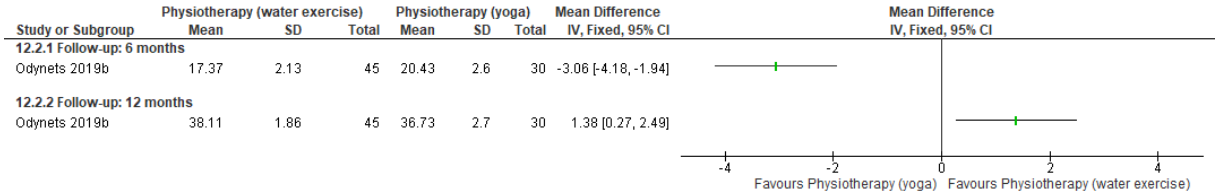
Figure 54 Quality of life: FACT-B4 overall score



Change from baseline calculated by reviewer

Physiotherapy (water exercise) compared to physiotherapy (yoga)

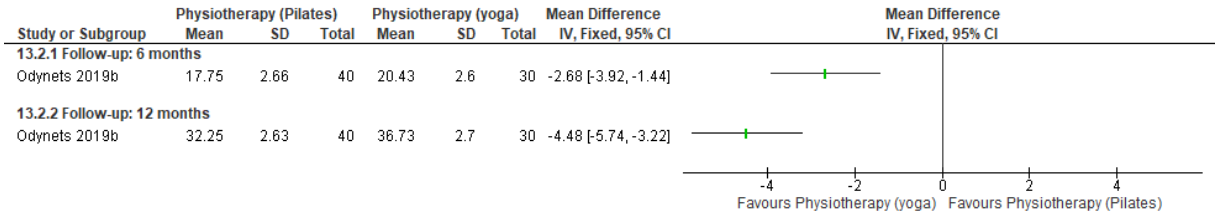
Figure 55 Quality of life: FACT-B4 overall score



Change from baseline calculated by reviewer

Physiotherapy (Pilates) compared to physiotherapy (yoga)

Figure 56 Quality of life: FACT-B4 overall score



Change from baseline calculated by reviewer

Physiotherapy (Pilates) compared to physiotherapy (combined exercises)

Upper limb function: DASH overall score (1 RCT without multiple time points)

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

Range of movement: shoulder internal rotation in degrees (1 RCT without multiple time points)

Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Upper limb muscle strength: shoulder flexion in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder abduction in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder internal rotation in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder external rotation in kg (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) motion (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) rest (1 RCT without multiple time points)

Physiotherapy (Pilates) compared to physiotherapy (home exercises)

Upper limb function: DASH overall score (1 RCT without multiple time points)

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

Range of movement: shoulder internal rotation in degrees (1 RCT without multiple time points)

Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Upper limb muscle strength: shoulder flexion in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder abduction in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder internal rotation in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder external rotation in kg (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) motion (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) rest (1 RCT without multiple time points)

Physiotherapy (combined exercises) compared to physiotherapy (home exercises)

Upper limb function: DASH overall score (1 RCT without multiple time points)

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

Range of movement: shoulder internal rotation in degrees (1 RCT without multiple time points)

Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Upper limb muscle strength: shoulder flexion in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder abduction in kg (1 RCT without multiple time points)

Upper limb muscle strength: shoulder internal rotation in kg (1 RCT without multiple time points)

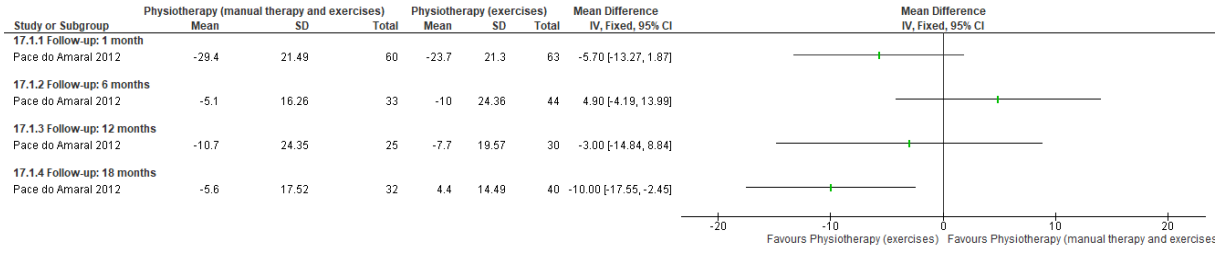
Upper limb muscle strength: shoulder external rotation in kg (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) motion (1 RCT without multiple time points)

Pain: numerical rating scale (0 to 10) rest (1 RCT without multiple time points)

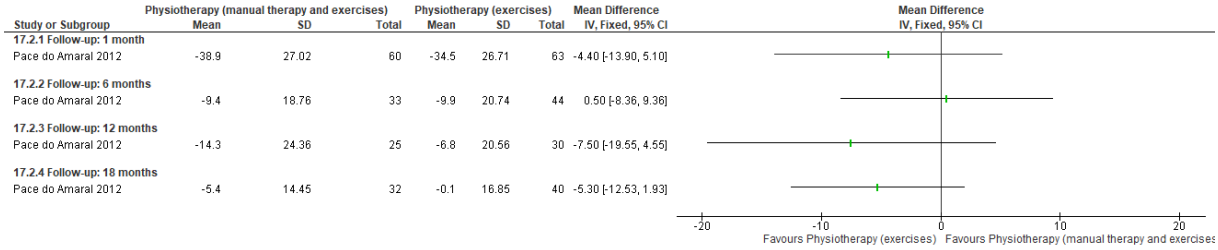
Physiotherapy (manual therapy and upper limb exercises) compared to Physiotherapy (upper limb exercises)

Figure 57 Range of movement: shoulder flexion in degrees



Change from baseline calculated by reviewer

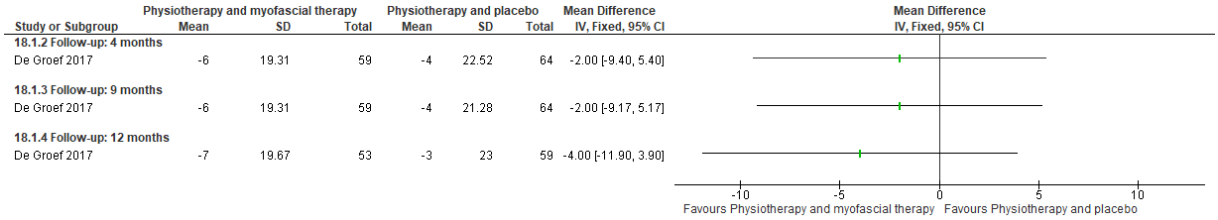
Figure 58 Range of movement: shoulder abduction in degrees



Change from baseline calculated by reviewer

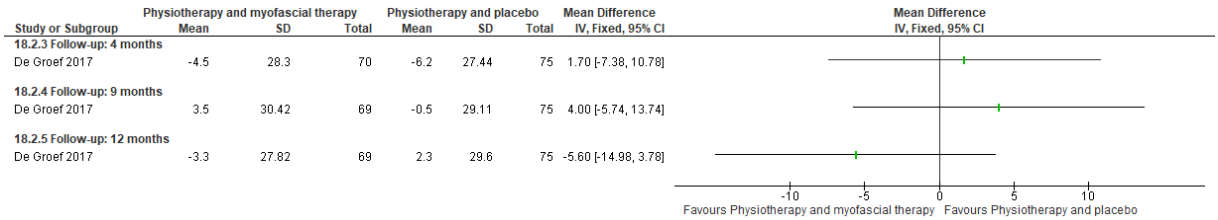
Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after surgery

Figure 59 Upper limb function: DASH overall score



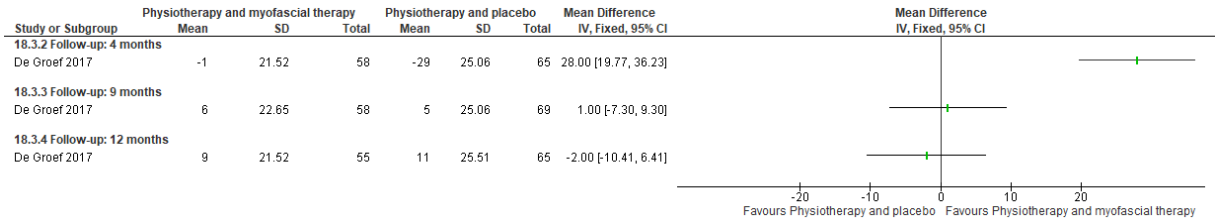
Change from baseline calculated by reviewer

Figure 60 Pain: visual analogue scale (0 to 100)



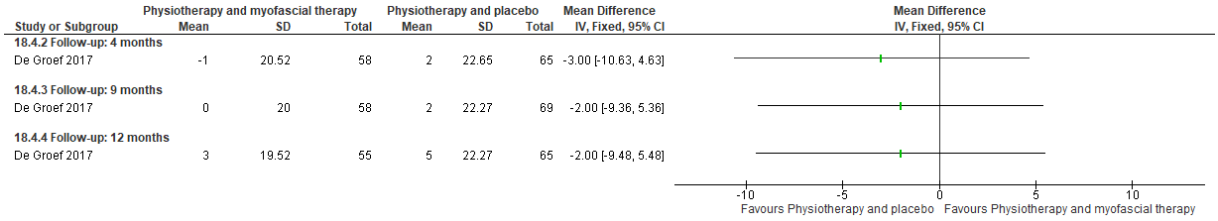
Change from baseline calculated by reviewer

Figure 61 Quality of life: SF-36 (physical functioning)



Change from baseline calculated by reviewer

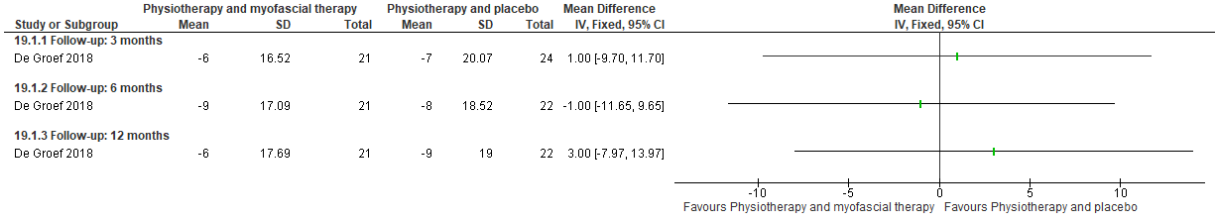
Figure 62 Quality of life: SF-36 (mental functioning)



Change from baseline calculated by reviewer

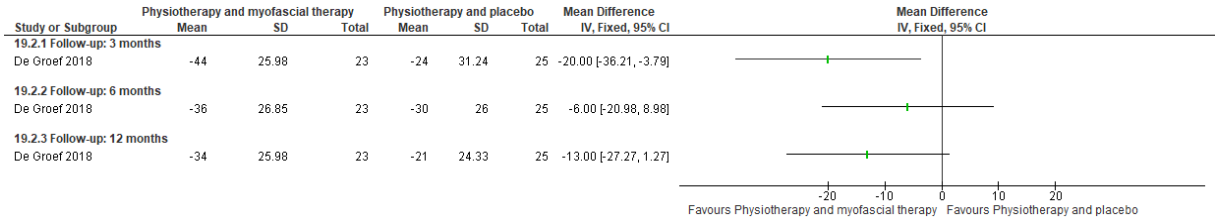
Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after radiotherapy

Figure 63 Upper limb function: DASH overall



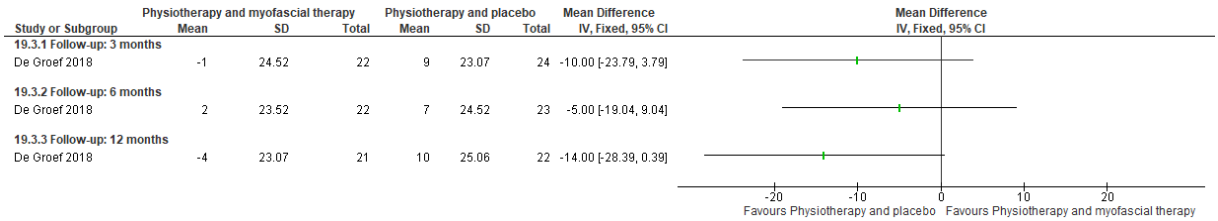
Change from baseline calculated by reviewer

Figure 64 Pain visual analogue scale (0 to 100)



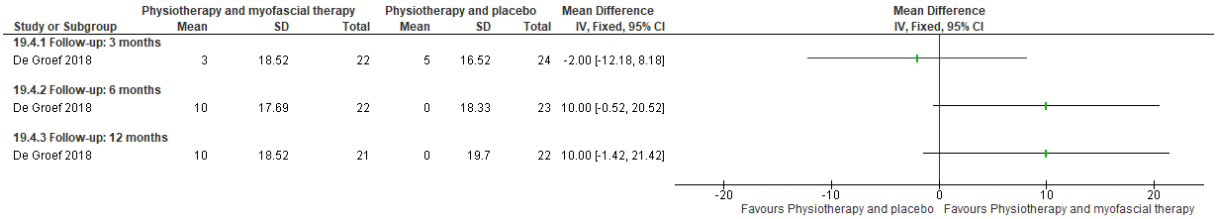
Change from baseline calculated by reviewer

Figure 65 Quality of life: SF-36 (physical functioning)



Change from baseline calculated by reviewer

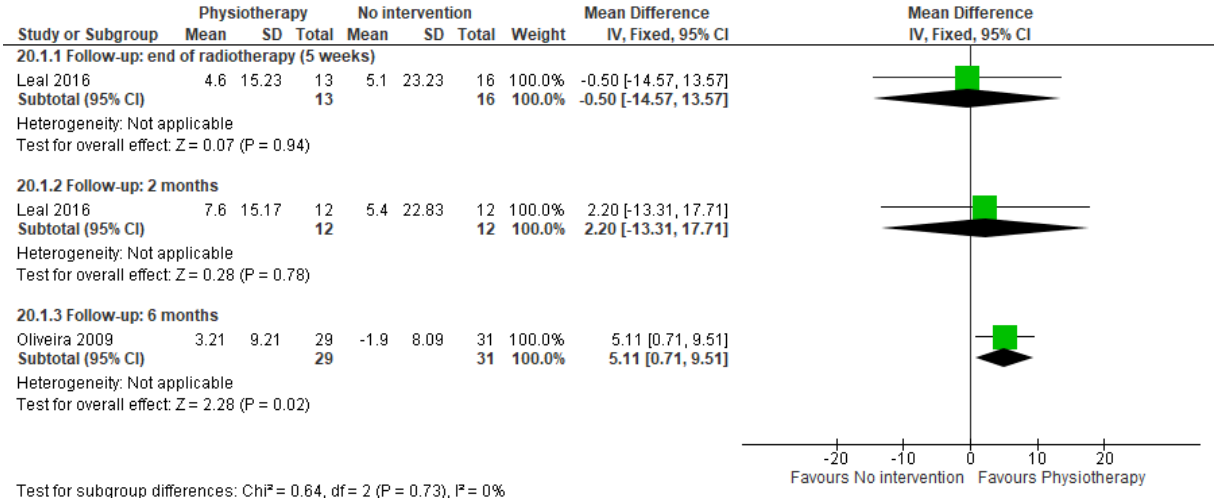
Figure 66 Quality of life: SF-36 (mental functioning)



Change from baseline calculated by reviewer

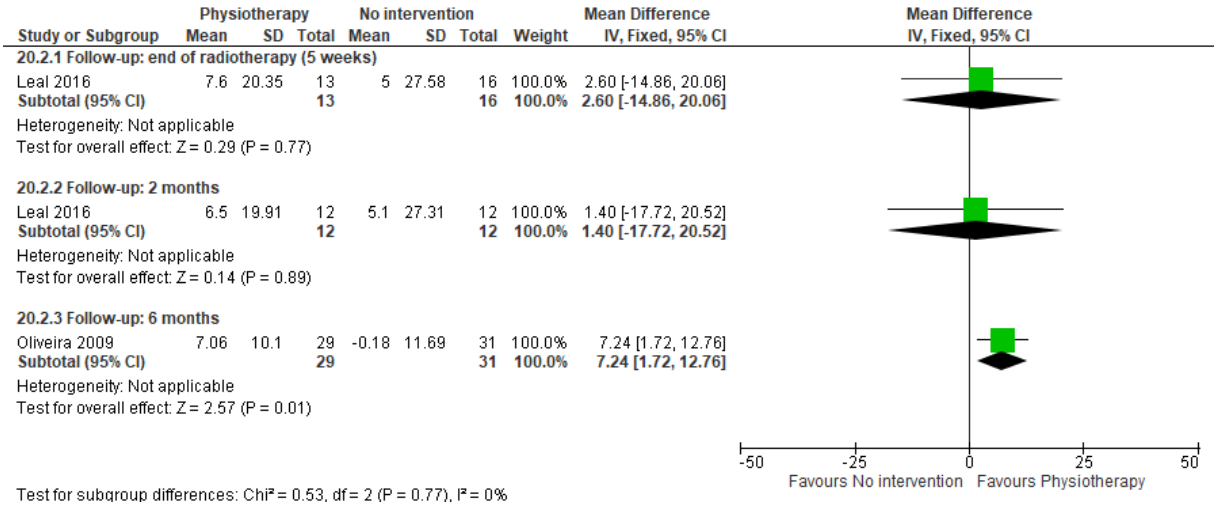
Physiotherapy compared to no intervention during radiotherapy

Figure 67 Range of movement: shoulder flexion in degrees



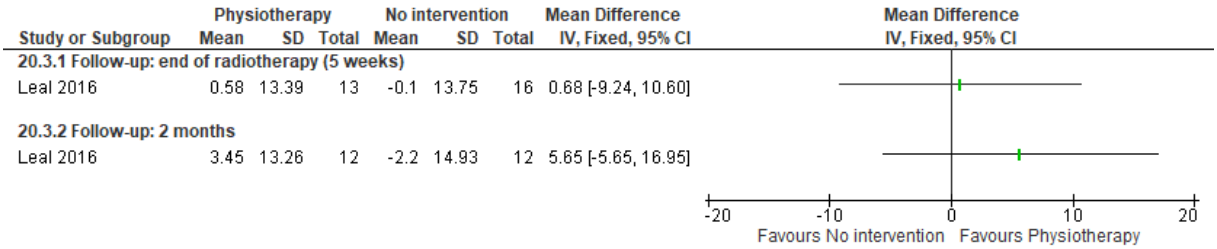
Change from baseline calculated by reviewer

Figure 68 Range of movement: shoulder abduction in degrees



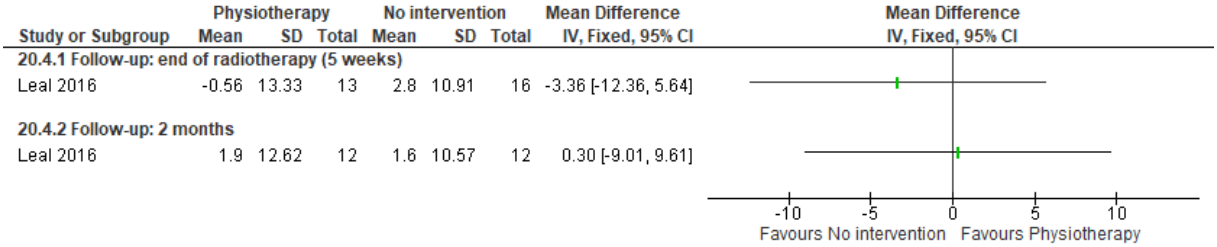
Change from baseline calculated by reviewer

Figure 69 Range of movement: shoulder external rotation in degrees



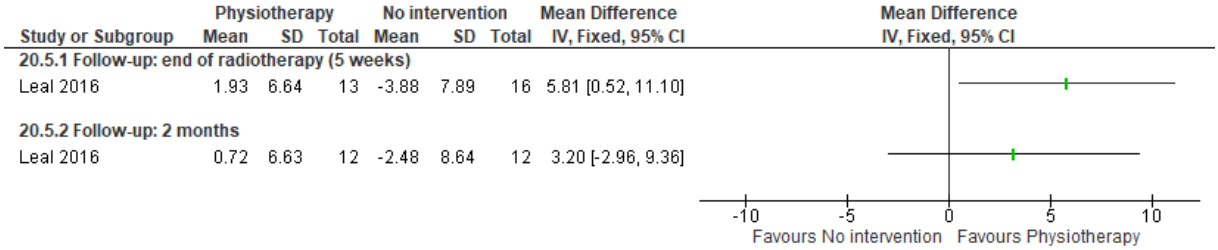
Change from baseline calculated by reviewer

Figure 70 Range of movement: shoulder internal rotation in degrees



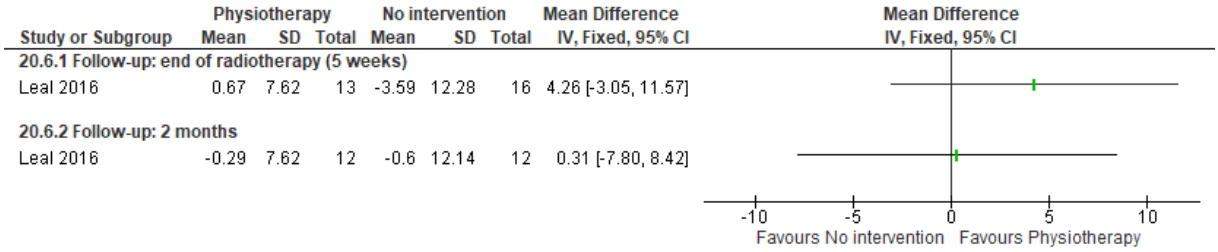
Change from baseline calculated by reviewer

Figure 71 Range of movement: shoulder extension in degrees



Change from baseline calculated by reviewer

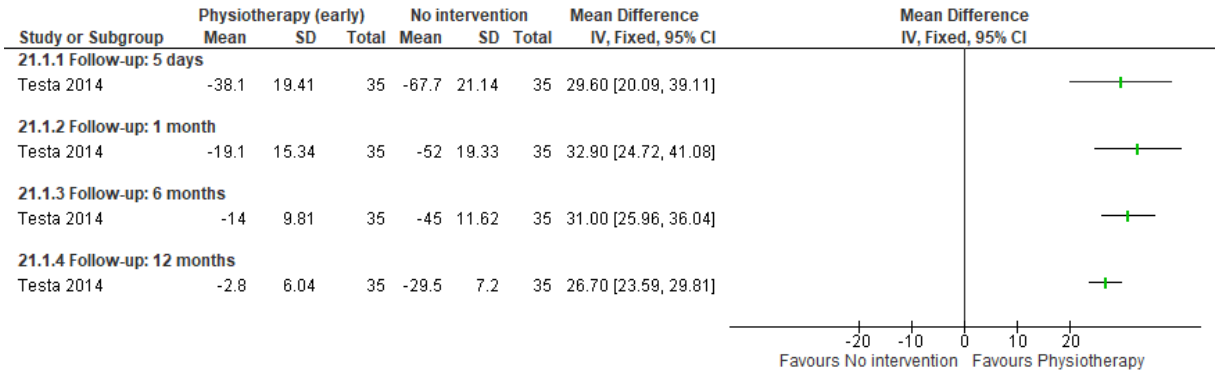
Figure 72 Range of movement: shoulder adduction in degrees



Change from baseline calculated by reviewer

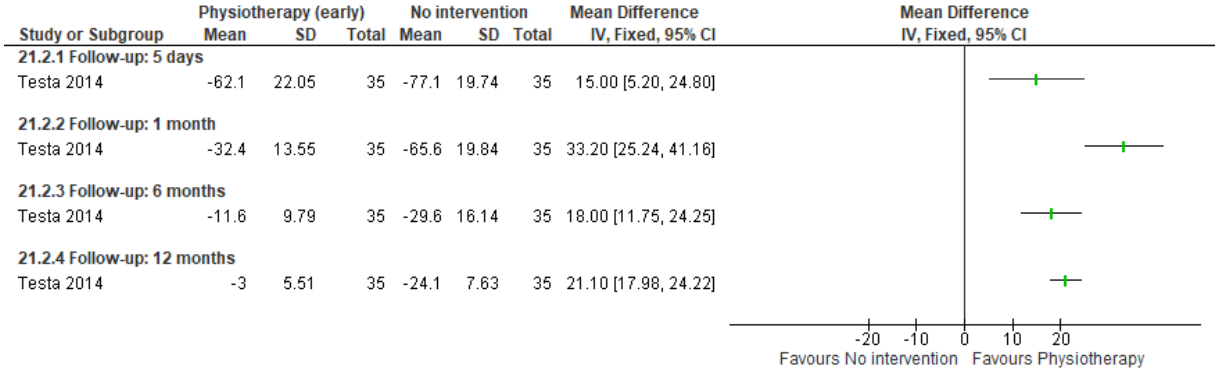
Physiotherapy (early) compared to no intervention

Figure 73 Range of movement: shoulder flexion in degrees



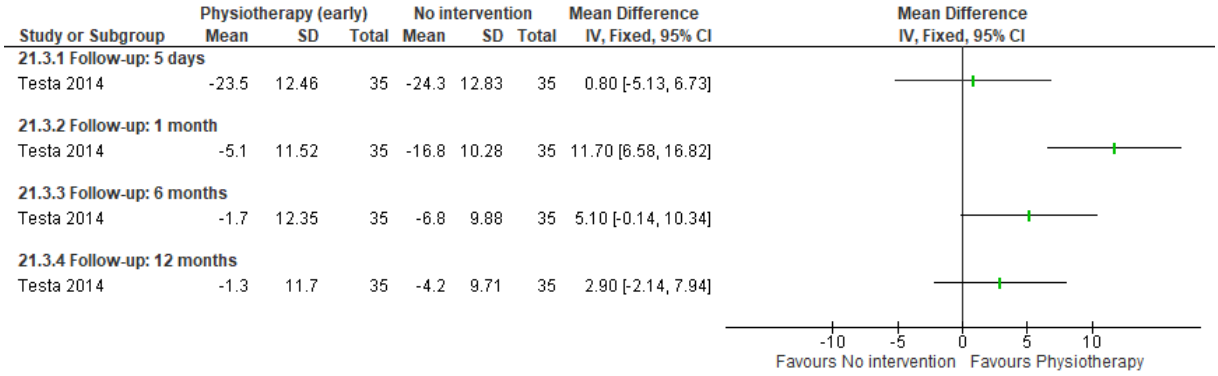
Change from baseline calculated by reviewer

Figure 74 Range of movement: shoulder abduction in degrees



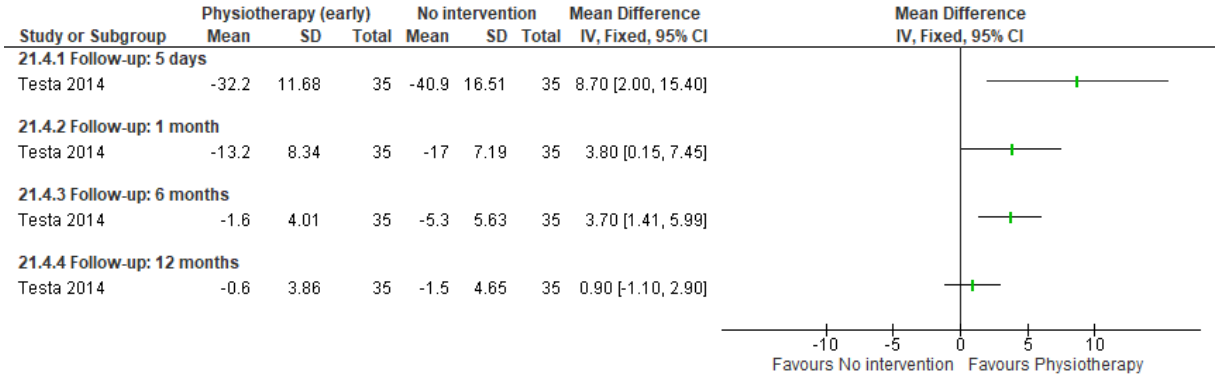
Change from baseline calculated by reviewer

Figure 75 Range of movement: shoulder internal rotation in degrees



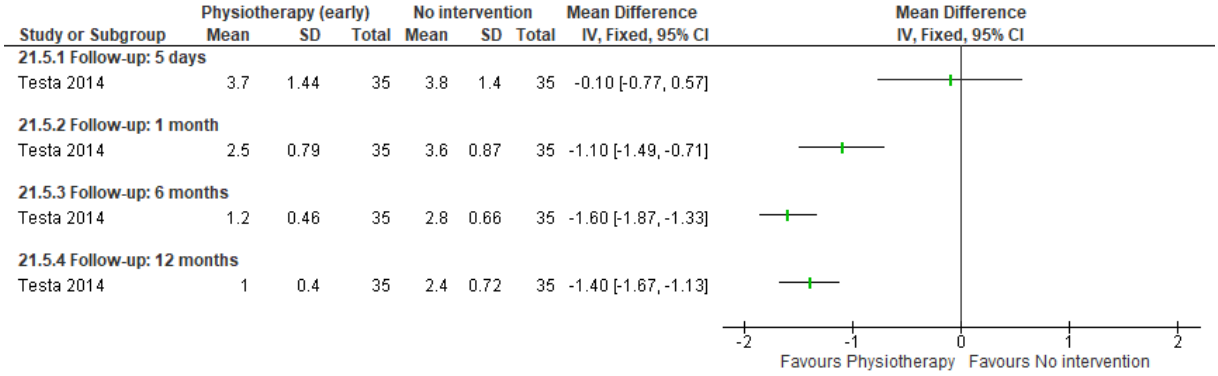
Change from baseline calculated by reviewer

Figure 76 Range of movement: shoulder external rotation in degrees



Change from baseline calculated by reviewer

Figure 77 Pain: visual analogue scale

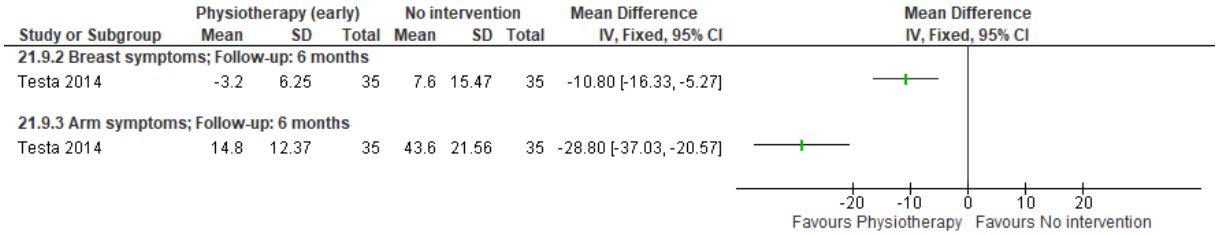


Change from baseline calculated by reviewer

Quality of life: EORTC QLQ-30 (global health) (1 RCT without multiple time points)

Quality of life: EORTC QLQ-30 (pain) (1 RCT without multiple time points)

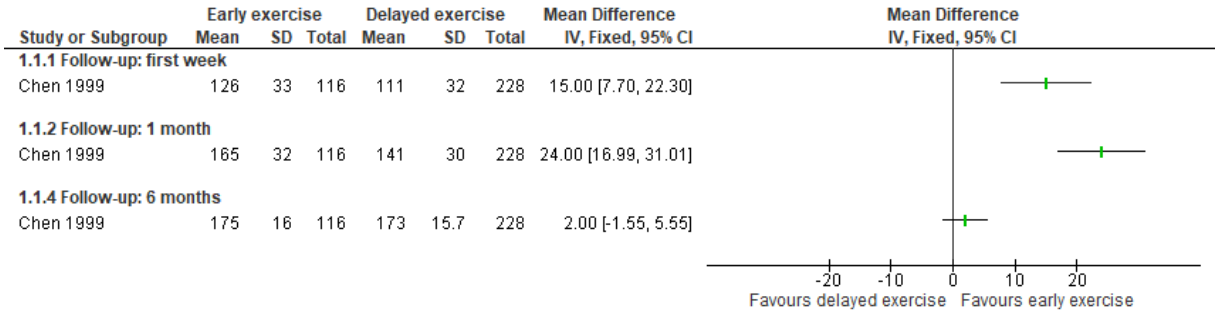
Figure 78 Quality of life: EORTC QLQ-BR23 (breast and arm symptom scales; lower scores better)



Change from baseline calculated by reviewer

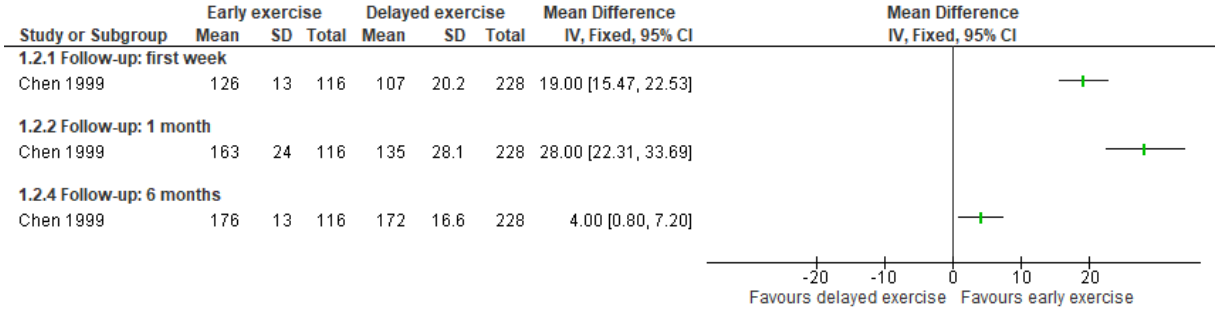
Exercise: early compared to delayed

Figure 79 Range of movement: shoulder flexion in degrees



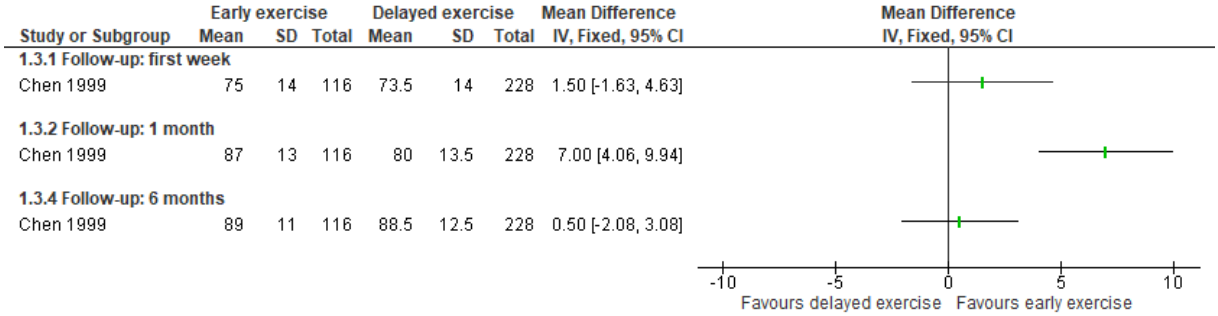
Baseline data was not reported only follow-up data. Delayed and later groups were combined as reported by McNeely 2010.

Figure 80 Range of movement: shoulder abduction in degrees



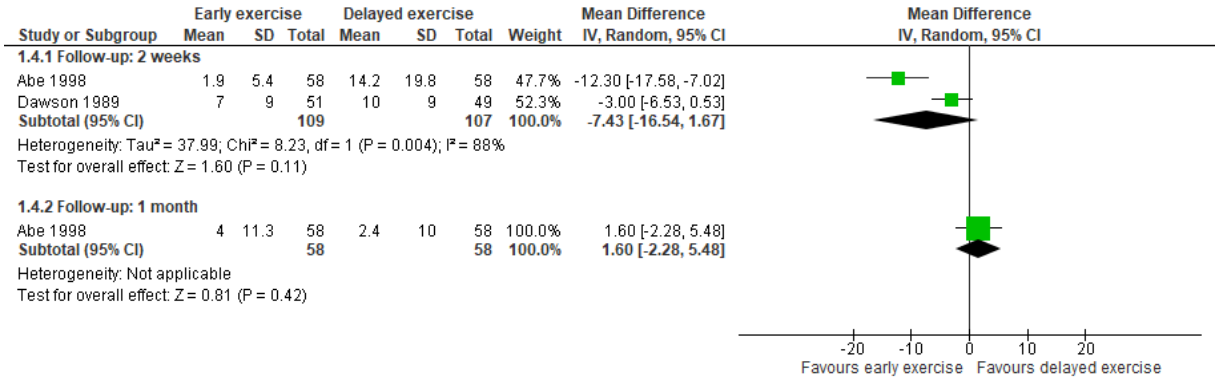
Baseline data was not reported only follow-up data. Delayed and later groups were combined as reported by McNeely 2010.

Figure 81 Range of movement: shoulder external rotation in degrees



Baseline data was not reported only follow-up data. Delayed and later groups were combined as reported by McNeely 2010.

Figure 82 Range of movement: limitation of shoulder flexion in degrees



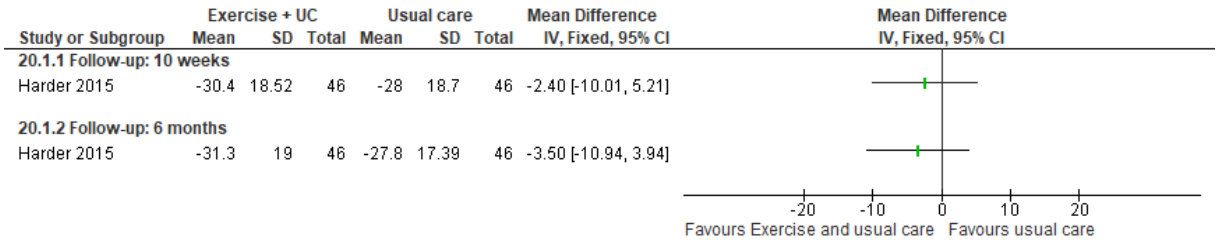
Baseline data was not reported only follow-up data. Limitation of the shoulder was defined as: 180 degrees minus actually obtained degree of flexion at follow-up (Abe 1998) and mean decrease of flexion in degrees (Dawson 1989)

Range of movement: limitation of shoulder abduction in degrees (1 RCT without multiple time points)

Incidence of lymphoedema (200 ml or more) (1 RCT without multiple time points)

Exercise and usual care compared to usual care

Figure 83 Upper limb function (Quick DASH)



Change from baseline calculated by reviewer

Figure 84 Range of movement: shoulder flexion in degrees at follow-up

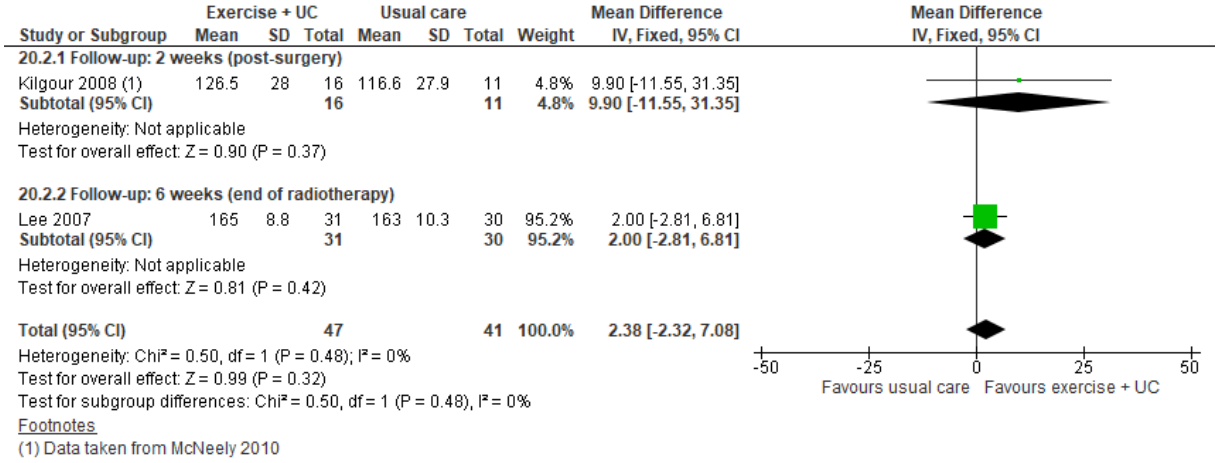
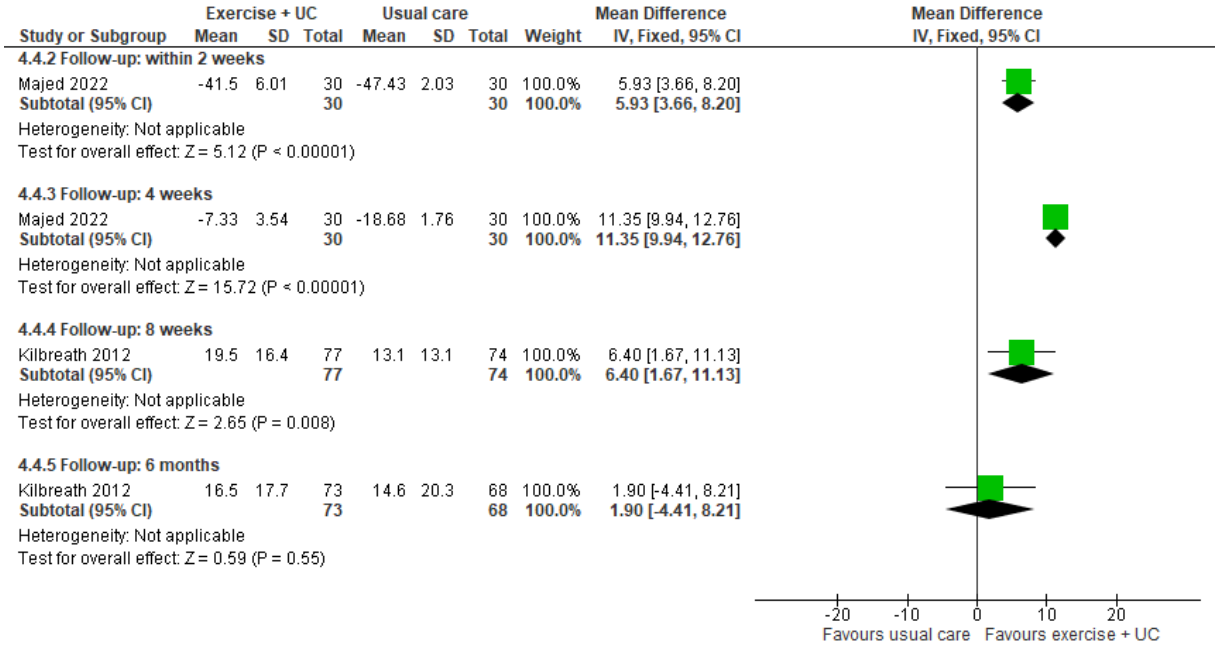


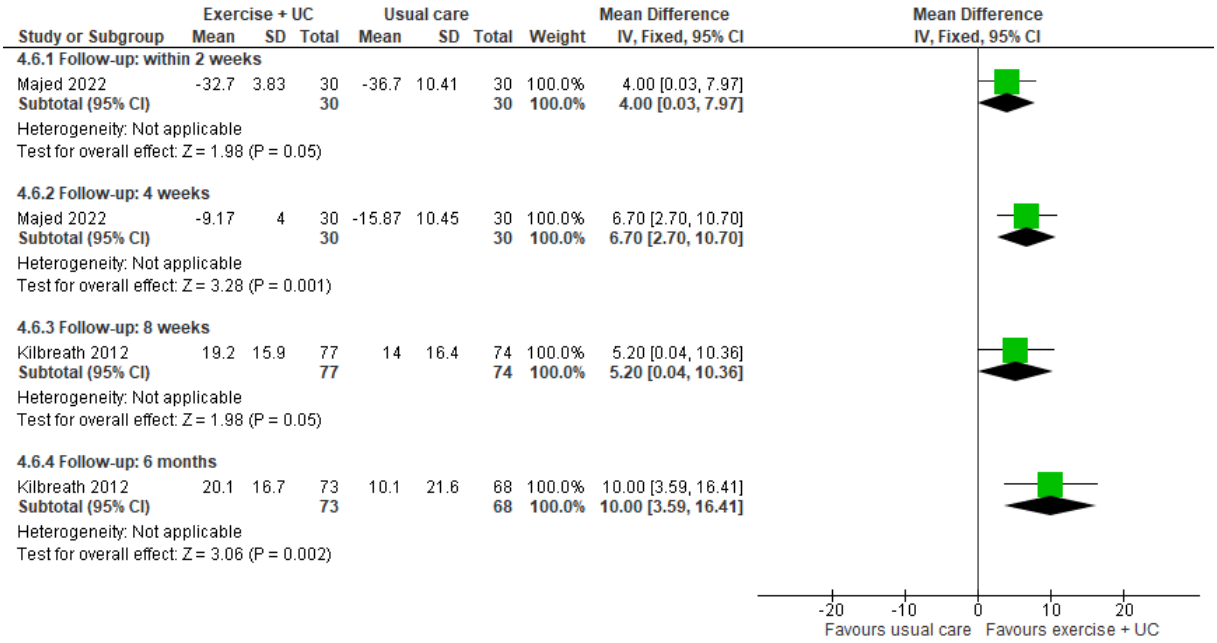
Figure 85 Range of movement: shoulder flexion in degrees (change from baseline)



Change from baseline calculated by reviewer

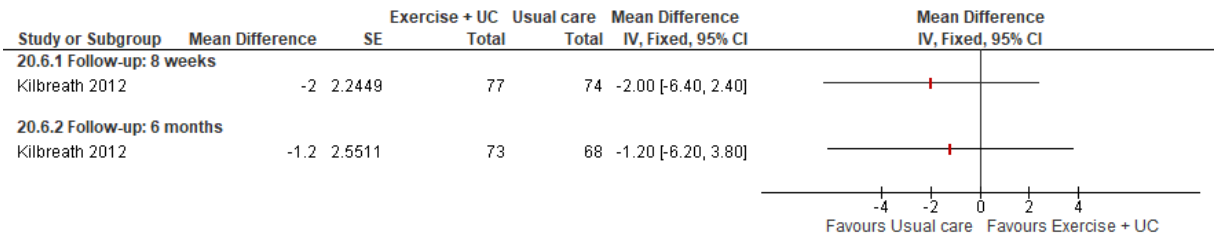
Range of movement: shoulder abduction in degrees at FU (1 RCT without multiple time points)

Figure 86 Range of movement: shoulder abduction in degrees (change from baseline)



Change from baseline calculated by reviewer

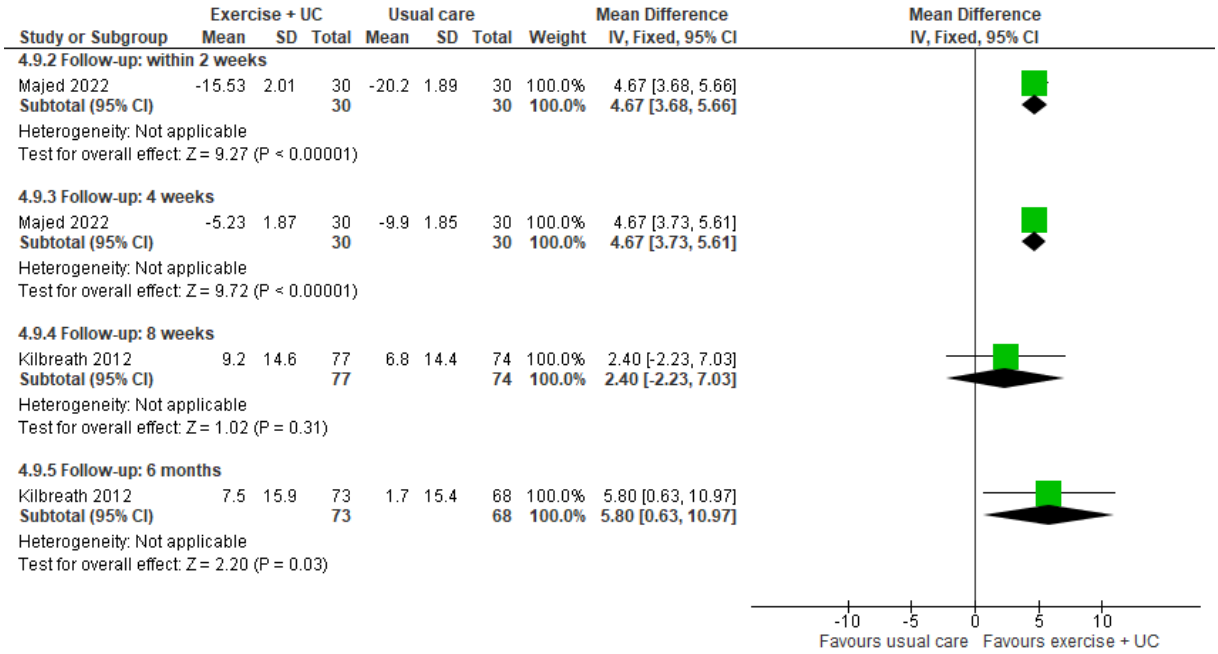
Figure 87 Range of movement: shoulder external rotation in degrees (change from baseline)



No data available for follow-up external rotation in exercise and control arm; study only reports between group difference

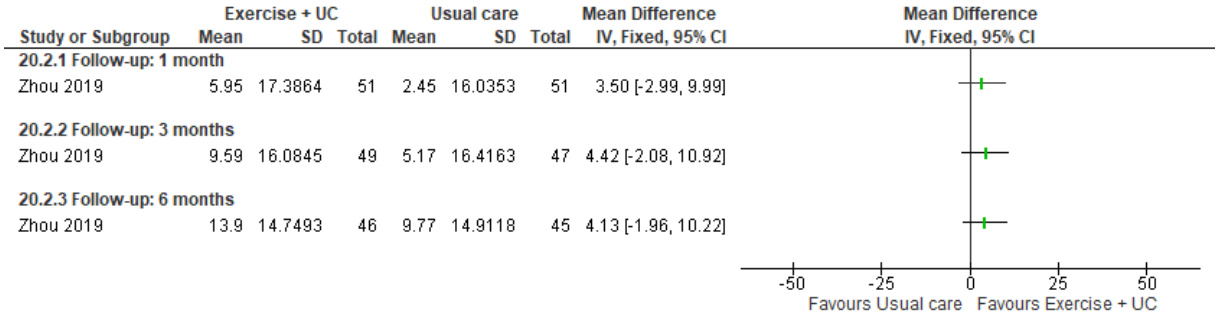
Range of movement: shoulder extension in degrees at FU (1 RCT without multiple time points)

Figure 88 Range of movement: shoulder extension in degrees (change from baseline)



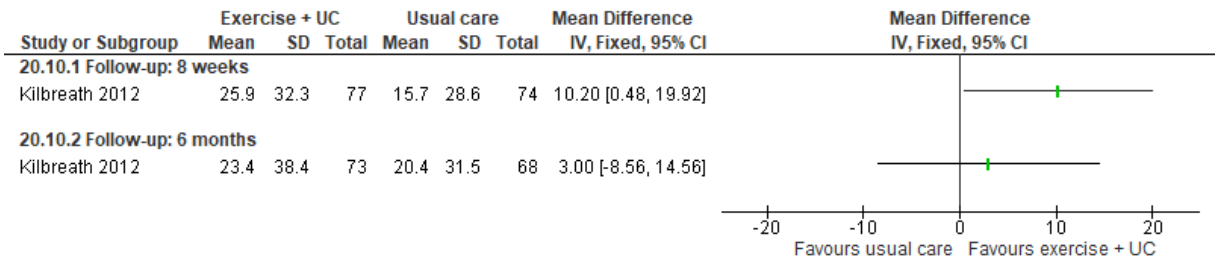
Change from baseline calculated by reviewer

Figure 89 Upper limb muscle strength (Constant Murley Score)



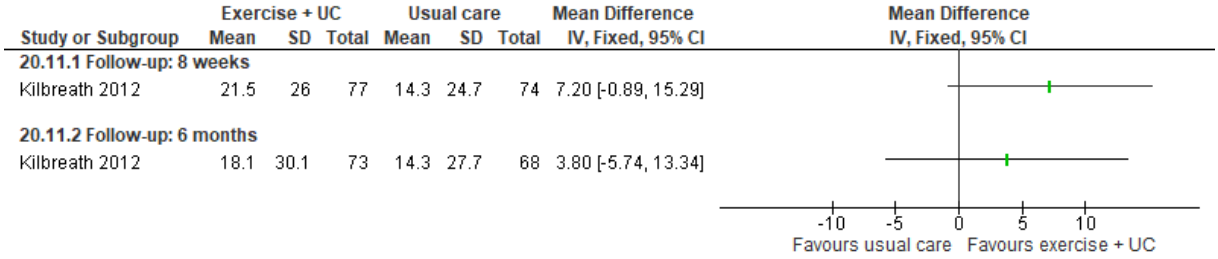
Change from baseline calculated by reviewer

Figure 90 Upper limb muscle strength: shoulder abduction in Newtons



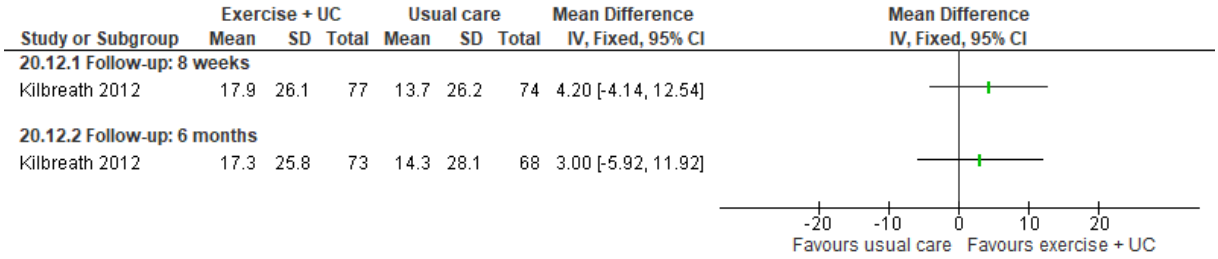
Change from baseline calculated by reviewer

Figure 91 Upper limb muscle strength: shoulder flexion in Newtons



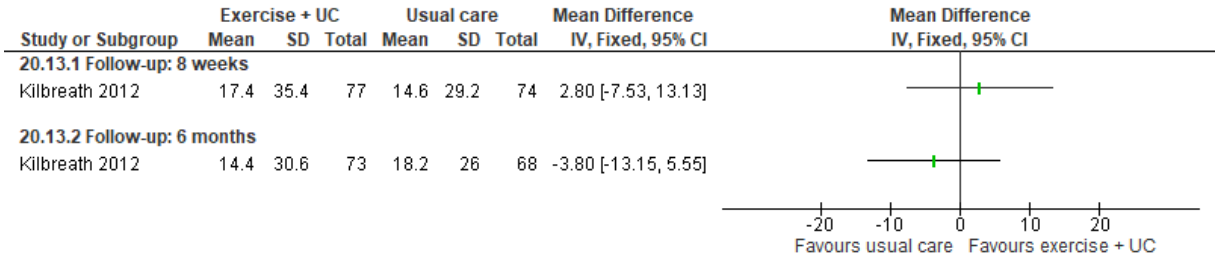
Change from baseline calculated by reviewer

Figure 92 Upper limb muscle strength: shoulder horizontal extension in Newtons



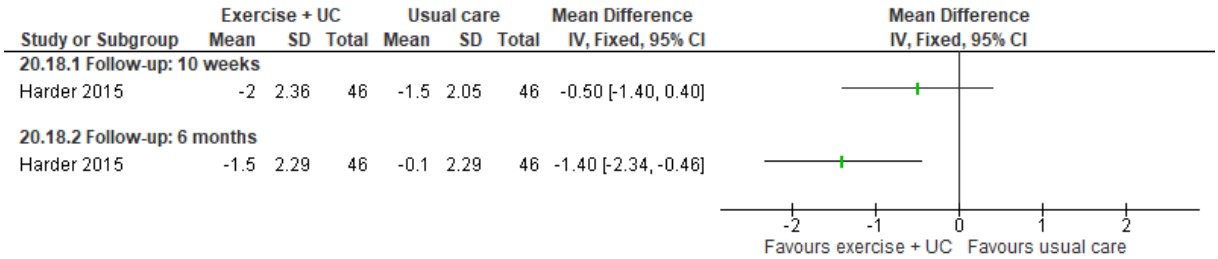
Change from baseline calculated by reviewer

Figure 93 Upper limb muscle strength: shoulder horizontal flexion in Newtons



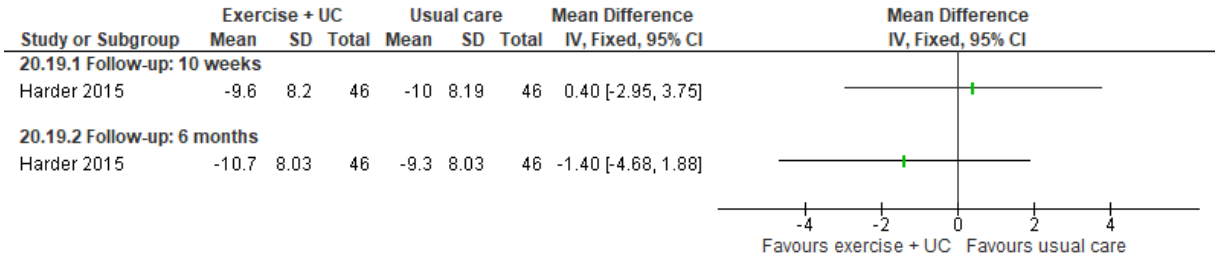
Change from baseline calculated by reviewer

Figure 94 Pain score (0 to 10)



Change from baseline calculated by reviewer

Figure 95 Pain (Oxford Shoulder Score)



Change from baseline calculated by reviewer

Figure 96 Incidence of lymphoedema (difference in arm circumference ≥2 cm)

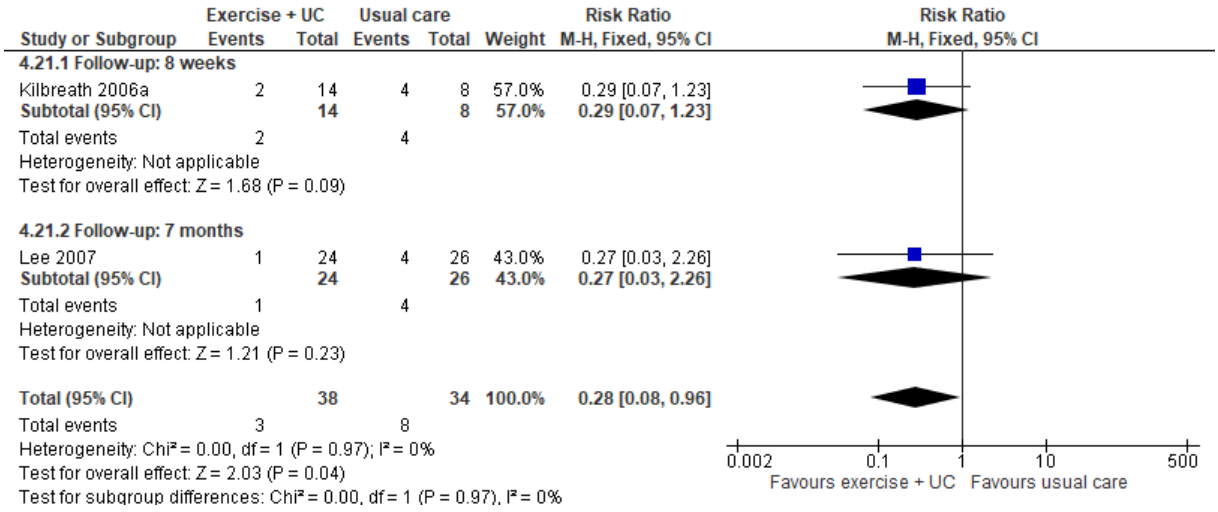


Figure 97 Incidence of lymphoedema: interlimb arm volume =>10%

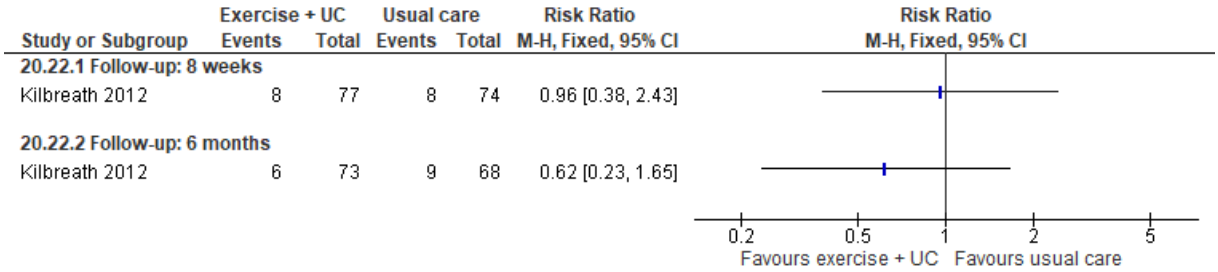
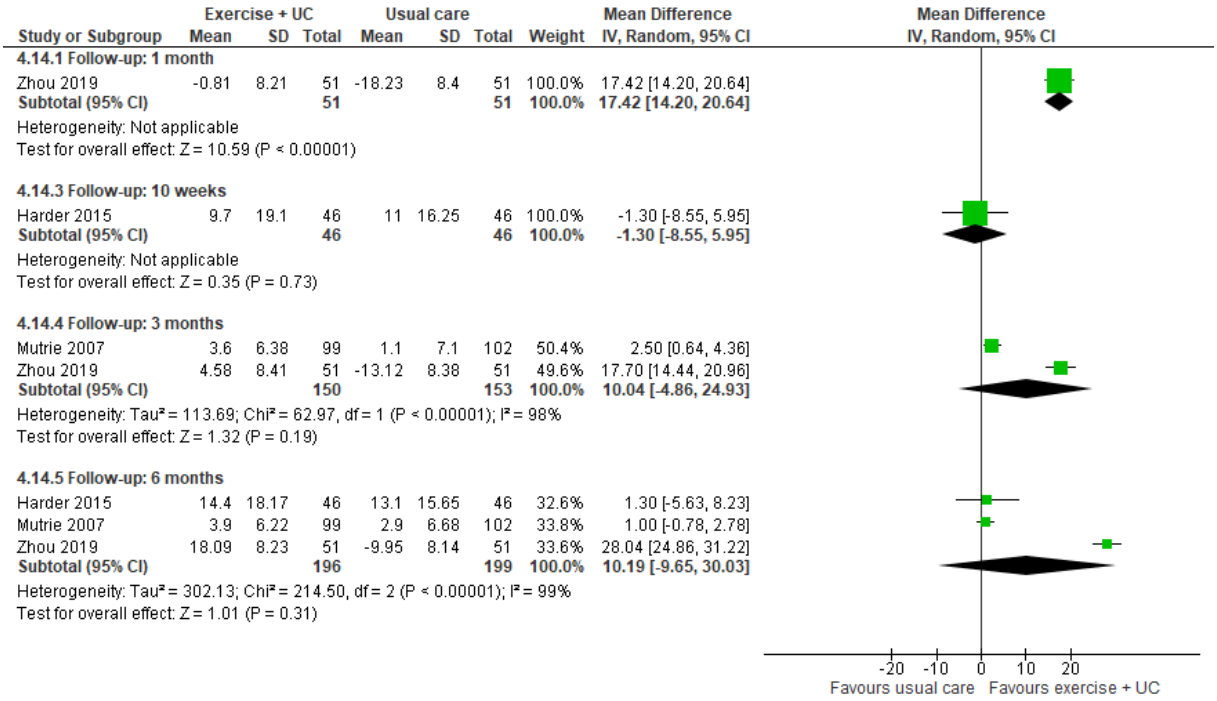
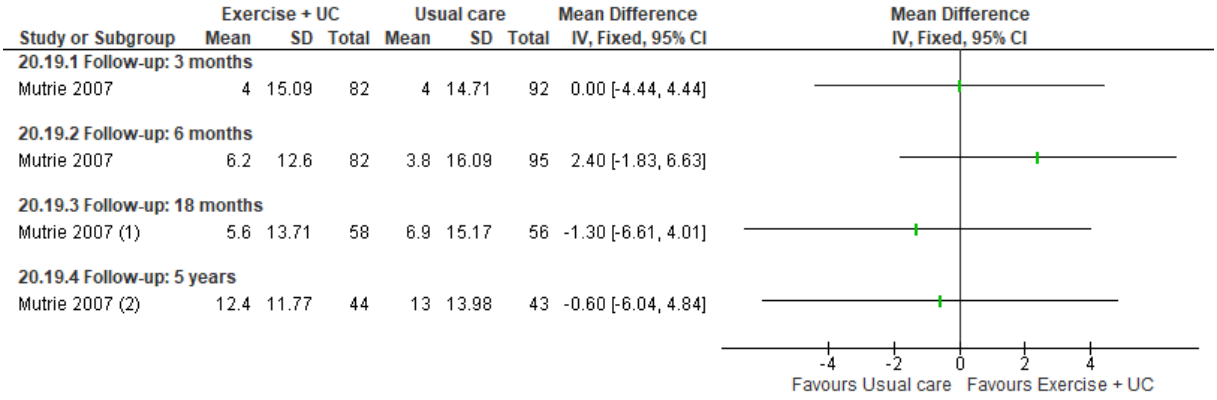


Figure 98 Quality of life: FACT B+4



Change from baseline calculated by reviewer

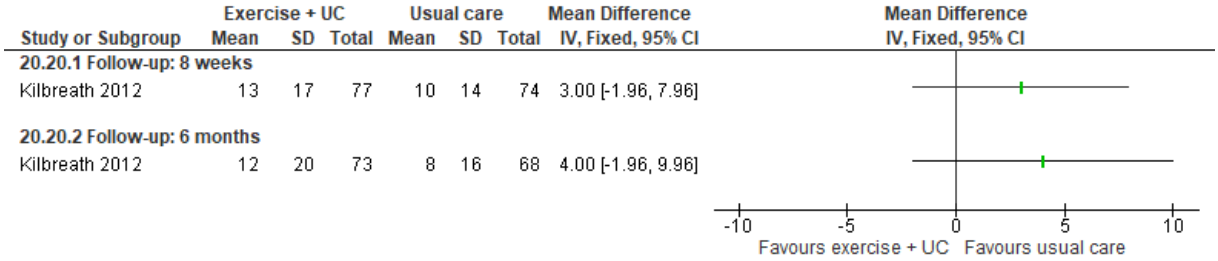
Figure 99 Quality of life: FACT G



Footnotes
(1) Reported by Mutrie 2012
(2) Reported by Mutrie 2012

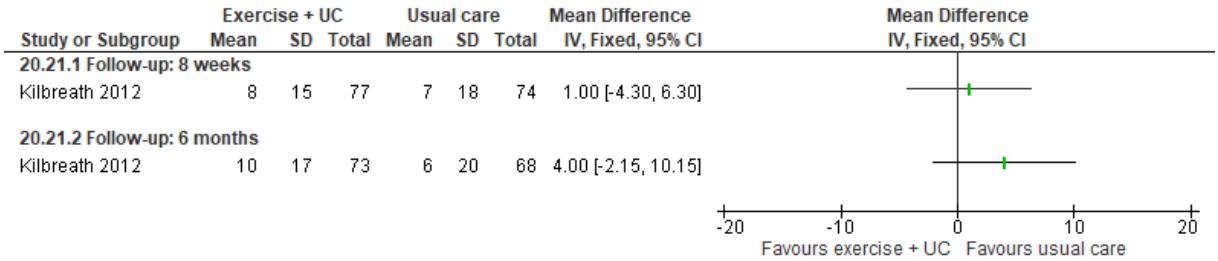
Change from baseline calculated by reviewer

Figure 100 Quality of life: EORTC-BR23 arm symptoms



Change from baseline calculated by reviewer

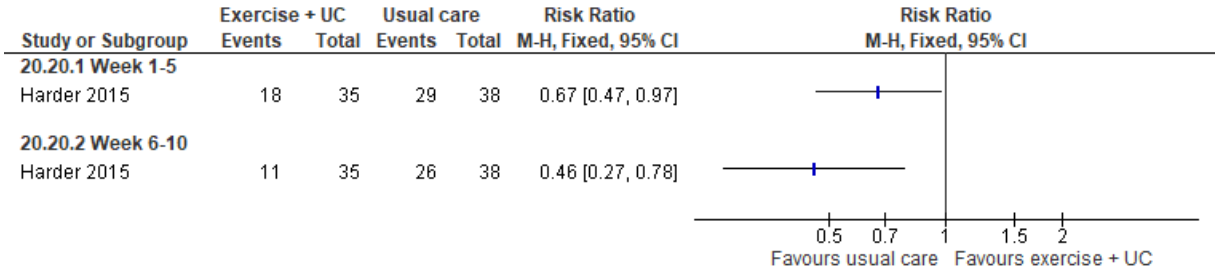
Figure 101 Quality of life: EORTC-BR23 breast symptoms



Change from baseline calculated by reviewer

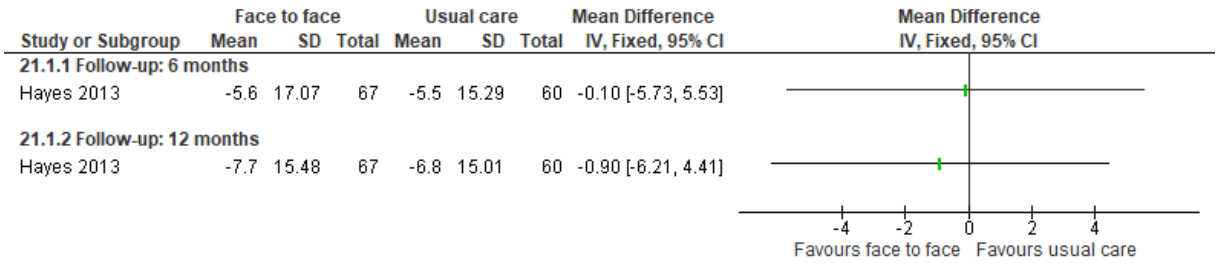
Quality of life: EORTC QoL 30 at FU (1 RCT without multiple time points)

Figure 102 Patient adherence (exercise >5 times a week)



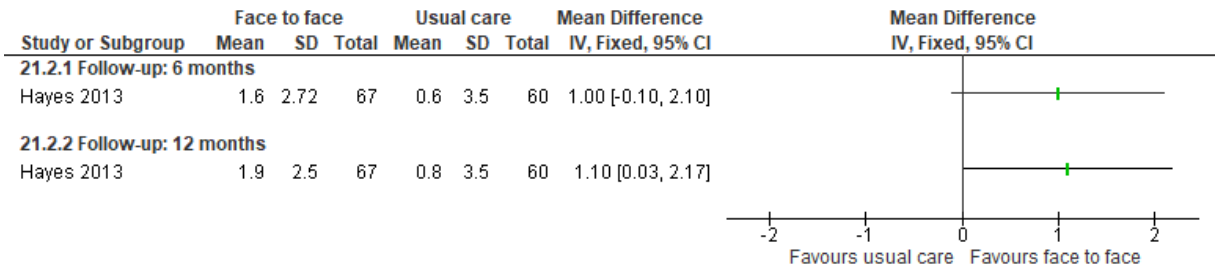
Exercise: face to face exercise compared to usual care

Figure 103 Upper body function (DASH 0 to 100)



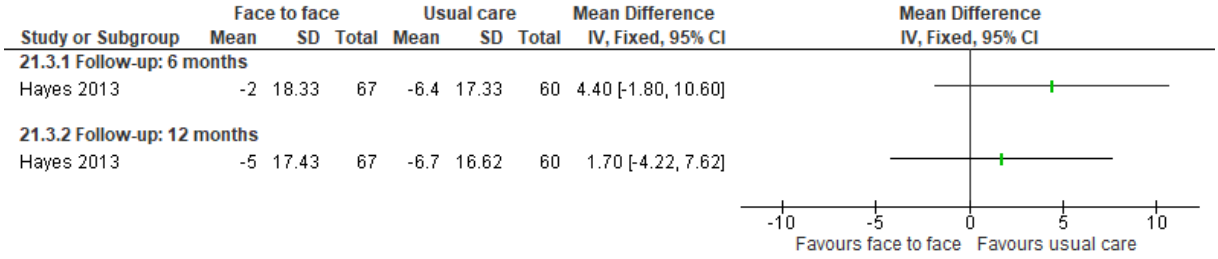
Change from baseline calculated by reviewer

Figure 104 Upper body function (strength and endurance test)



Change from baseline calculated by reviewer

Figure 105 Neuropathic pain (0 to 100)



Change from baseline calculated by reviewer

Figure 106 Incidence of lymphoedema (measured by bioimpedance spectroscopy)

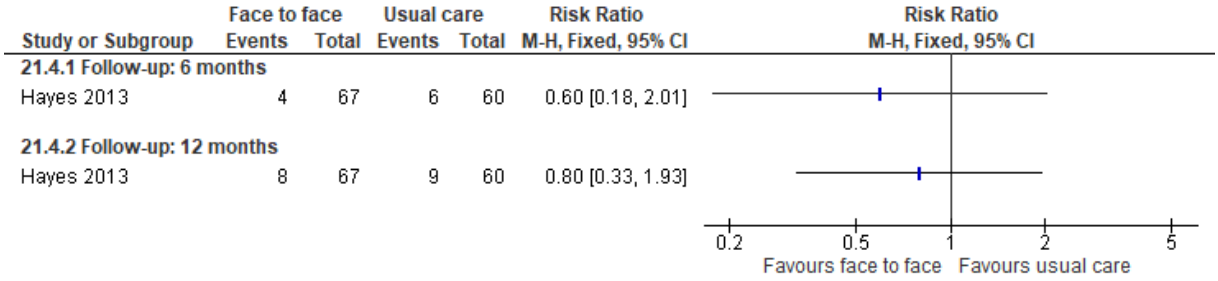
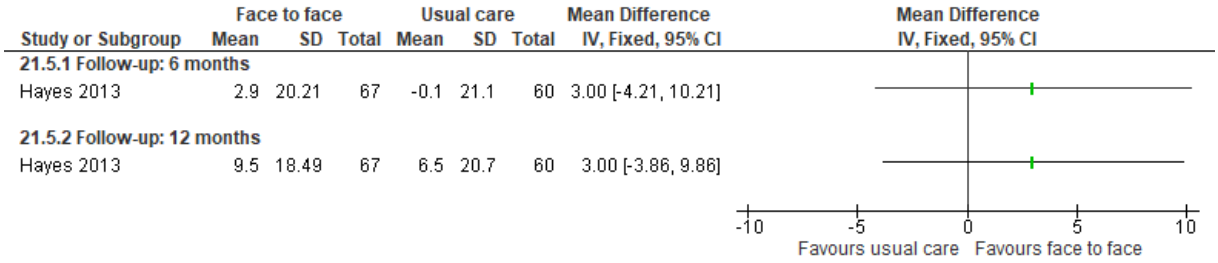


Figure 107 Quality of life: FACT B+4

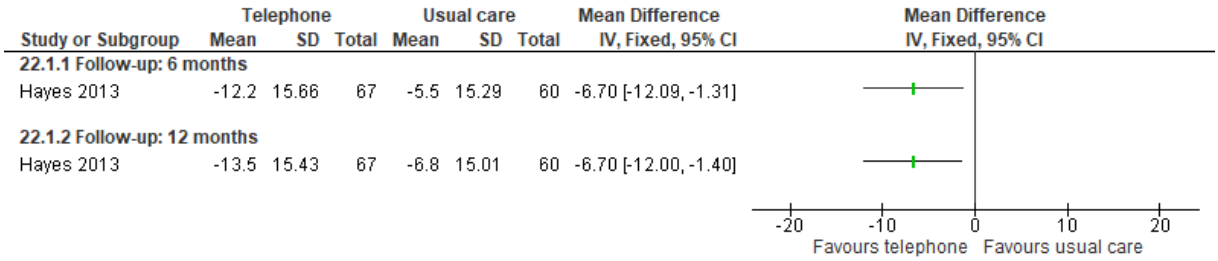


Change from baseline calculated by reviewer

Patient adherence to exercise (at 6 or 12 months) (1 RCT without multiple time points)

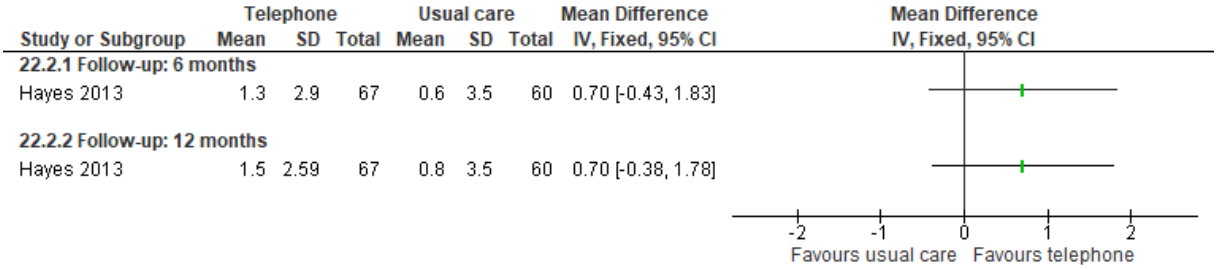
Exercise: telephone delivered exercise compared to usual care

Figure 108 Upper body function (DASH 0 to 100)



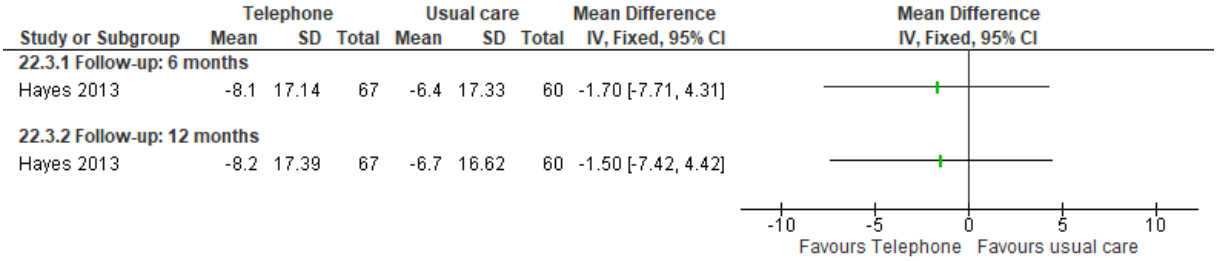
Change from baseline calculated by reviewer

Figure 109 Upper body function (strength and endurance test)



Change from baseline calculated by reviewer

Figure 110 Neuropathic pain (0 to 100)



Change from baseline calculated by reviewer

Figure 111 Incidence of lymphoedema (measured by bioimpedance spectroscopy)

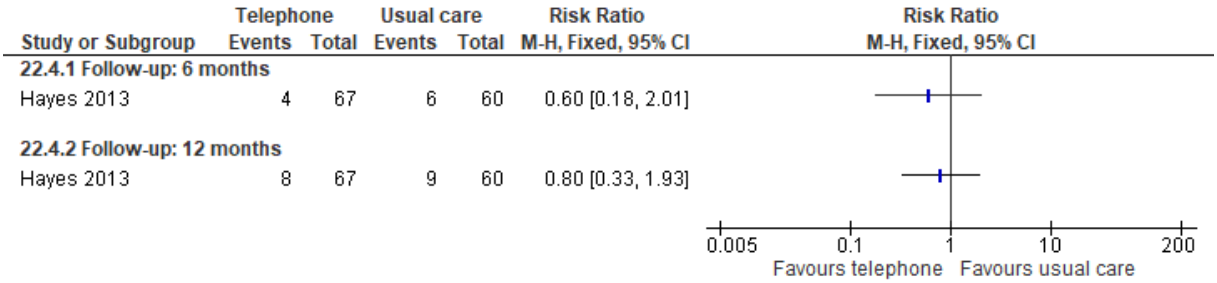
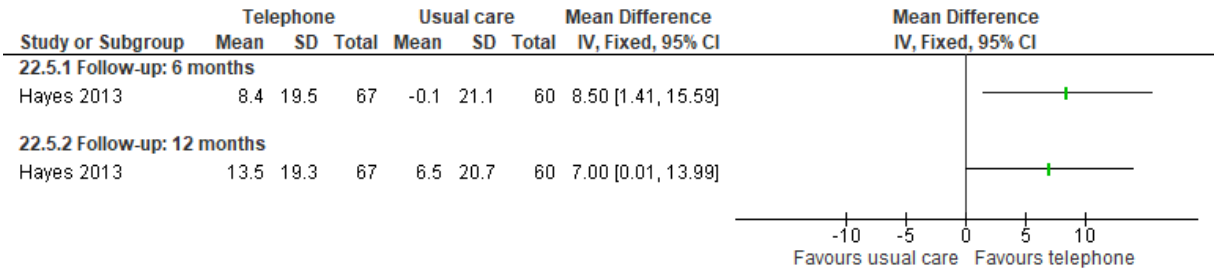


Figure 112 Quality of life: FACT B+4



Change from baseline calculated by reviewer

Patient adherence to exercise (at 6 or 12 months) (1 RCT without multiple time points)

Exercise: rehabilitation compared to usual care

Upper limb function (DASH 0 to 100) (1 RCT without multiple time points)

Range of movement: shoulder flexion in degrees (1 RCT without multiple time points)

Range of movement: shoulder abduction in degrees (1 RCT without multiple time points)

Range of movement: shoulder extension in degrees (1 RCT without multiple time points)

Range of movement: shoulder adduction in degrees (1 RCT without multiple time points)

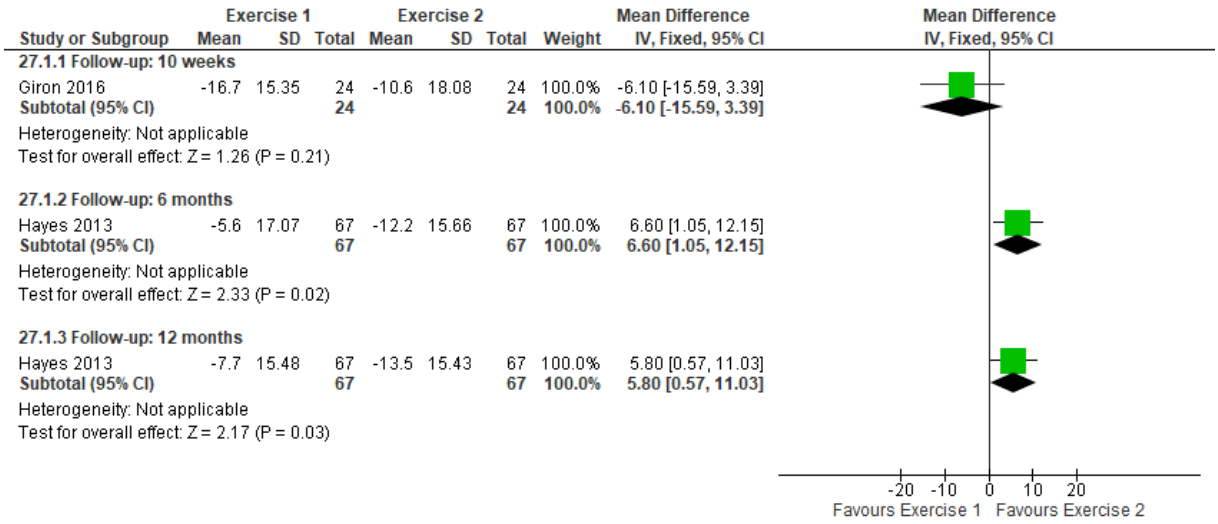
Range of movement: shoulder internal rotation in degrees (1 RCT without multiple time points)

Range of movement: shoulder external rotation in degrees (1 RCT without multiple time points)

Pain score (VAS 1 to 10) (1 RCT without multiple time points)

Exercise compared to exercise

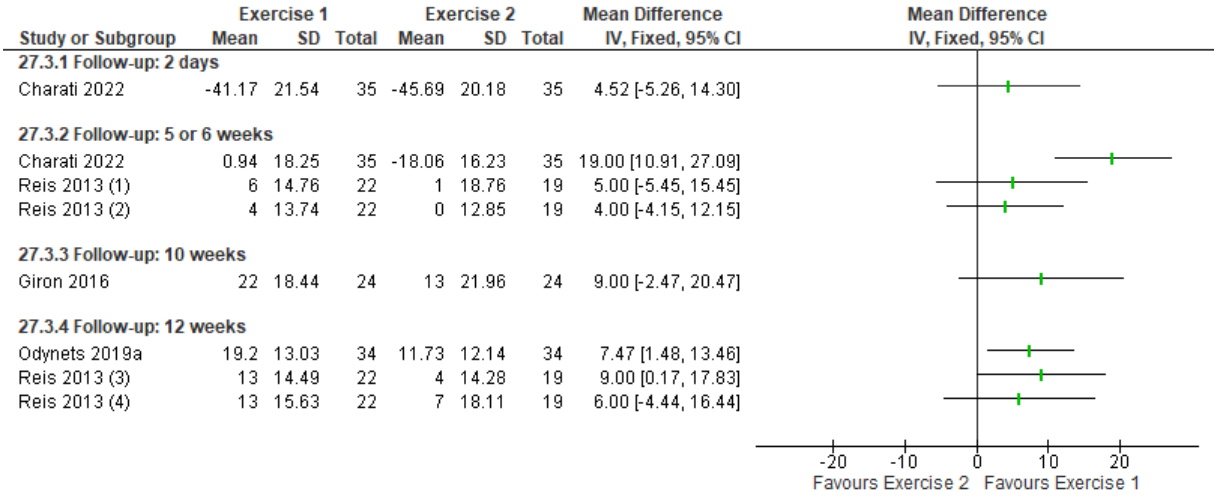
Figure 113 Upper body function (DASH 0 to 100)



Change from baseline calculated by reviewer

Range of movement: shoulder flexion in degrees at FU (1 RCT without multiple time points)

Figure 114 Range of movement: shoulder flexion in degrees (change from baseline)

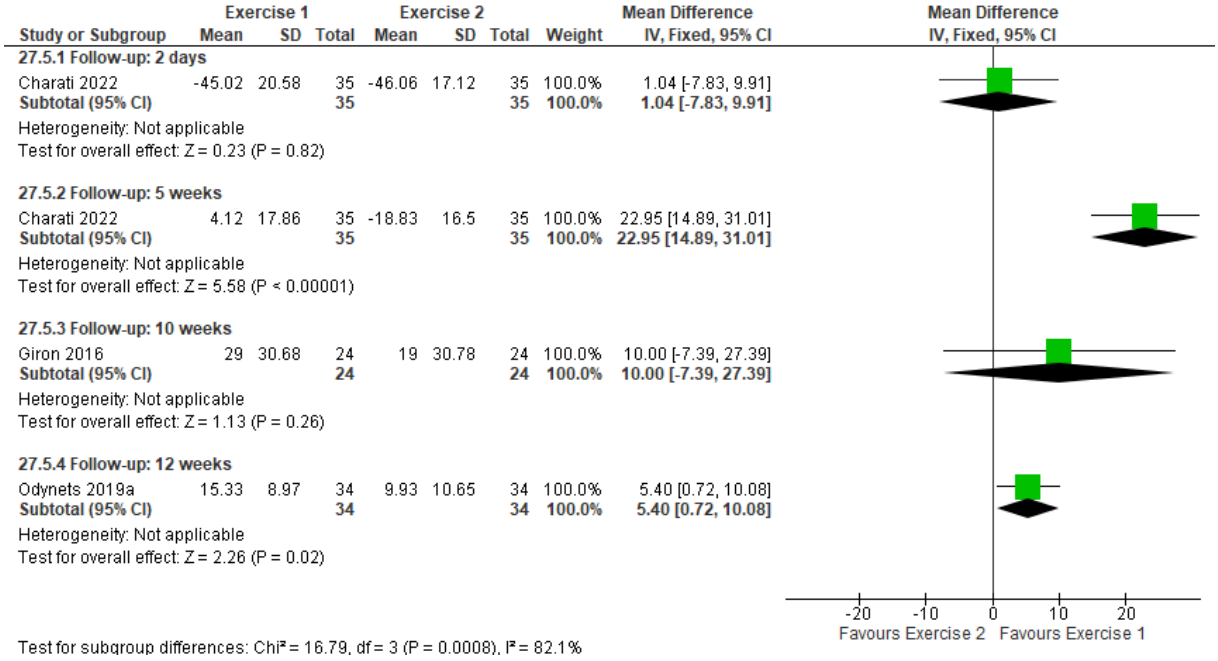


Footnotes
(1) Right shoulder
(2) Left shoulder
(3) Right shoulder
(4) Left shoulder

Change from baseline calculated by reviewer

Range of movement: shoulder abduction in degrees at FU (1 RCT without multiple time points)

Figure 115 Range of movement: shoulder abduction in degrees (change from baseline)



Change from baseline calculated by reviewer

Range of movement: reported as number of participants with 180 degrees shoulder abduction (1 RCT without multiple time points)

Figure 116 Range of movement: reported as number of participants with <180 or <90% degrees shoulder abduction

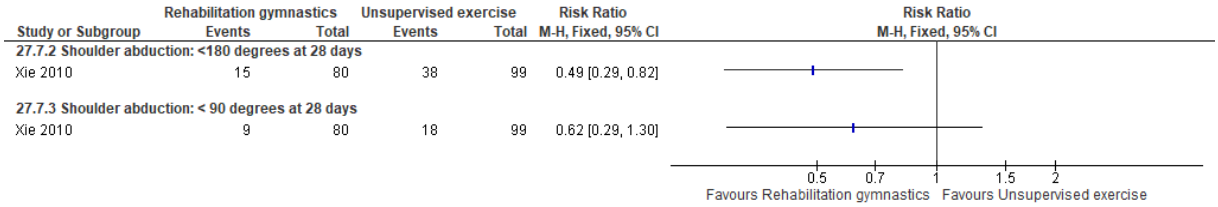
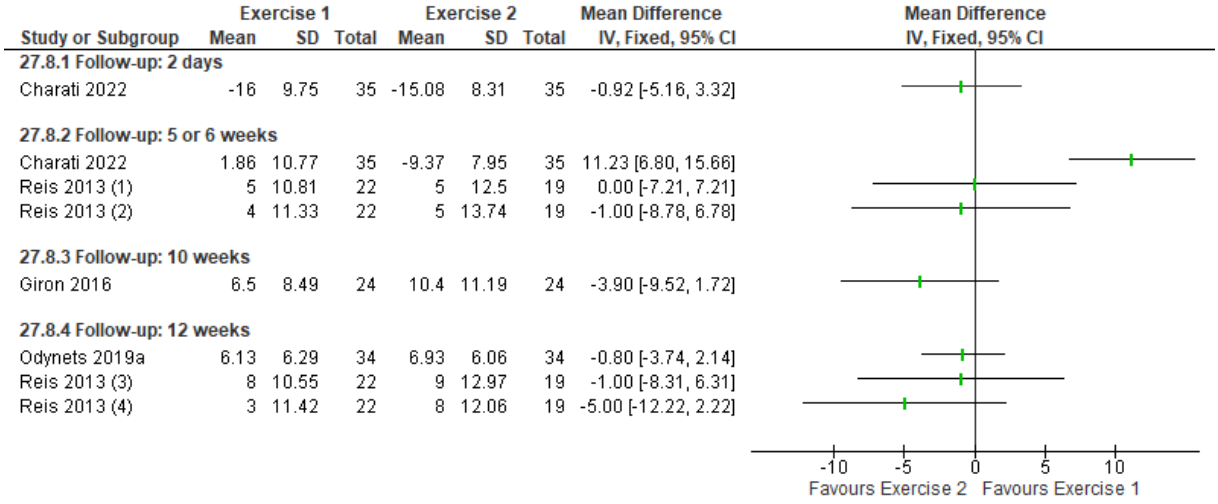


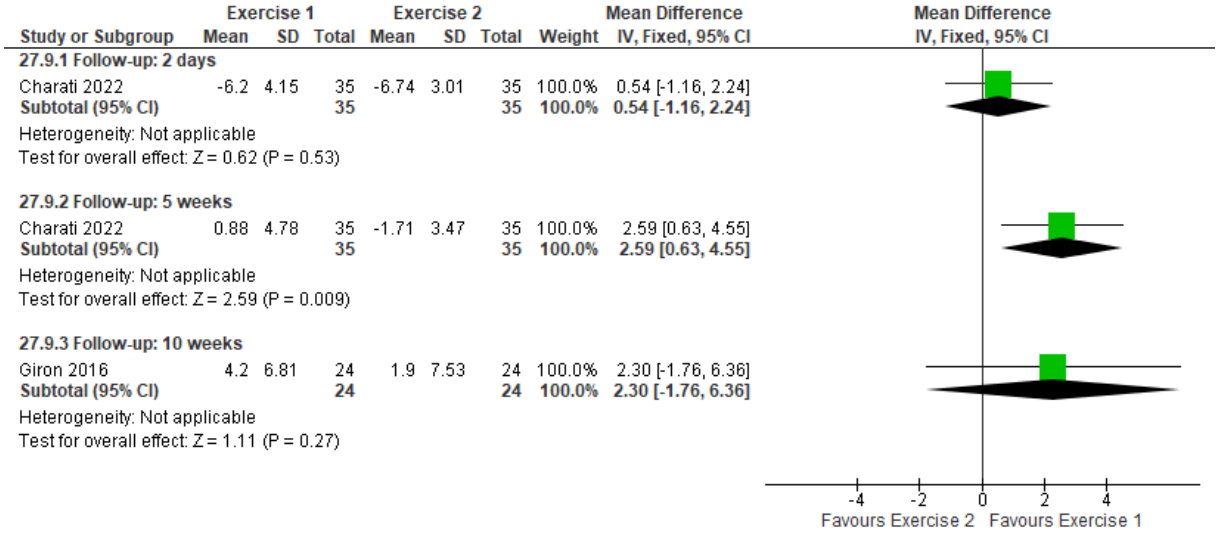
Figure 117 Range of movement: shoulder extension in degrees (change from baseline)



Footnotes
(1) Right shoulder
(2) Left shoulder
(3) Right shoulder
(4) Left shoulder

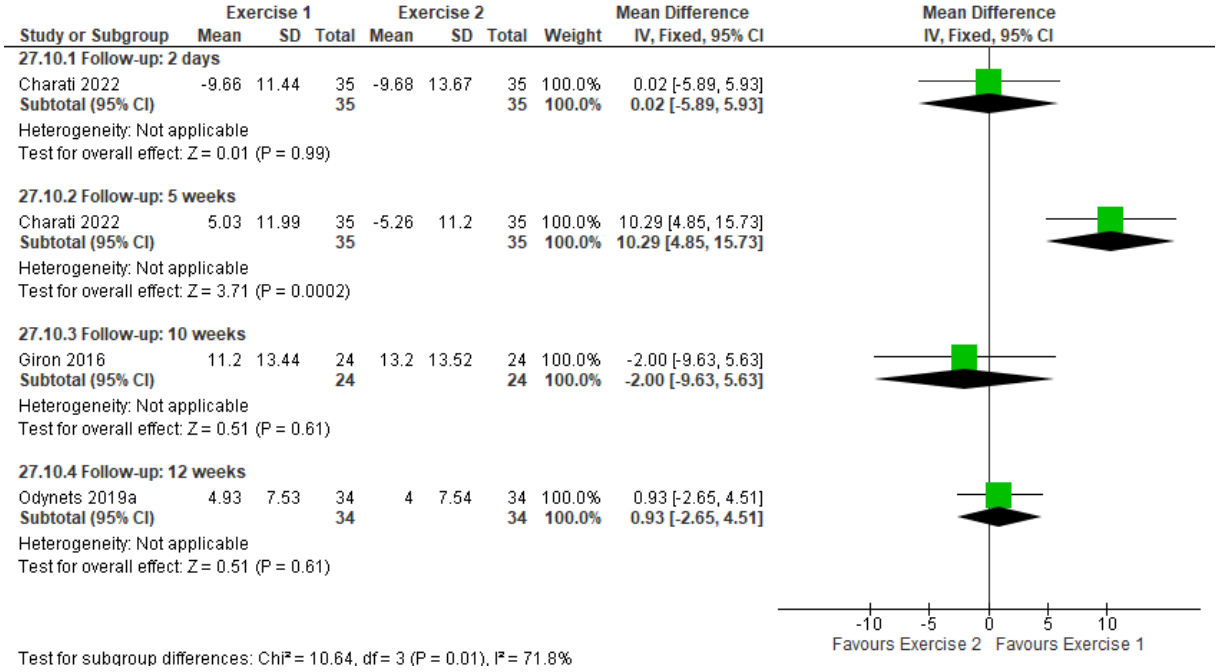
Change from baseline calculated by reviewer

Figure 118 Range of movement: shoulder adduction (change from baseline)



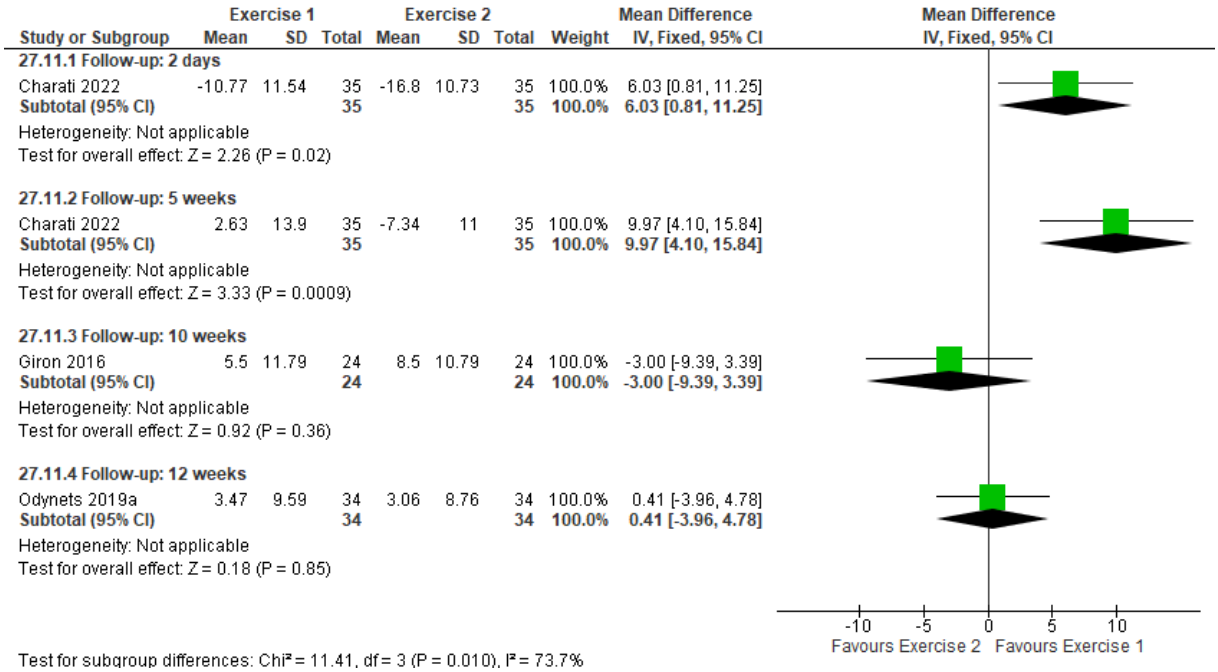
Change from baseline calculated by reviewer

Figure 119 Range of movement: shoulder internal rotation in degrees (change from baseline)



Change from baseline calculated by reviewer

Figure 120 Range of movement: shoulder external rotation in degrees (change from baseline)

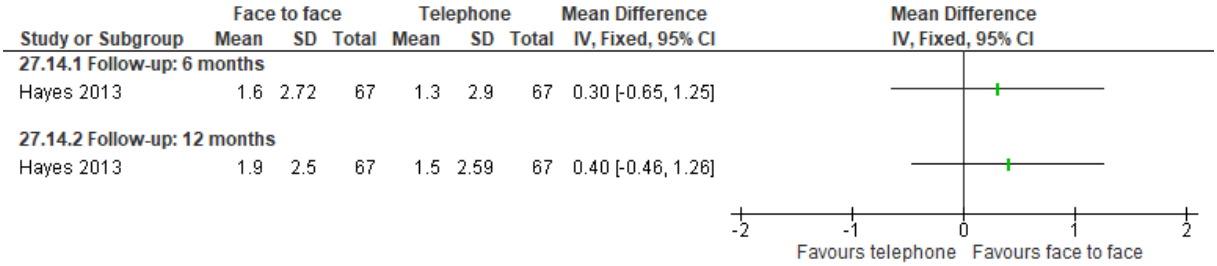


Change from baseline calculated by reviewer

Upper limb muscle strength: shoulder internal rotation at 43 degrees (maximal voluntary isometric contraction) (1 RCT without multiple time points)

Upper limb muscle strength of affected side in kg (1 RCT without multiple time points)

Figure 121 Upper body function (strength and endurance test)

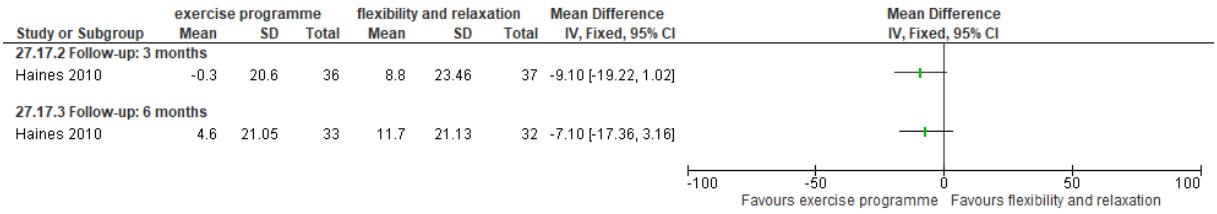


Change from baseline calculated by reviewer

Pain: VAS (0 to 100) at FU (1 RCT without multiple time points)

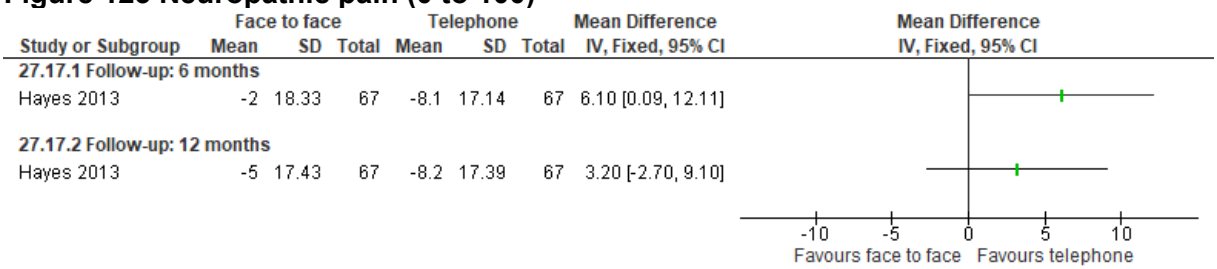
Pain: VAS 0 to 10 (change from baseline) (1 RCT without multiple time points)

Figure 122 Pain: EORTC-C30 pain scale 0 to 100 (change from baseline)



Change from baseline calculated by reviewer

Figure 123 Neuropathic pain (0 to 100)



Change from baseline calculated by reviewer

Figure 124 Incidence of lymphoedema (measured by bioimpedance spectroscopy)

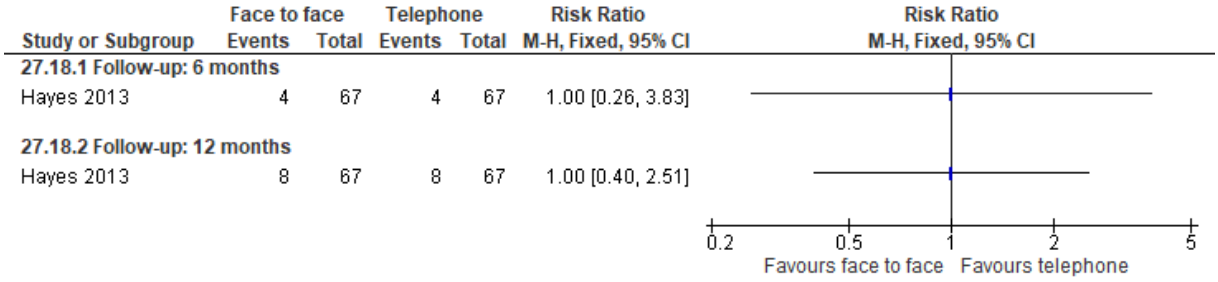
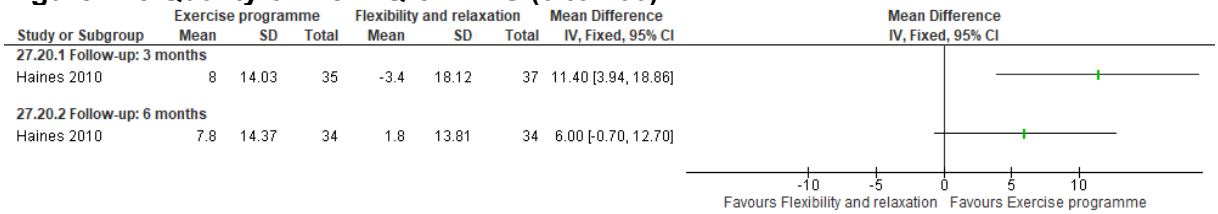
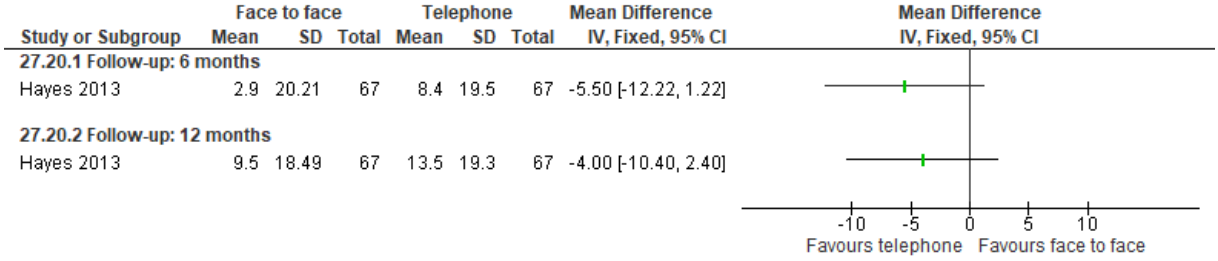


Figure 125 Quality of life: EQ-5D VAS (0 to 100)



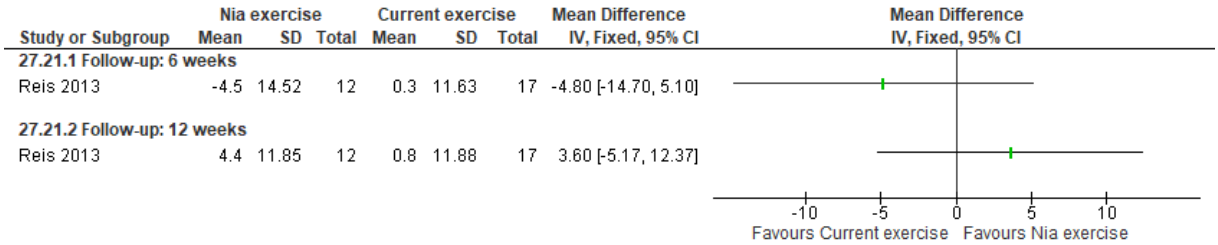
Change from baseline calculated by reviewer

Figure 126 Quality of life: FACT B+4



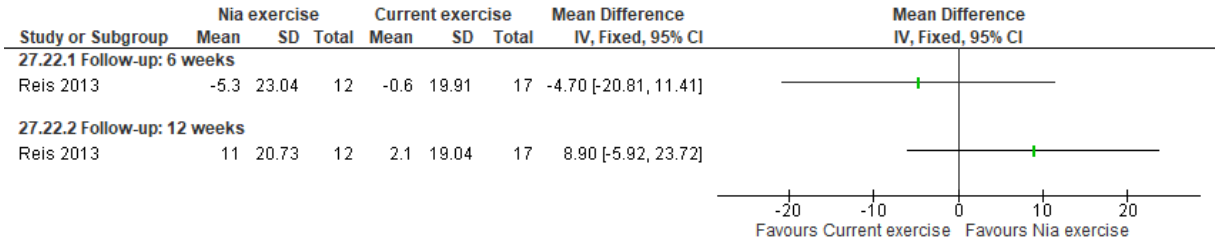
Change from baseline calculated by reviewer

Figure 127 Quality of life: FACT-G (0 to 108)



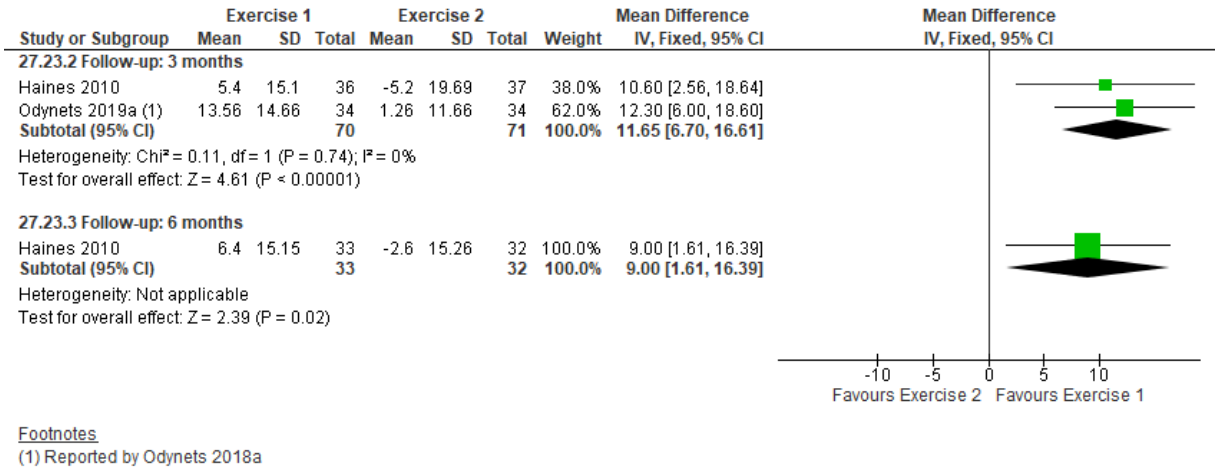
Change from baseline calculated by reviewer

Figure 128 Quality of life: FACIT-F



Change from baseline calculated by reviewer

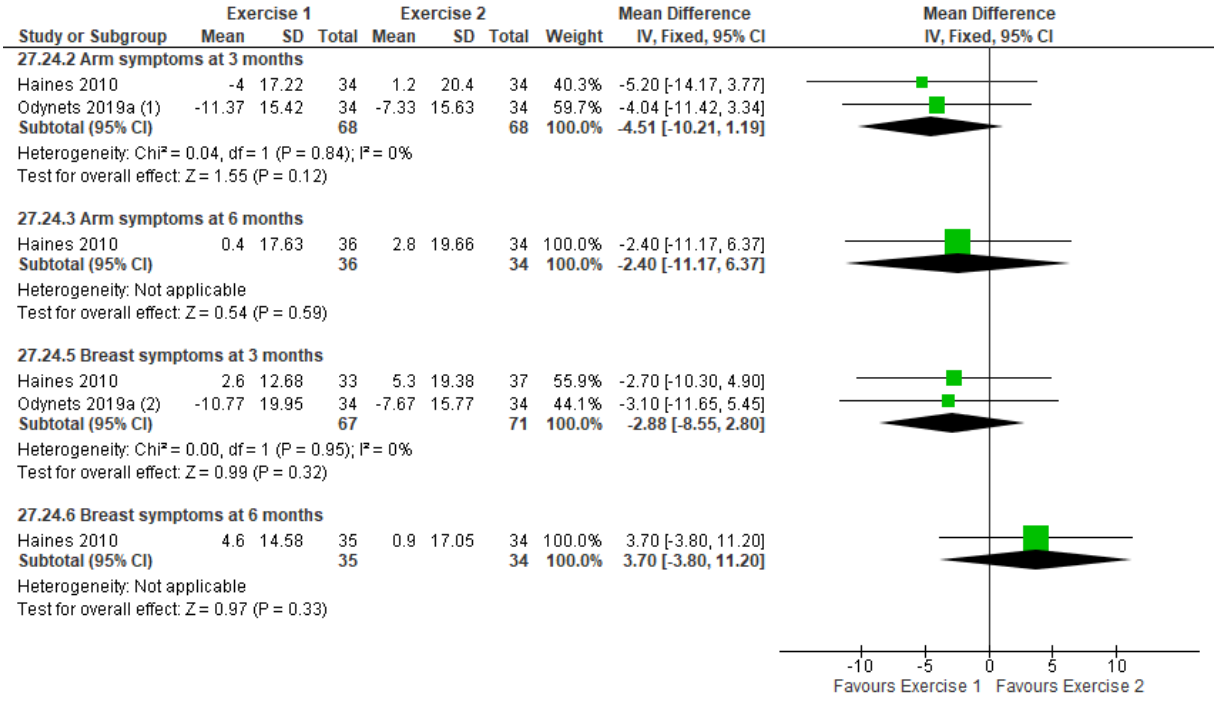
Figure 129 Quality of life: EORTC C30



Footnotes
(1) Reported by Odynets 2018a

Change from baseline calculated by reviewer

Figure 130 Quality of life: EORTC BR23



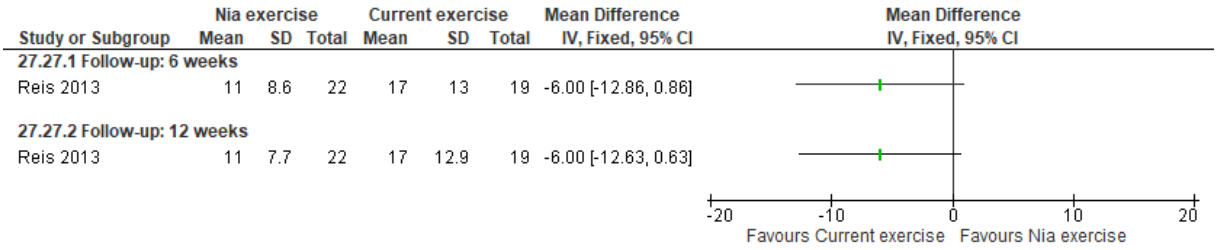
Footnotes
(1) Reported by Odynets 2018a
(2) Reported by Odynets 2018a

Change from baseline calculated by reviewer

Quality of life: WHOQOL (1 to 5) (1 RCT without multiple time points)

Patient adherence to exercise (at 6 or 12 months) (1 RCT without multiple time points)

Figure 131 Patient adherence: number of days engaged in aerobic exercise



Change from baseline calculated by reviewer

Appendix F – GRADE tables

Physiotherapy: early compared to delayed

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy: early compared to delayed	Control	Relative (95% CI)	Absolute		
Range of movement: shoulder flexion in degrees - Follow-up: 5 days [MID +/-11.07] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27	30	-	MD 25.01 higher (12.18 to 37.84 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 2 weeks [MID +/- 8.41] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	101	104	-	MD 11 higher (6.44 to 15.56 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 8.23] (Better indicated by higher values)												
2	randomised trials[6]	very serious[7]	very serious[8]	no serious indirectness	serious[5]	none	128	134	-	MD 19.76 higher (7.66 lower to 47.19 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 3 months [MID +/- 10.12] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27	30	-	MD 22.82 higher (15.11 to 30.53 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 5.93] (Better indicated by higher values)												
2	randomised trials[6]	very serious[7]	very serious[8]	no serious indirectness	serious[5]	none	128	134	-	MD 8.78 higher (0.74 lower to 18.29 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 2 years [MID +/- 6.77] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	85	86	-	MD 2 higher (1.69 lower to 5.69 higher)	⊕⊕OO LOW	CRITICAL

Range of movement: shoulder abduction in degrees - Follow-up: 5 days [MID +/- 13.01] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 19.42 higher (6.99 to 31.85 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 2 weeks [MID +/- 12.01] (Better indicated by higher values)												
1	randomised trials[1]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	101	104	-	MD 4 higher (2.17 lower to 10.17 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 12.36] (Better indicated by higher values)												
2	randomised trials[6]	very serious[7]	very serious[8]	no serious indirectness	very serious[9]	none	128	134	-	MD 21 higher (20.55 lower to 62.56 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 3 months [MID +/- 8.95] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27	30	-	MD 29.92 higher (22.72 to 37.12 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 11.35] (Better indicated by higher values)												
2	randomised trials[6]	very serious[7]	very serious[8]	no serious indirectness	serious[5]	none	128	134	-	MD 10.26 higher (9.88 lower to 30.4 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 2 years [MID +/- 14.03] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	85	86	-	MD 3 higher (4.72 lower to 10.72 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 5 days [MID +/- 12.68] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 2.04 lower (13.87 lower to 9.79 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 2 weeks [MID +/- 6.27] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	101	104	-	MD 3 higher (0.29 lower to 6.29 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 1 month [MID +/- 5.05] (Better indicated by higher values)												

2	randomised trials[6]	very serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	128	134	-	MD 0.02 lower (2.57 lower to 2.53 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 3 months[10] (Better indicated by higher values)												
1	randomised trials[1]	[2]				none	27	30	-[10]	not pooled[10]		
Range of movement: shoulder internal rotation in degrees - Follow-up: 6 months [mid +/- 6.0] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	101	104	-	MD 2.00 higher (1.09 lower to 5.09 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 2 years [MID +/- 5.77] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	85	86	-	MD 0 higher (3.31 lower to 3.31 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 5 days [MID +/- 12.97] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 14.41 higher (1.91 to 26.91 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 2 weeks [MID +/- 7.81] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	101	104	-	MD 7 higher (2.97 to 11.03 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 1 month [MID +/- 7.59] (Better indicated by higher values)												
2	randomised trials[6]	very serious[7]	very serious[8]	no serious indirectness	serious[5]	none	128	134	-	MD 7.69 higher (2.6 lower to 17.97 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 3 months[10] (Better indicated by higher values)												
1	randomised trials[1]					none	27	30	-[10]	not pooled[10]		
Range of movement: shoulder external rotation in degrees - Follow-up: 6 months [MID +/- 5.57] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	101	104	-	MD 1 higher (2.1 lower to 4.1 higher)	⊕⊕OO LOW	CRITICAL

Range of movement: shoulder external rotation in degrees - Follow-up: 2 years [MID +/- 5.27] (Better indicated by higher values)												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	85	86	-	MD 2 higher (1.31 lower to 5.31 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 5 days [MID +/- 4.76] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 3.12 higher (1.4 lower to 7.64 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 1 month [MID +/- 3.64] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 2.48 higher (1.22 lower to 6.18 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 3 months [MID +/- 3.56] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 2.36 higher (1.33 lower to 6.05 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 6 months [MID +/- 3.19] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 1.5 higher (2 lower to 5 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 5 days [MID +/- 7.62] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 5.12 higher (1.82 lower to 12.06 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 1 month [MID +/- 5.99] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 5.25 higher (0.1 to 10.4 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 3 months [MID +/- 4.33] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 2.44 higher (1.62 lower to 6.5 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 6 months [MID +/- 4.05] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	27	30	-	MD 1.33 higher (2.59 lower to 5.25 higher)	⊕⊕OO LOW	CRITICAL
Impaired shoulder mobility - Follow-up: 1 week [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[11]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/89 (18%)	34/74 (45.9%)	RR 0.39 (0.24 to 0.65)	280 fewer per 1000 (from 161 fewer to 349 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Impaired shoulder mobility - Follow-up: 4 months [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[12]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	13/34 (38.2%)	8/29 (27.6%)	RR 1.39 (0.67 to 2.87)	108 more per 1000 (from 91 fewer to 516 more)	⊕OOO VERY LOW	CRITICAL
Impaired shoulder mobility - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
3	randomised trials[13]	very serious[7]	no serious inconsistency	no serious indirectness	very serious[9]	none	23/198 (11.6%)	23/161 (14.3%)	RR 0.85 (0.5 to 1.43)[15]	21 fewer per 1000 (from 71 fewer to 61 more)	⊕OOO VERY LOW	CRITICAL
Pain (mild or moderate) - Follow-up: 2 weeks [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	23/101 (22.8%)	23/104 (22.1%)	RR 1.03 (0.62 to 1.71)	7 more per 1000 (from 84 fewer to 157 more)	⊕OOO VERY LOW	CRITICAL
Pain (mild or moderate) - Follow-up: 1 month [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	15/101 (14.9%)	12/104 (11.5%)	RR 1.29 (0.63 to 2.61)	33 more per 1000 (from 43 fewer to 186 more)	⊕OOO VERY LOW	CRITICAL
Pain (mild or moderate) - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	12/101 (11.9%)	7/104 (6.7%)	RR 1.77 (0.72 to 4.3)	52 more per 1000 (from 19 fewer to 222 more)	⊕OOO VERY LOW	CRITICAL
Pain (mild or moderate) - Follow-up: 2 years [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	12/85 (14.1%)	12/86 (14%)	RR 1.01 (0.48 to 2.12)	1 more per 1000 (from 73 fewer to 156 more)	⊕OOO VERY LOW	CRITICAL

Incidence of lymphoedema - Follow-up: 1 month [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	1/101 (0.99%)	3/104 (2.9%)	RR 0.34 (0.04 to 3.25)	19 fewer per 1000 (from 28 fewer to 65 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema - Follow-up: 4 months [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[12]	very serious[4]	no serious inconsistency	no serious indirectness	serious[5]	none	10/34 (29.4%)	19/29 (65.5%)	RR 0.45 (0.25 to 0.8)	360 fewer per 1000 (from 131 fewer to 491 fewer)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
3	randomised trials[14]	very serious[7]	no serious inconsistency	no serious indirectness	very serious[9]	none	9/210 (4.3%)	7/198 (3.5%)	RR 1.23 (0.47 to 3.23)[16]	8 more per 1000 (from 19 fewer to 79 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema - Follow-up: 2 years [MID 0.8 to 1.25; RR less than 1 favours early physiotherapy]												
1	randomised trials[3]	very serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	13/85 (15.3%)	12/86 (14%)	RR 1.1 (0.53 to 2.26)	14 more per 1000 (from 66 fewer to 176 more)	⊕OOO VERY LOW	CRITICAL

[1] Cinar 2008
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] Bendz 2002
[4] Study at high risk of bias. Quality of the outcome downgraded twice.
[5] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[6] Bendz 2002; Cinar 2008
[7] >33.3% of weighted data from studies at high risk of bias. Quality of the outcome downgraded twice.
[8] i-squared >66.7%. Quality of the outcome downgraded twice.
[9] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[10] Study reported SD as 0.00. There was no variability. Mean difference could not be estimated
[11] Schultz 1997
[12] Flew 1979
[13] Van Der Horst 1985; Schultz 1997; Jansen 1990
[14] Bendz 2002; Jansen 1990; Van Der Horst 1985
[15] Data for Schultz 1997 and Van Der Horst 1985 was taken from McNeely 2010.
[16] Data for Van Der Horst 1985 was taken from McNeely 2010.

Physiotherapy and usual care compared to usual care

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy and usual care compared to usual care	Control	Relative (95% CI)	Absolute		
Upper limb function: DASH overall score - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	121	118	-	MD 4.6 lower (8.9 to 0.3 lower)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: DASH overall score - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	132	138	-	MD 7.81 lower (12.44 to 3.18 lower)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: DASH activity limitation score - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	196	196	-	MD 5.21 lower (9.78 to 0.64 lower)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: DASH activity limitation score - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	196	196	-	MD 8.04 lower (12.93 to 3.15 lower)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 12 months [MID +/- 6.10] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	6	9	-	MD 1.1 lower (14.33 lower to 12.13 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 12 months [MID +/- 16.75] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	6	9	-	MD 4.9 higher (30.83 lower to 40.63 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 12 months [MID +/- 8.00] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	6	9	-	MD 15.4 lower (41.66 lower to 10.86 higher)	⊕⊕OO LOW	CRITICAL

Upper limb muscle strength: shoulder flexion in kg - Follow-up: 12 months [MID +/- 2.25] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	2	5	-	MD 1.5 higher (3.4 lower to 6.4 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in kg - Follow-up: 12 months [MID +/- 1.60] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	2	5	-	MD 0 higher (3.07 lower to 3.07 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder external rotation in kg - Follow-up: 12 months [MID +/- 0.90] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2	5	-	MD 4.3 higher (1.23 to 7.37 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 6 weeks (pain at rest) [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	153	150	-	MD 0.58 lower (1.09 to 0.07 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 6 weeks (pain on movement) [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	153	150	-	MD 0.55 lower (1.1 lower to 0 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 6 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	145	133	-	MD 0.17 lower (0.7 lower to 0.36 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 12 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	135	139	-	MD 0.68 lower (1.23 to 0.13 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Neuropathic pain: DN4 (≥ 4 indicative of neuropathic pain) - Follow-up: 6 weeks [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	24/153 (15.7%)	21/150 (14%)	RR 1.12 (0.65 to 1.92)	17 more per 1000 (from 49 fewer to 129 more)	⊕⊕OO LOW	CRITICAL

Neuropathic pain: DN4 (≥ 4 indicative of neuropathic pain) - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	26/145 (17.9%)	29/133 (21.8%)	RR 0.82 (0.51 to 1.32)	39 fewer per 1000 (from 107 fewer to 70 more)	⊕⊕OO LOW	CRITICAL
Neuropathic pain: DN4 (≥ 4 indicative of neuropathic pain) - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	22/135 (16.3%)	32/139 (23%)	RR 0.71 (0.43 to 1.15)	67 fewer per 1000 (from 131 fewer to 35 more)	⊕⊕⊕O MODERATE	CRITICAL
Pain: FACT-B4 (arm symptom scale, 0 to 4) - Follow-up: 6 weeks [MID +/- 2.20] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	153	150	-	MD 0.48 lower (1.4 lower to 0.44 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: FACT-B4 (arm symptom scale, 0 to 4) - Follow-up: 6 months [MID +/- 2.20] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	145	133	-	MD 1.11 lower (2.01 to 0.21 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: FACT-B4 (arm symptom scale, 0 to 4) - Follow-up: 12 months [MID +/- 2.60] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	135	139	-	MD 2.02 lower (3.11 to 0.93 lower)	⊕⊕⊕O MODERATE	CRITICAL
Incidence of lymphoedema - Follow-up: 6 weeks [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	22/153 (14.4%)	20/150 (13.3%)	RR 1.08 (0.61 to 1.89)	11 more per 1000 (from 52 fewer to 119 more)	⊕⊕OO LOW	CRITICAL
Incidence of lymphoedema - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	29/145 (20%)	32/133 (24.1%)	RR 0.83 (0.53 to 1.3)	41 fewer per 1000 (from 113 fewer to 72 more)	⊕⊕OO LOW	CRITICAL
Incidence of lymphoedema - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy and usual care]												

2	randomised trials[5]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	33/154 (21.4%)	37/157 (23.6%)	RR 0.92 (0.61 to 1.38)	19 fewer per 1000 (from 92 fewer to 90 more)	⊕⊕OO LOW	CRITICAL
Quality of life: EQ-5D-5L - Follow-up: 6 months [MID +/-0.08] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	196	196	-	MD 0.02 higher (0.02 lower to 0.06 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: EQ-5D-5L - Follow-up: 12 months [MID +/-0.08] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	196	196	-	MD 0.05 higher (0 to 0.1 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-12 physical health composite scale - Follow-up: 6 months [MID +/- 5.60] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	145	133	-	MD 2.73 higher (0.24 to 5.22 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-12 physical health composite scale - Follow-up: 12 months [MID +/- 5.75] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	135	139	-	MD 4.39 higher (1.74 to 7.04 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-12 mental health composite scale - Follow-up: 6 months [MID +/- 5.55] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	145	133	-	MD 2.12 higher (0.37 lower to 4.61 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-12 mental health composite scale - Follow-up: 12 months [MID +/- 5.60] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	135	139	-	MD 1.99 higher (0.58 lower to 4.56 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: FACT-B+4 overall score - Follow-up: 6 months [MID +/- 8.86] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	21	19	-	MD 1.17 higher (8.8 lower to 11.14 higher)	⊕⊕⊕O MODERATE	CRITICAL

Quality of life: FACT-B+4 overall score - Follow-up: 12 months [MID +/- 7.60] (Better indicated by higher values)												
1	randomised trials[3]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	21	19	-	MD 0.44 lower (9.43 lower to 8.55 higher)	⊕⊕OO LOW	CRITICAL
Adherence: number of participants doing arm or shoulder exercises - Follow-up: 6 weeks [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	148/153 (96.7%)	135/150 (90%)	RR 1.07 (1.01 to 1.14)	63 more per 1000 (from 9 more to 126 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Adherence: number of participants doing arm or shoulder exercises - Follow-up: 6 months [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	114/145 (78.6%)	82/133 (61.7%)	RR 1.28 (1.09 to 1.49)	173 more per 1000 (from 55 more to 302 more)	⊕⊕⊕O MODERATE	IMPORTANT
Adherence: number of participants doing arm or shoulder exercises - Follow-up: 12 months [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy and usual care]												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	101/134 (75.4%)	99/138 (71.7%)	RR 1.05 (0.91 to 1.21)	36 more per 1000 (from 65 fewer to 151 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Adherence: number of participants attending physiotherapy sessions - Follow-up: 6 weeks [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy and usual care]												
1	randomised trials[6]	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64/72 (88.9%)	58/67 (86.6%)	RR 1.03 (0.91 to 1.16)	26 more per 1000 (from 78 fewer to 139 more)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Bruce 2022
[2] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[3] Rafn 2018
[4] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[5] Bruce 2022; Rafn 2018
[6] Lauridsen 2005
[7] Study at moderate risk of bias. Quality of the outcome downgraded once.

Physiotherapy (exercise programme) compared to usual care

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy (exercise programme) compared to usual care	Control	Relative (95% CI)	Absolute		
Upper limb function: QuickDASH overall score - Follow-up: 1 month [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	85	-	MD 4.20 lower (8.78 lower to 0.38 higher)	⊕⊕OO LOW	CRITICAL
Upper limb function: QuickDASH overall score - Follow-up: 3 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	85	-	MD 2.30 lower (5.32 lower to 0.72 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: QuickDASH overall score - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	85	-	MD 2.10 lower (4.26 lower to 0.06 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 10.21] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	82	-	MD 1.10 higher (6.2 lower to 8.4 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 3 months [MID +/- 10.81] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	82	-	MD 11.30 higher (5.83 to 16.77 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 8.23] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	82	-	MD 6.50 higher (2.08 to 10.92 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 12 months [MID +/- 10.50] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	62	-	MD 1.1 lower (8.3 lower to 6.1 higher)	⊕⊕⊕O MODERATE	CRITICAL

Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 11.19] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	82	-	MD 5.80 higher (0.52 lower to 12.12 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 3 months [MID +/- 10.86] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	82	-	MD 8.90 higher (3.5 to 14.3 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 7.58] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	72	82	-	MD 3.80 higher (0.5 lower to 8.1 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction (ipsilateral) in degrees - Follow-up: 12 months [MID +/- 19.00] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	68	62	-	MD 0.8 lower (14.2 lower to 12.6 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder external rotation (ipsilateral) in degrees - Follow-up: 12 months [MID +/- 7.50] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	68	62	-	MD 2.7 lower (8.4 lower to 3 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength (dynamic muscle strength): shoulder abduction (ipsilateral) in kg - Follow-up: 12 months [MID +/- 0.49] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	66	61	-	MD 0.3 higher (0.1 lower to 0.7 higher)	⊕⊕OO LOW	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 1 month [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	82	-	MD 0.60 lower (0.95 to 0.25 lower)	⊕⊕⊕O MODERATE	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 3 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	82	-	MD 0.30 lower (0.61 lower to 0.01 higher)	⊕⊕⊕O MODERATE	CRITICAL

Pain: numerical rating scale (0 to 10) - Follow-up: 20 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	82	76	-	MD 0.35 lower (0.89 lower to 0.19 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 6 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	72	82	-	MD 0.50 lower (0.78 to 0.22 lower)	⊕⊕⊕O MODERATE	CRITICAL
Pain: numerical rating scale (0 to 10) - Follow-up: 12 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	82	76	-	MD 0.54 lower (1.11 lower to 0.03 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neuropathic pain: NeuPPS (0 to 5) - Follow-up: 5 months [MID +/- 0.44] (Better indicated by lower values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	82	76	-	MD 0.39 lower (0.68 to 0.1 lower)	⊕⊕OO LOW	CRITICAL
Neuropathic pain: NeuPPS (0 to 5) - Follow-up: 12 months [MID +/- 1.58] (Better indicated by lower values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	82	76	-	MD 0.13 lower (0.88 lower to 0.62 higher)	⊕⊕⊕O MODERATE	CRITICAL
Incidence of lymphoedema - Follow-up: 6 and 12 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
2	randomised trials[1,4]	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	27/154 (17.5%)	20/161 (12.4%)	RR 1.35 (0.8 to 2.29)	43 more per 1000 (from 25 fewer to 160 more)	⊕OOO VERY LOW	CRITICAL
Quality of life: EORTC-C30 (global health scale) - Follow-up: 5 months [MID -8 to +12] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0	-	-	MD 1.5 higher (5.5 lower to 8.5 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: EORTC-C30 (global health scale) - Follow-up: 12 months [MID -8 to +12] (Better indicated by higher values)												

1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	0	-	-	MD 5.8 higher (1 lower to 12.6 higher)	⊕⊕OO LOW	CRITICAL
Adherence: any regular exercise (on a weekly basis) in the study period [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy]												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	53/61 (86.9%)	36/53 (67.9%)	RR 1.28 (1.04 to 1.58)	190 more per 1000 (from 27 more to 394 more)	⊕⊕OO LOW	CRITICAL

[1] Klein 2021
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] Ammitzboll 2020
[5] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Physiotherapy (water exercise programme) compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (water exercise programme) compared to usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Pain: visual analogue scale (0 to 100) - Neck pain; follow-up: 8 weeks Pain – [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	32	33	-	MD 31 lower (46.5 to 15.5 lower)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 100) - Shoulder/axillary pain; follow-up: 8 weeks [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	32	33	-	MD 20 lower (34.64 to 5.36 lower)	⊕⊕OO LOW	CRITICAL

[1] Cantarero-Villanueva 2012
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) compared to usual care

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy (tissue massage, passive mobilisation, and Xbox 360 Kinect™) compared to usual care	Control	Relative (95% CI)	Absolute		
Upper limb function: DASH overall score - Follow-up: 6 weeks [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	19	17	-	MD 8.34 lower (15.42 to 1.26 lower)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 weeks [MID +/- 10.80] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	very serious[5]	none	19	17	-	MD 2.8 lower (16.48 lower to 10.88 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 weeks [MID +/- 13.21] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	very serious[5]	none	19	17	-	MD 2.24 lower (18.88 lower to 14.4 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 6 weeks [MID +/- 6.16] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	very serious[5]	none	19	17	-	MD 2.56 lower (11.3 lower to 6.18 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder flexion in kg - Follow-up: 6 weeks [MID +/- 0.62] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	19	17	-	MD 0.54 lower (1.36 lower to 0.28 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in kg - Follow-up: 6 weeks [MID +/- 0.49] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	very serious[5]	none	19	17	-	MD 0.31 lower (1.24 lower to 0.62 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder external rotation in kg - Follow-up: 6 weeks [MID +/- 0.62] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	19	17	-	MD 0.81 lower (1.64 lower to 0.02 higher)	⊕OOO VERY LOW	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 6 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	19	17	-	MD 1.03 higher (0.05 lower to 2.11 higher)	⊕⊕OO LOW	CRITICAL

[1] Feyzioglu 2020
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[5] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Physiotherapy (myofascial release massage) compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (myofascial release massage) compared to usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function: DASH overall score - Follow-up: 4 weeks [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	10	-	MD 5.5 lower (12.25 lower to 1.25 higher)	⊕⊕OO LOW	CRITICAL
Upper limb function: DASH overall score - Follow-up: 3 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	9	-	MD 9 lower (17.81 to 0.19 lower)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 4 weeks [MID +/- 5.04] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	10	-	MD 10.2 higher (0.84 lower to 21.24 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 3 months [MID +/- 5.83] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	9	-	MD 9.1 higher (3.4 lower to 21.6 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 4 weeks [MID +/- 4.45] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14	10	-	MD 21.6 higher (12 to 31.2 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 3 months [MID +/- 5.09] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	9	-	MD 16.5 higher (5.84 to 27.16 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 4 weeks [MID +/- 6.99] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	10	-	MD 12.5 higher (1.29 to 23.71 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 3 months [MID +/- 7.60] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	9	-	MD 14.9 higher (2.32 to 27.48 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 4 weeks [MID +/- 3.30] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	10	-	MD 4.6 higher (1.06 lower to 10.26 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 3 months [MID +/- 3.52] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	9	-	MD 3.1 higher (3.14 lower to 9.34 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: combination movement of abduction/flexion/external rotation in degrees - Follow-up: 4 weeks [MID +/- 6.03] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	10	-	MD 13.3 higher (1.17 to 25.43 higher)	⊕⊕OO LOW	CRITICAL

Range of movement: combination movement of abduction/flexion/external rotation in degrees - Follow-up: 3 months [MID +/- 6.21] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	9	-	MD 9 higher (4.09 lower to 22.09 higher)	⊕⊕OO LOW	CRITICAL

[1] Marshall-Mckenna 2014
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (group-based educational program and visual material) compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (group-based educational program and visual material) compared to usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Pain: visual analogue scale (0 to 10) - Follow-up: 3 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	79	82	-	MD 1 lower (1.73 to 0.27 lower)	⊕⊕OO LOW	CRITICAL
Adherence to advice provided during interventions: ≥80% - Follow-up: 3 months [MID 0.8 to 1.25; RR greater than 1 favours physiotherapy]												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	14/79 (17.7%)	10/82 (12.2%)	RR 1.45 (0.69 to 3.08)	55 more per 1000 (from 38 fewer to 254 more)	⊕OOO VERY LOW	IMPORTANT

[1] Simoncini 2017
[2] Study at high risk of bias. Quality of the outcome downgraded twice.
[3] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Physiotherapy compared to information about unsupervised exercise

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy compared to information about unsupervised exercise**	**Control**	**Relative (95% CI)**	**Absolute**		

Upper limb function: DASH overall score - Follow-up: 3 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	15	15	-	MD 13.5 lower (24.3 to 2.7 lower)	⊕OOO VERY LOW	CRITICAL
Upper limb function: DASH overall score - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	15	14	-	MD 9 lower (17.2 to 0.8 lower)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 5 days [MID +/- 11.05] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	32	33	-	MD 2.70 lower (14.16 lower to 8.76 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 11.85] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	32	33	-	MD 2.30 lower (14.61 lower to 10.01 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 3 months [MID +/- 9.08] (Better indicated by higher values)												
2	randomised trials[6]	serious[2]	very serious[7]	no serious indirectness	serious[4]	none	47	48	-	MD 12.97 higher (1.05 lower to 27.00 higher)[6]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 7.88] (Better indicated by higher values)												
2	randomised trials[6]	serious[2]	serious[8]	no serious indirectness	serious[4]	none	45	47	-	MD 10.15 higher (1.17 lower to 21.47 higher)[6]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 12 months [MID +/- 4.10] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	28	33	-	MD 5.4 higher (1.13 to 9.67 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 24 months [MID +/- 4.85] (Better indicated by higher values)												

1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	27	33	-	MD 4.7 higher (0.32 lower to 9.72 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 5 days [MID +/- 9.55] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	32	33	-	MD 9 lower (18.92 lower to 0.92 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 11.45] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	32	33	-	MD 9 higher (2.9 lower to 20.9 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 3 months [MID +/- 13.40] (Better indicated by higher values)												
2	randomised trials[6]	serious[2]	serious[8]	no serious indirectness	serious[4]	none	47	48	-	MD 19.86 higher (1.97 to 37.74 higher)[6]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 11.55] (Better indicated by higher values)												
2	randomised trials[6]	serious[2]	very serious[7]	no serious indirectness	serious[4]	none	47	47	-	MD 14.23 higher (3.85 lower to 32.31 higher)[6]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 12 months [MID +/- 5.50] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	28	33	-	MD 7 higher (1.3 to 12.7 higher)[6]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 24 months [MID +/- 7.55] (Better indicated by higher values)												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	27	33	-	MD 7 higher (0.82 lower to 14.82 higher)[6]	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 3 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	15	15	-	MD 2.7 lower (3.6 to 1.8 lower)	⊕OOO VERY LOW	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 6 months [MID reduction of 2 points] (Better indicated by lower values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	15	14	-	MD 2.5 lower (3.5 to 1.5 lower)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: increase of ≥200 ml - Follow-up: 1 month [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4,9]	none	1/32 (3.1%)	1/33 (3%)	RR 1.03 (0.07 to 15.79)[6]	1 more per 1000 (from 28 fewer to 448 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: increase of ≥200 ml - Follow-up: 3 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	very serious[9]	none	3/32 (9.4%)	8/33 (24.2%)	RR 0.39 (0.11 to 1.33)[6]	148 fewer per 1000 (from 216 fewer to 80 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: increase of ≥200 ml - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	very serious[9]	none	1/32 (3.1%)	5/33 (15.2%)	RR 0.21 (0.03 to 1.67)[6]	120 fewer per 1000 (from 147 fewer to 102 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: increase of ≥200 ml - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	very serious[9]	none	2/32 (6.3%)	4/33 (12.1%)	RR 0.52 (0.1 to 2.62)[6]	58 fewer per 1000 (from 109 fewer to 196 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: increase of ≥200 ml - Follow-up: 24 months [MID 0.8 to 1.25; RR less than 1 favours physiotherapy]												
1	randomised trials[5]	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	3/32 (9.4%)	9/33 (27.3%)	RR 0.34 (0.1 to 1.16)[6]	180 fewer per 1000 (from 245 fewer to 44 more)	⊕⊕OO LOW	CRITICAL

[1] Beurskens 2007
[2] >33.3% of weighted data from studies at moderate risk of bias. Quality of the outcome downgraded once.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[5] Box 2002a
[6] Data for Box 2002a was taken from McNeely 2010.
[7] Beurskens 2007; Box 2002a
[7] i-squared >66.7%. Quality of the outcome downgraded twice.
[9] i-squared >33.3%. Quality of the outcome downgraded once.
[10] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Physiotherapy (free-range exercises) compared to physiotherapy (limited-range exercises)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy (free-range exercises) compared to physiotherapy (limited-range exercises)	Control	Relative (95% CI)	Absolute		
Upper limb function: DASH overall score - Follow-up: 1 month [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 10.5 lower (17.84 to 3.16 lower)	⊕⊕OO LOW	CRITICAL
Upper limb function: DASH overall score - Follow-up: 3 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 2.5 lower (8.82 lower to 3.82 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 7 days [MID +/- 8.80] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 10.3 higher (1.4 to 19.2 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 15 days [MID +/- 10.09] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.1 higher (6.49 lower to 12.69 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 9.86] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 11.1 higher (2.12 to 20.08 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 2 months [MID +/- 13.34] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 13.2 higher (2.25 to 24.15 higher)	⊕⊕OO LOW	CRITICAL

Range of movement: shoulder flexion in degrees - Follow-up: 3 months [MID +/- 7.96] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 4.6 higher (2.82 lower to 12.02 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 7 days [MID +/- 10.09] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 11.8 higher (0.65 to 22.95 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 15 days [MID +/- 13.73] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.4 higher (11.6 lower to 14.4 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 13.86] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 16.5 higher (3.35 to 29.65 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 2 months [MID +/- 14.95] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 11.5 higher (1.68 lower to 24.68 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 3 months [MID +/- 13.27] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 8.2 higher (3.21 lower to 19.61 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 7 days [MID +/- 5.20] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 4.5 lower (9.82 lower to 0.82 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 15 days [MID +/- 5.23] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3 lower (8.41 lower to 2.41 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 1 month [MID +/- 4.81] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.2 lower (6.25 lower to 3.85 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 2 months [MID +/- 5.09] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.8 higher (2.95 lower to 6.55 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 3 months [MID +/- 4.59] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.4 lower (5.95 lower to 3.15 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 7 days [MID +/- 5.63] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 5.3 lower (10.76 lower to 0.16 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 15 days [MID +/- 6.66] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.6 lower (9.36 lower to 2.16 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 1 month [MID +/- 5.91] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.4 lower (6.95 lower to 4.15 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 2 months [MID +/- 6.19] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.5 lower (9.06 lower to 2.06 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 3 months [MID +/- 5.08] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.2 lower (6.07 lower to 3.67 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 7 days [MID +/- 6.65] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 6.6 lower (14.04 lower to 0.84 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 15 days [MID +/- 7.97] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 5.9 lower (14.24 lower to 2.44 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 1 month [MID +/- 7.02] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.6 lower (10.67 lower to 3.47 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 2 months [MID +/- 6.96] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 2.1 lower (8.8 lower to 4.6 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 3 months [MID +/- 7.56] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 2.1 higher (4.85 lower to 9.05 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 7 days [MID +/- 6.06] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 5 higher (0.6 lower to 10.6 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 15 days [MID +/- 4.44] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1 higher (3.84 lower to 5.84 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 1 month [MID +/- 4.25] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.5 higher (0.25 lower to 7.25 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 2 months [MID +/- 4.39] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 3.5 higher (0.49 lower to 7.49 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 3 months [MID +/- 4.00] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.3 higher (2.31 lower to 4.91 higher)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 7 days [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31	31	-	MD 0.2 higher (1.17 lower to 1.57 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 15 days [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31	31	-	MD 0.4 lower (1.76 lower to 0.96 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 1 month [MID reduction of 2 points] (Better indicated by lower values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31	31	-	MD 0.8 lower (1.83 lower to 0.23 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 2 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 1.6 lower (2.84 to 0.36 lower)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale (0 to 10) - Follow-up: 3 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	31	31	-	MD 0.9 lower (2.02 lower to 0.22 higher)	⊕⊕OO LOW	CRITICAL

[1] de Almeida Rizzi 2020
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (directed exercises) compared to physiotherapy (free exercises)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (directed exercises) compared to physiotherapy (free exercises)**	**Control**	**Relative (95% CI)**	**Absolute**		
Range of movement: shoulder flexion in degrees - Follow-up: 14 days [MID +/- 10.28] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 3.3 higher (8.3 lower to 14.9 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 28 days [MID +/- 8.41] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 8.8 higher (0.55 lower to 18.15 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 42 days [MID +/- 7.67] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 10.8 higher (2.15 to 19.45 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 14 days [MID +/- 9.51] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 3.2 higher (6.27 lower to 12.67 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 28 days [MID +/- 10.15] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 10.7 higher (0.13 lower to 21.53 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 42 days [MID +/- 10.19] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 15 higher (3.9 to 26.1 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 14 days [MID +/- 3.17] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1 lower (4.62 lower to 2.62 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 28 days [MID +/- 3.28] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1.1 higher (2.29 lower to 4.49 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 42 days [MID +/- 4.38] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 4.3 higher (0.27 to 8.33 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 14 days [MID +/- 4.18] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1.9 higher (2.13 lower to 5.93 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 28 days [MID +/- 3.83] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 0.2 lower (3.97 lower to 3.57 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 42 days [MID +/- 3.77] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 2.3 higher (1.77 lower to 6.37 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 14 days [MID +/- 10.38] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 11.4 higher (0.78 to 22.02 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 28 days [MID +/- 9.18] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 7.2 higher (1.88 lower to 16.28 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 42 days [7.76] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 8.3 higher (0.95 to 15.65 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 14 days [MID +/- 13.51] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 9.9 higher (4.64 lower to 24.44 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 28 days [MID 13.27] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 13.6 higher (0.77 to 26.43 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 42 days [MID +/- 13.51] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 13.9 higher (1.41 to 26.39 higher)	⊕⊕OO LOW	CRITICAL

Adherence: number of physiotherapy sessions [MID +/- 0.95] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 0.64 higher (0.65 lower to 1.93 higher)	⊕⊕OO LOW	IMPORTANT

[1] De Rezende 2006
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (water exercise) compared to physiotherapy (Pilates)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (water exercise) compared to physiotherapy (Pilates)**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life: FACT-B4 overall score - Follow-up: 6 months [MID +/- 1.33] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	45	40	-	MD 0.38 lower (1.41 lower to 0.65 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT-B4 overall score - Follow-up: 12 months [MID +/- 1.32] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	45	40	-	MD 5.86 higher (4.88 to 6.84 higher)	⊕⊕OO LOW	CRITICAL

[1] Odynets 2019b
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interva. Quality of the outcome downgraded once.l

Physiotherapy (water exercise) compared to physiotherapy (yoga)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (water exercise) compared to physiotherapy (yoga)**	**Control**	**Relative (95% CI)**	**Absolute**		

Quality of life: FACT-B4 overall score - Follow-up: 6 months [MID +/- 1.30] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	45	30	-	MD 3.06 lower (4.18 to 1.94 lower)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT-B4 overall score - Follow-up: 12 months [MID +/- 1.35] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	serious[4]	none	45	30	-	MD 1.38 higher (0.27 to 2.49 higher)	⊕OOO VERY LOW	CRITICAL

[1] Odynets 2019b
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (Pilates) compared to physiotherapy (yoga)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (Pilates) compared to physiotherapy (yoga)**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life: FACT-B4 overall score - Follow-up: 6 months [MID +/- 1.30] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	40	30	-	MD 2.68 lower (3.92 to 1.44 lower)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT-B4 overall score - Follow-up: 12 months [MID +/- 1.35] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	40	30	-	MD 4.48 lower (5.74 to 3.22 lower)	⊕⊕OO LOW	CRITICAL

[1] Odynets 2019b
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] Partially applicable. Quality of the outcome downgraded once.

Physiotherapy (Pilates) compared to physiotherapy (combined exercises)

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physiotherapy (Pilates) compared to physiotherapy (combined exercises)	Control	Relative (95% CI)	Absolute		
Upper limb function: DASH overall score - Follow-up: 8 weeks [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 3.07 lower (12.18 lower to 6.04 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 8 weeks [MID +/- 4.42] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 7.36 lower (14.46 to 0.26 lower)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 8 weeks [MID +/- 9.05] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 6.93 lower (20.23 lower to 6.37 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 8 weeks [MID +/- 4.15] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 8.04 lower (13.44 to 2.64 lower)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 8 weeks [MID +/- 5.54] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 7.87 lower (14.77 to 0.97 lower)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder flexion in kg - Follow-up: 8 weeks [MID +/- 1.71] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	18	-	MD 0.24 higher (0.68 lower to 1.16 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength: shoulder abduction in kg - Follow-up: 8 weeks [MID +/- 0.65] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	18	18	-	MD 0.09 higher (0.8 lower to 0.98 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder internal rotation in kg - Follow-up: 8 weeks [MID +/- 1.07] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	18	18	-	MD 0.09 lower (1.31 lower to 1.13 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder external rotation in kg - Follow-up: 8 weeks [MID +/- 0.92] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	18	18	-	MD 0.02 higher (1.19 lower to 1.23 higher)	⊕OOO VERY LOW	CRITICAL
Pain: numerical rating scale (0 to 10) motion - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	18	-	MD 0 higher (1.14 lower to 1.14 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: numerical rating scale (0 to 10) rest - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	18	-	MD 0.67 lower (1.94 lower to 0.6 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Zengin Alpozgen 2017
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Physiotherapy (Pilates) compared to physiotherapy (home exercises)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (Pilates) compared to physiotherapy (home exercises)**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function: DASH overall score - Follow-up: 8 weeks [MID +/- 7] (Better indicated by lower values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 8.19 lower (19.78 lower to 3.4 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 8 weeks [MID +/- 9.86] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.9 lower (11.5 lower to 9.7 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 8 weeks [MID +/- 14.58] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 4 higher (12.7 lower to 20.7 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 8 weeks [MID +/- 5.91] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 1.23 higher (5.31 lower to 7.77 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 8 weeks [MID +/- 7.97] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.6 lower (9.13 lower to 7.93 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder flexion in kg - Follow-up: 8 weeks [MID +/- 0.69] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.63 higher (0.27 lower to 1.53 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in kg - Follow-up: 8 weeks [MID +/- 0.61] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.6 higher (0.25 lower to 1.45 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder internal rotation in kg - Follow-up: 8 weeks [MID +/- 0.93] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.85 higher (0.25 lower to 1.95 higher)	⊕⊕OO LOW	CRITICAL

Upper limb muscle strength: shoulder external rotation in kg - Follow-up: 8 weeks [MID +/- 0.88] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.92 higher (0.25 lower to 2.09 higher)	⊕⊕OO LOW	CRITICAL
Pain: numerical rating scale (0 to 10) motion - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 1.01 lower (2.31 lower to 0.29 higher)	⊕⊕OO LOW	CRITICAL
Pain: numerical rating scale (0 to 10) rest - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	19	-	MD 0.3 lower (1.68 lower to 1.08 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Zengin Alpozgen 2017
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (combined exercises) compared to physiotherapy (home exercises)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (combined exercises) compared to physiotherapy (home exercises)**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function: DASH overall score - Follow-up: 8 weeks [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 5.12 lower (15.72 lower to 5.48 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 8 weeks [MID +/- 9.86] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 6.46 higher (3.3 lower to 16.22 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 8 weeks [MID +/- 14.58] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 10.93 higher (4.62 lower to 26.48 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 8 weeks [MID +/- 5.91] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 9.27 higher (2.72 to 15.82 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 8 weeks [MID +/- 7.97] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 7.27 higher (1.53 lower to 16.07 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder flexion in kg - Follow-up: 8 weeks [MID +/- 0.69] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.39 higher (0.51 lower to 1.29 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in kg - Follow-up: 8 weeks [MID +/- 0.61] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.51 higher (0.3 lower to 1.32 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder internal rotation in kg - Follow-up: 8 weeks [MID +/- 0.93] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.94 higher (0.35 lower to 2.23 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder external rotation in kg - Follow-up: 8 weeks [MID +/- 0.88] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 0.9 higher (0.26 lower to 2.06 higher)	⊕⊕OO LOW	CRITICAL
Pain: numerical rating scale (0 to 10) motion - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	19	-	MD 1.01 lower (2.26 lower to 0.24 higher)	⊕⊕OO LOW	CRITICAL
Pain: numerical rating scale (0 to 10) rest - Follow-up: 8 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18	19	-	MD 0.37 higher (0.82 lower to 1.56 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Zengin Alpozgen 2017
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (manual therapy and upper limb exercises) compared to Physiotherapy (upper limb exercises)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (manual therapy and upper limb exercises) compared to Physiotherapy (upper limb exercises)**	**Control**	**Relative (95% CI)**	**Absolute**		
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 10.65] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	60	63	-	MD 5.7 lower (13.27 lower to 1.87 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 12.18] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	33	44	-	MD 4.9 higher (4.19 lower to 13.99 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 12 months [MID +/- 9.79] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	25	30	-	MD 3 lower (14.84 lower to 8.84 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 18 months [MID +/- 7.25] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	32	40	-	MD 10 lower (17.55 to 2.45 lower)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 13.36] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	60	63	-	MD 4.4 lower (13.9 lower to 5.1 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 10.37] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	33	44	-	MD 0.5 higher (8.36 lower to 9.36 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 12 months [MID +/- 10.28] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	25	30	-	MD 7.5 lower (19.55 lower to 4.55 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 18 months [MID +/- 8.43] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	32	40	-	MD 5.3 lower (12.53 lower to 1.93 higher)	⊕⊕OO LOW	CRITICAL

[1] Pace do Amaral 2012
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after surgery

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after surgery**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function: DASH overall score - Follow-up: 4 months [MID +/- 7] (Better indicated by lower values)												

1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	59	64	-	MD 2 lower (9.4 lower to 5.4 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: DASH overall score - Follow-up: 9 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	59	64	-	MD 2 lower (9.17 lower to 5.17 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb function: DASH overall score - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	53	59	-	MD 4 lower (11.9 lower to 3.9 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 4 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	75	-	MD 1.7 higher (7.38 lower to 10.78 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 9 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	69	75	-	MD 4 higher (5.74 lower to 13.74 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 12 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	69	75	-	MD 5.6 lower (14.98 lower to 3.78 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 4 months [1MID +/- 2.53] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	58	65	-	MD 28 higher (19.77 to 36.23 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 9 months [MID +/- 12.53] (Better indicated by higher values)												

1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	58	69	-	MD 1 higher (7.3 lower to 9.3 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 12 months [MID +/- 12.76] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55	65	-	MD 2 lower (10.41 lower to 6.41 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 4 months [MID +/- 11.33] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	58	65	-	MD 3 lower (10.63 lower to 4.63 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 9 months [MID +/- 11.14] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	58	69	-	MD 2 lower (9.36 lower to 5.36 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 12 months [MID +/- 11.14] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55	65	-	MD 2 lower (9.48 lower to 5.48 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

[1] De Groef 2017
[2] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after radiotherapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy and myofascial therapy compared to physiotherapy and placebo - after radiotherapy**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function: DASH overall score - Follow-up: 3 months [MID +/- 7] (Better indicated by lower values)												

1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	21	24	-	MD 1 higher (9.7 lower to 11.7 higher)	⊕⊕OO LOW	CRITICAL
Upper limb function: DASH overall score - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	21	22	-	MD 1 lower (11.65 lower to 9.65 higher)	⊕⊕OO LOW	CRITICAL
Upper limb function: DASH overall score - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	21	22	-	MD 3 higher (7.97 lower to 13.97 higher)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 3 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	23	25	-	MD 20 lower (36.21 to 3.79 lower)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 6 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	23	25	-	MD 6 lower (20.98 lower to 8.98 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: visual analogue scale (0 to 100) - Follow-up: 12 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	23	25	-	MD 13 lower (27.27 lower to 1.27 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 3 months [MID +/- 11.54] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22	24	-	MD 10 lower (23.79 lower to 3.79 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 6 months [MID +/- 12.26] (Better indicated by higher values)												

1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22	23	-	MD 5 lower (19.04 lower to 9.04 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (physical functioning) - Follow-up: 12 months [MID +/- 12.53] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	21	22	-	MD 14 lower (28.39 lower to 0.39 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 3 months [MID +/- 8.26] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22	24	-	MD 2 lower (12.18 lower to 8.18 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 6 months [MID +/- 9.17] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22	23	-	MD 10 higher (0.52 lower to 20.52 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: SF-36 (mental functioning) - Follow-up: 12 months [MID +/- 9.85] (Better indicated by higher values)												
1	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	21	22	-	MD 10 higher (1.42 lower to 21.42 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] De Groef 2018
[2] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy compared to no intervention during radiotherapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy compared to no intervention during radiotherapy**	**Control**	**Relative (95% CI)**	**Absolute**		
Range of movement: shoulder flexion in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 11.62] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	13	16	-	MD 0.5 lower (14.57 lower to 13.57 higher)	⊕OOO VERY LOW	CRITICAL

Range of movement: shoulder flexion in degrees - Follow-up: 2 months [MID +/- 11.42] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12	12	-	MD 2.2 higher (13.31 lower to 17.71 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 4.05] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	29	31	-	MD 5.11 higher (0.71 to 9.51 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 13.79] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	13	16	-	MD 2.6 higher (14.86 lower to 20.06 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 2 months [MID +/- 13.66] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12	12	-	MD 1.4 higher (17.72 lower to 20.52 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 5.85] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	29	31	-	MD 7.24 higher (1.72 to 12.76 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 6.88] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	13	16	-	MD 0.68 higher (9.24 lower to 10.6 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 2 months [MID +/- 7.47] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	12	12	-	MD 5.65 higher (5.65 lower to 16.95 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 5.46] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	13	16	-	MD 3.36 lower (12.36 lower to 5.64 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 2 months [MID +/- 5.29] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12	12	-	MD 0.3 higher (9.01 lower to 9.61 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 3.95] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	13	16	-	MD 5.81 higher (0.52 to 11.1 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 2 months [MID +/- 4.32] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	12	12	-	MD 3.2 higher (2.96 lower to 9.36 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: end of radiotherapy (5 weeks) [MID +/- 6.14] (Better indicated by higher values)												

1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	13	16	-	MD 4.26 higher (3.05 lower to 11.57 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 2 months [MID +/- 6.07] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12	12	-	MD 0.31 higher (7.8 lower to 8.42 higher)	⊕OOO VERY LOW	CRITICAL

[1] Leal 2016
[2] Study at moderate risk of bias
[3] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[4] Oliveira 2009
[5] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Physiotherapy (early) compared to no intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Physiotherapy (early) compared to no intervention**	**Control**	**Relative (95% CI)**	**Absolute**		
Range of movement: shoulder flexion in degrees - Follow-up: 5 days [MID +/- 10.57] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 29.6 higher (20.09 to 39.11 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 9.67] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 32.9 higher (24.72 to 41.08 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 5.81] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 31 higher (25.96 to 36.04 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 12 months [MID +/- 3.60] (Better indicated by higher values)												

1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 26.7 higher (23.59 to 29.81 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 5 days [MID +/- 9.87] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 15 higher (5.2 to 24.8 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 9.92] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 33.2 higher (25.24 to 41.16 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 8.07] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 18 higher (11.75 to 24.25 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 12 months [MID +/- 3.82] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 21.1 higher (17.98 to 24.22 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 5 days [MID +/- 6.42] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 0.8 higher (5.13 lower to 6.73 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 1 month [MID +/- 5.14] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 11.7 higher (6.58 to 16.82 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 6 months [MID +/- 4.94] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 5.1 higher (0.14 lower to 10.34 higher)	⊕OOO VERY LOW	CRITICAL

Range of movement: shoulder internal rotation in degrees - Follow-up: 12 months [MID +/- 4.86] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 2.9 higher (2.14 lower to 7.94 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 5 days [MID +/- 8.26] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 8.7 higher (2 to 15.4 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 1 month [MID +/- 3.60] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 3.8 higher (0.15 to 7.45 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 6 months [MID +/- 2.82] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 3.7 higher (1.41 to 5.99 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 12 months [MID +/- 2.33] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 0.9 higher (1.1 lower to 2.9 higher)	⊕OOO VERY LOW	CRITICAL
Pain: visual analogue scale - Follow-up: 5 days [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 0.1 lower (0.77 lower to 0.57 higher)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale - Follow-up: 1 month [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 1.1 lower (1.49 to 0.71 lower)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale - Follow-up: 6 months [MID reduction of 2 points] (Better indicated by lower values)												

1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 1.6 lower (1.87 to 1.33 lower)	⊕⊕OO LOW	CRITICAL
Pain: visual analogue scale - Follow-up: 12 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 1.4 lower (1.67 to 1.13 lower)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC QLQ-30 (global health; higher scores better) - Follow-up: 6 months [MID -8 to +12] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 17.5 higher (11.71 to 23.29 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC QLQ-30 (pain; lower scores better) - Follow-up: 6 months [MID +/- 2.04] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 6.8 lower (8.28 to 5.32 lower)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC QLQ-BR23 (symptom scales; lower scores better) - Breast symptoms; Follow-up: 6 months [MID +/- 7.74] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	35	35	-	MD 10.8 lower (16.33 to 5.27 lower)	⊕OOO VERY LOW	CRITICAL
Quality of life: EORTC QLQ-BR23 (symptom scales; lower scores better) - Arm symptoms; Follow-up: 6 months [MID +/- 10.78] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 28.8 lower (37.03 to 20.57 lower)	⊕⊕OO LOW	CRITICAL

[1] Testa 2014
[2] Study at high risk of bias. Quality of the outcome downgraded twice.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.

Exercise: early compared to delayed

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise: early compared to delayed**	**Control**	**Relative (95% CI)**	**Absolute**		

Range of movement: shoulder flexion in degrees - Follow-up: first week [MID +/- 16.00] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	116	228	-	MD 15 higher (7.7 to 22.3 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 1 month [MID +/- 15.00] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 24 higher (16.99 to 31.01 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 6 months [MID +/- 7.85] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 2 higher (1.55 lower to 5.55 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: first week [MID +/- 10.10] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 19 higher (15.47 to 22.53 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 1 month [MID +/- 14.05] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 28 higher (22.31 to 33.69 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 6 months [MID +/- 8.30] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 4 higher (0.8 to 7.2 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: first week [MID +/- 7.00] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 1.5 higher (1.63 lower to 4.63 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 1 month [MID +/- 6.75] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	116	228	-	MD 7 higher (4.06 to 9.94 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 6 months [MID +/- 6.25] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	no serious imprecision	none	116	228	-	MD 0.5 higher (2.08 lower to 3.08 higher)[5]	⊕OOO VERY LOW	CRITICAL
Range of movement: limitation of shoulder flexion in degrees - Follow-up: 2 weeks [MID +/- 7.20] (Better indicated by lower values)												
2	randomised trials[5]	very serious[2]	very serious[6]	no serious indirectness	serious[4]	none	109	107	-	MD 7.43 lower (16.54 lower to 1.67 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: limitation of shoulder flexion in degrees - Follow-up: 1 month [MID +/- 5.00] (Better indicated by lower values)												
1	randomised trials[7]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	58	58	-	MD 1.6 higher (2.28 lower to 5.48 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: limitation of shoulder abduction in degrees - Follow-up: at discharge (average 2 weeks) [MID +/- 5.00] (Better indicated by lower values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	serious[4]	none	51	49	-	MD 1 lower (5.12 lower to 3.12 higher)	⊕⊕OO LOW	CRITICAL
Incidence of lymphoedema (200 ml or more) - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours early exercise]												
1	randomised trials[10]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	16/57 (28.1%)	6/58 (10.3%)	RR 2.71 (1.14 to 6.44)	177 more per 1000 (from 14 more to 563 more)	⊕⊕⊕O MODERATE	CRITICAL

[1] Chen 1999
[2] >33.3% of weighted data from studies at high risk of bias. Quality of the outcome downgraded twice.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[5] Baseline data was not reported only follow-up data. Delayed and later groups were combined as reported by McNeely 2010.
[6] Abe 1998; Dawson 1989
[7] i-squared >66.7%. Quality of the outcome downgraded twice.
[8] Abe 1998
[9] Dawson 1989
[10] Study at moderate risk of bias. Quality of the outcome downgraded once.
[11] Todd 2008

Exercise and usual care compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise and usual care compared to usual care	Control	Relative (95% CI)	Absolute		
Upper limb function (Quick DASH) - Follow-up: 10 weeks [MID +/- 8] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	46	46	-	MD 2.4 lower (10.01 lower to 5.21 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb function (Quick DASH) - Follow-up: 6 months [MID +/- 8] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	46	46	-	MD 3.5 lower (10.94 lower to 3.94 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees at FU (2 to 6 weeks) [MID +/- 9.55] (Better indicated by higher values)												
2	randomised trials[4,5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	47	41	-	MD 2.38 higher (2.32 lower to 7.08 higher)[7]	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: within 2 weeks [MID +/- 1.02] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 5.93 higher (3.66 to 8.2 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 4 weeks [MID +/- 0.88] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 11.35 higher (9.94 to 12.76 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 8 weeks [MID +/- 6.55] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 6.4 higher (1.67 to 11.13 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 6 months [MID +/- 10.15] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73	68	-	MD 1.9 higher (4.41 lower to 8.21 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder abduction in degrees at FU - Follow-up: 2 weeks (post-surgery) [MID +/- 18.60] (Better indicated by higher values)												

1	randomised trials[4]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	16	11	-	MD 17.7 higher (10.73 lower to 46.13 higher)[7]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: within 2 weeks [MID +/- 5.21] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 4 higher (0.03 to 7.97 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 4 weeks [MID +/- 5.23] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 6.7 higher (2.7 to 10.7 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 8 weeks [MID +/- 8.20] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 5.2 higher (0.04 to 10.36 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 6 months [MID +/- 10.80] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	73	68	-	MD 10 higher (3.59 to 16.41 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 8 weeks [MID +/- 6.40] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 2 lower (6.4 lower to 2.4 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 6 months [SDs were not reported] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	[11]	none	73	68	-	MD 1.20 lower (6.2 lower to 3.8 higher)		CRITICAL
Range of movement: shoulder extension in degrees at FU - Follow-up: 6 weeks (end of radiotherapy) [MID +/- 4.65] (Better indicated by higher values)												
1	randomised trials[5]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	31	30	-	MD 0.5 higher (4.14 lower to 5.14 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: within 2 weeks [MID +/- 0.95] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 4.67 higher (3.68 to 5.66 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 4 weeks [MID +/- 0.93] (Better indicated by higher values)												
1	randomised trials[8]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 4.67 higher (3.73 to 5.61 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 8 weeks [MID +/- 7.20] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77	74	-	MD 2.4 higher (2.23 lower to 7.03 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 6 months [MID +/- 7.70] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	73	68	-	MD 5.8 higher (0.63 to 10.97 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength (Constant Murley Score) - Follow-up: 1 month [MID +/- 8.02] (Better indicated by higher values)												
1	randomised trials[11]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	51	51	-	MD 3.5 higher (2.99 lower to 9.99 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength (Constant Murley Score) - Follow-up: 3 months [MID +/- 8.21] (Better indicated by higher values)												

1	randomised trials[12]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	49	47	-	MD 4.42 higher (2.08 lower to 10.92 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength (Constant Murley Score) - Follow-up: 6 months [MID +/- 7.46] (Better indicated by higher values)												
1	randomised trials[12]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	46	45	-	MD 4.13 higher (1.96 lower to 10.23 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in Newtons - Follow-up: 8 weeks [MID +/- 14.30] (Better indicated by lower values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 10.2 higher (0.48 to 19.92 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder abduction in Newtons - Follow-up: 6 months [MID +/- 15.75] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73	68	-	MD 3 higher (8.56 lower to 14.56 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength: shoulder flexion in Newtons - Follow-up: 8 weeks [MID +/- 12.35] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 7.2 higher (0.89 lower to 15.29 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: shoulder flexion in Newtons - Follow-up: 6 months [MID +/- 13.85] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73	68	-	MD 3.8 higher (5.74 lower to 13.34 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength: horizontal extension in Newtons - Follow-up: 8 weeks [MID +/- 13.10] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	77	74	-	MD 4.2 higher (4.14 lower to 12.54 higher)	⊕⊕OO LOW	CRITICAL
Upper limb muscle strength: horizontal extension in Newtons - Follow-up: 6 months [MID +/- 14.05] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73	68	-	MD 3 higher (5.92 lower to 11.92 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength: horizontal flexion in Newtons - Follow-up: 8 weeks [MID +/- 14.60] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77	74	-	MD 2.8 higher (7.53 lower to 13.13 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength: horizontal flexion in Newtons - Follow-up: 6 months [MID +/- 13.00] (Better indicated by higher values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	73	68	-	MD 3.8 lower (13.15 lower to 5.55 higher)	⊕⊕OO LOW	CRITICAL
Pain Score (0 to 10) - Follow-up: 10 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	46	46	-	MD 0.5 lower (1.4 lower to 0.4 higher)	⊕⊕OO LOW	CRITICAL
Pain Score (0 to 10) - Follow-up: 6 months [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	46	46	-	MD 1.4 lower (2.34 to 0.46 lower)	⊕OOO VERY LOW	CRITICAL
Pain (Oxford Shoulder Score) - Follow-up: 10 weeks [MID +/- 6] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	46	46	-	MD 0.4 higher (2.95 lower to 3.75 higher)	⊕⊕OO LOW	CRITICAL
Pain (Oxford Shoulder Score) - Follow-up: 6 months [MID +/- 6] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	46	46	-	MD 1.4 lower (4.68 lower to 1.88 higher)	⊕⊕OO LOW	CRITICAL

Incidence of lymphoedema (difference in arm circumference ≥2cm) [MID 0.8 to 1.25; RR less than 1 favours exercise and usual care]												
2	randomised trials[5,10]	serious[6]	no serious inconsistency	no serious indirectness	serious[3]	none	3/38 (7.9%)	8/34 (23.5%)	RR 0.28 (0.08 to 0.96)	169 fewer per 1000 (from 9 fewer to 216 fewer)	⊕⊕OO LOW	CRITICAL
Incidence of lymphoedema: interlimb arm volume =>10% - Follow-up: 8 weeks [MID 0.8 to 1.25; RR less than 1 favours exercise and usual care]												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	very serious[13]	none	8/77 (10.4%)	8/74 (10.8%)	RR 0.96 (0.38 to 2.43)	4 fewer per 1000 (from 67 fewer to 155 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema: interlimb arm volume =>10% - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours exercise and usual care]												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	very serious[13]	none	6/73 (8.2%)	9/68 (13.2%)	RR 0.62 (0.23 to 1.65)	50 fewer per 1000 (from 102 fewer to 86 more)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 1 month [MID +/- 4.20] (Better indicated by higher values)												
1	randomised trials[12]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	51	-	MD 17.42 higher (14.2 to 20.64 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 10 weeks [MID +/- 8.13] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	46	46	-	MD 1.3 lower (8.55 lower to 5.95 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 3 months [MID +/- 3.87] (Better indicated by higher values)												
2	randomised trials[12,14]	very serious[15]	very serious[16]	no serious indirectness	very serious[13]	none	150	153	-	MD 10.04 higher (4.86 lower to 24.93 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 6 months [MID +/- 4.07] (Better indicated by higher values)												
3	randomised trials[1,12,14]	very serious[15]	very serious[16]	no serious indirectness	very serious[13]	none	196	199	-	MD 10.19 higher (9.65 lower to 30.03 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT-G - Follow-up: 3 months [MID +/- 7.36] (Better indicated by higher values)												
1	randomised trials[14]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	82	92	-	MD 0 higher (4.44 lower to 4.44 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: FACT-G - Follow-up: 6 months [MID +/- 8.05] (Better indicated by higher values)												
1	randomised trials[14]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	82	95	-	MD 2.4 higher (1.83 lower to 6.63 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: FACT-G - Follow-up: 18 months [MID +/- 7.59] (Better indicated by higher values)												
1	randomised trials[17]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	58	56	-	MD 1.3 lower (6.61 lower to 4.01 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: FACT-G - Follow-up: 5 years [MID +/- 6.99] (Better indicated by higher values)												
1	randomised trials[17]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	44	43	-	MD 0.6 lower (6.04 lower to 4.84 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: EORTC-BR23 arm symptoms - Follow-up: 8 weeks [MID +/- 7.00] (Better indicated by lower values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness		none	77	74	-	MD 3 higher (1.96 lower to 7.96 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC-BR23 arm symptoms - Follow-up: 6 months [MID +/- 8.00] (Better indicated by lower values)												

1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	73	68	-	MD 4 higher (1.96 lower to 9.96 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC-BR23 breast symptoms - Follow-up: 8 weeks [MID +/- 9.00] (Better indicated by lower values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77	74	-	MD 1 higher (4.3 lower to 6.3 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: EORTC-BR23 breast symptoms - Follow-up: 6 months [MID +/- 10.00] (Better indicated by lower values)												
1	randomised trials[10]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	73	68	-	MD 4 higher (2.15 lower to 10.15 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC QoL 30 at FU - Post-intervention [MID -8 to +12] (Better indicated by higher values)												
1	randomised trials[18]	serious[9]	no serious inconsistency	no serious indirectness	serious[3]	none	31	30	-	MD 5.3 higher (4.57 lower to 15.17 higher)	⊕⊕OO LOW	CRITICAL
Patient adherence (exercise > 5 times a week) - Week 1-5 [MID 0.8 to 1.25; RR greater than 1 favours exercise and usual care]												
1	randomised trials[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18/35 (51.4%)	29/38 (76.3%)	RR 0.67 (0.47 to 0.97)	252 fewer per 1000 (from 23 fewer to 404 fewer)	⊕OOO VERY LOW	IMPORTANT
Patient adherence (exercise > 5 times a week) - Week 6-10 [MID 0.8 to 1.25; RR greater than 1 favours exercise and usual care]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/35 (31.4%)	26/38 (68.4%)	RR 0.46 (0.27 to 0.78)	369 fewer per 1000 (from 151 fewer to 499 fewer)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Harder 2015
[2] Study at high risk of bias. Quality of the outcome downgraded twice.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] Kilgour 2008
[5] Lee 2007
[6] >33.3% of weighted data from studies at moderate or high risk of bias. Quality of the outcome downgraded once.
[7] Data for Kilgour 2008 was taken from McNeely 2010.
[8] Majed 2022
[9] Study at moderate risk of bias. Quality of the outcome downgraded once.
[10] Kilbreath 2012
[11] SDs were not reported. Therefore, MID could not be calculated
[12] Zhou 2019
[13] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[14] Mutrie 2007
[15] >33.3% of weighted data from studies at high risk of bias. Quality of the outcome downgraded twice.
[16] i-squared >66.7%. Quality of the outcome downgraded twice.
[17] Mutrie 2007 (reported by Mutrie 2012)
[18] Lee 2007 (data extracted from McNeely 2010)

Exercise: face to face exercise compared to usual care

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise: face to face exercise compared to usual care	Control	Relative (95% CI)	Absolute		
Upper body function (DASH 0 to 100) - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 0.1 lower (5.73 lower to 5.53 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper body function (DASH 0 to 100) - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 0.9 lower (6.21 lower to 4.41 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 6 months [MID +/- 1.75] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 1 higher (0.1 lower to 2.1 higher)	⊕⊕OO LOW	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 12 months [MID +/- 1.75] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 1.1 higher (0.03 to 2.17 higher)	⊕⊕OO LOW	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 6 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 4.4 higher (1.8 lower to 10.6 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 12 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 1.7 higher (4.22 lower to 7.62 higher)	⊕⊕⊕O MODERATE	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours face to face exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/67 (6%)	6/60 (10%)	RR 0.6 (0.18 to 2.01)	40 fewer per 1000 (from 82 fewer to 101 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours face to face exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	8/67 (11.9%)	9/60 (15%)	RR 0.8 (0.33 to 1.93)	30 fewer per 1000 (from 101 fewer to 139 more)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 6 months [MID +/- 10.55] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 3 higher (4.21 lower to 10.21 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: FACT B+4 - Follow-up: 12 months [MID +/- 10.35] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 3 higher (3.86 lower to 9.86 higher)	⊕⊕⊕O MODERATE	CRITICAL
Patient adherence to exercise (at 6 or 12 months) [MID 0.8 to 1.25; RR greater than 1 favours face to face exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	50/67 (74.6%)	40/60 (66.7%)	RR 1.12 (0.89 to 1.4)	80 more per 1000 (from 73 fewer to 267 more)	⊕⊕OO LOW	IMPORTANT

[1] Hayes 2013
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.

[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Exercise: telephone delivered exercise compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise: telephone delivered exercise compared to usual care	Control	Relative (95% CI)	Absolute		
Upper body function (DASH 0 to 100) - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 6.7 lower (12.09 to 1.31 lower)	⊕⊕OO LOW	CRITICAL
Upper body function (DASH 0 to 100) - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 6.7 lower (12 to 1.4 lower)	⊕⊕OO LOW	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 6 months [MID +/- 1.75] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 0.7 higher (0.43 lower to 1.83 higher)	⊕⊕OO LOW	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 12 months [MID +/- 1.75] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 0.7 higher (0.38 lower to 1.78 higher)	⊕⊕OO LOW	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 6 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 1.7 lower (7.71 lower to 4.31 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 12 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	60	-	MD 1.5 lower (7.42 lower to 4.42 higher)	⊕⊕⊕O MODERATE	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours telephone delivered exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/67 (6%)	6/60 (10%)	RR 0.6 (0.18 to 2.01)	40 fewer per 1000 (from 82 fewer to 101 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours telephone delivered exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	8/67 (11.9%)	9/60 (15%)	RR 0.8 (0.33 to 1.93)	30 fewer per 1000 (from 101 fewer to 139 more)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 6 months [MID +/- 10.55] (Better indicated by higher values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 8.5 higher (1.41 to 15.59 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 12 months [MID +/- 10.35] (Better indicated by higher values)												
1	randomised trials[1]	serious[3]	no serious inconsistency	no serious indirectness	serious[3]	none	67	60	-	MD 7 higher (0.01 to 13.99 higher)	⊕⊕OO LOW	CRITICAL

Patient adherence to exercise (at 6 or 12 months) [MID 0.8 to 1.25; RR greater than 1 favours telephone delivered exercise]												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	50/67 (74.6%)	40/60 (66.7%)	RR 1.12 (0.89 to 1.4)	80 more per 1000 (from 73 fewer to 267 more)	⊕⊕OO LOW	IMPORTANT

[1] Hayes 2013
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.
[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.

Exercise: rehabilitation compared to usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise: rehabilitation compared to usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Upper limb function (DASH 0 to 100) - Follow-up: 18 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	29	30	-	MD 5.62 higher (0.29 lower to 11.53 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees - Follow-up: 4 weeks [MID +/- 11.36] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20	12	-	MD 24.35 lower (40.37 to 8.33 lower)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees - Follow-up: 4 weeks [MID +/- 11.76] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20	12	-	MD 28.45 lower (45.04 to 11.86 lower)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder extension in degrees - Follow-up: 4 weeks [MID +/- 3.68] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	20	12	-	MD 1.5 lower (6.69 lower to 3.69 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder adduction in degrees - Follow-up: 4 weeks [MID +/- 4.60] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20	12	-	MD 1.95 higher (4.54 lower to 8.44 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees - Follow-up: 4 weeks [MID +/- 8.22] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20	12	-	MD 8.85 lower (20.43 lower to 2.73 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees - Follow-up: 4 weeks [MID +/- 6.64] (Better indicated by higher values)												
1	randomised trials[4]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20	12	-	MD 10.15 lower (19.52 to 0.78 lower)	⊕⊕OO LOW	CRITICAL
Pain score (VAS 1 to 10) - Follow-up: 18 months [MID +/- 1.33] (Better indicated by lower values)												
1	randomised trials[6]	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	29	30	-	MD 0.26 higher (1.05 lower to 1.57 higher)	⊕⊕OO LOW	CRITICAL

[1] Ibrahim 2017
[2] Study at moderate risk of bias. Quality of the outcome downgraded once.

[3] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[4] da Silveira 2020
[5] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[6] Ibrahim 2017 (reported by Ibrahim 2018a)

Exercise compared to exercise

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise compared to exercise	Control	Relative (95% CI)	Absolute		
Upper body function (DASH 0 to 100) - Follow-up: 10 weeks [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 6.1 lower (15.59 lower to 3.39 higher)	⊕OOO VERY LOW	CRITICAL
Upper body function (DASH 0 to 100) - Follow-up: 6 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	67	67	-	MD 6.6 higher (1.05 to 12.15 higher)	⊕⊕OO LOW	CRITICAL
Upper body function (DASH 0 to 100) - Follow-up: 12 months [MID +/- 7] (Better indicated by lower values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	67	67	-	MD 5.8 higher (0.57 to 11.03 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees at FU - Follow-up: after radiotherapy [MID +/- 6.40] (Better indicated by higher values)												
1	randomised trials[7]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	17	20	-	MD 13 higher (6.33 to 19.67 higher)[8]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 2 days [MID +/- 10.09] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 4.52 higher (5.26 lower to 14.3 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 8.12] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 19.00 higher (10.91 to 27.09 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 6 weeks (right shoulder) [MID +/- 9.38] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 5.00 higher (5.45 lower to 15.45 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 6 weeks (left shoulder) [MID +/- 6.43] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 4.00 higher (4.15 lower to 12.15 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 10 weeks [MID +/- 10.98] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 9 higher (2.47 lower to 20.47 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 12 weeks [MID +/- 6.07] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 7.47 higher (1.48 to 13.46 higher)	⊕OOO VERY LOW	CRITICAL

Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 12 weeks (right shoulder) [MID +/- 7.14] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 9.00 higher (0.17 to 17.83 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder flexion in degrees (change from baseline) - Follow-up: 12 weeks (left shoulder) [MID +/- 9.06] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 6.00 higher (4.44 lower to 16.44 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees at FU - Follow-up: after radiotherapy [MID +/- 8.85] (Better indicated by higher values)												
1	randomised trials[7]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	17	20	-	MD 11 higher (2.38 to 19.62 higher)[8]	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 2 days [MID +/- 8.56] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 1.04 higher (7.83 lower to 9.91 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 8.25] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 22.95 higher (14.89 to 31.01 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 10 weeks [MID +/- 15.39] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 10 higher (7.39 lower to 27.39 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder abduction in degrees (change from baseline) - Follow-up: 12 weeks {MID +/- 5.33] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 5.4 higher (0.72 to 10.08 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: reported as number of participants with 180 degrees shoulder abduction - Shoulder abduction: 180 degrees at 28 days [MID 0.8 to 1.25; RR greater than 1 favours rehabilitation gymnastics]												
1	randomised trials[11]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	56/80 (70%)	33/99 (33.3%)	RR 2.1 (1.54 to 2.87)	367 more per 1000 (from 180 more to 623 more)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: reported as number of participants with <180 degrees shoulder abduction at 28 days [MID 0.8 to 1.25; RR less than 1 favours rehabilitation gymnastics]												
1	randomised trials[11]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	15/80 (18.8%)	38/99 (38.4%)	RR 0.49 (0.29 to 0.82)	196 fewer per 1000 (from 69 fewer to 273 fewer)	⊕⊕OO LOW	CRITICAL
Range of movement: reported as number of participants with <90 degrees shoulder abduction at 28 days [MID 0.8 to 1.25; RR less than 1 favours rehabilitation gymnastics]												
1	randomised trials[11]	serious[6]	no serious inconsistency	no serious indirectness	very serious[12]	none	9/80 (11.3%)	18/99 (18.2%)	RR 0.62 (0.29 to 1.3)	69 fewer per 1000 (from 129 fewer to 55 more)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 2 days [MID +/- 4.16] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	very serious[12]	none	35	35	-	MD 0.92 lower (5.16 lower to 3.32 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 3.98] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 11.23 higher (6.8 to 15.66 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 6 weeks (rigth shouder) [MID +/- 6.25] (Better indicated by higher values)												

1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[12]	none	22	19	-	MD 0.00 higher (7.21 lower to 7.21 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 6 weeks (left shoulder) [MID +/- 6.87] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 1.00 lower (8.78 lower to 6.78 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 10 weeks [MID 5.60] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 3.9 lower (9.52 lower to 1.72 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 12 weeks [MID +/- 3.03] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 0.80 lower (3.74 lower to 2.14 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 12 weeks (right shoulder) [MID +/- 6.49] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 1.00 lower (8.31 lower to 6.31 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder extension in degrees (change from baseline) - Follow-up: 12 weeks (left shoulder) [MID +/- 6.03] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 5.00 lower (12.22 lower to 2.22 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder adduction in degrees (change from baseline) - Follow-up: 2 days [MID +/- 1.51] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 0.54 higher (1.16 lower to 2.24 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 1.74] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 2.59 higher (0.63 to 4.55 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder adduction in degrees (change from baseline) - Follow-up: 10 weeks [MID +/- 3.77] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 2.3 higher (1.76 lower to 6.36 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees (change from baseline) - Follow-up: 2 days [MID +/- 6.84] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 0.02 higher (5.89 lower to 5.93 higher)	⊕⊕⊕O MODERATE	CRITICAL
Range of movement: shoulder internal rotation in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 5.60] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 10.29 higher (4.85 to 15.73 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees (change from baseline) - Follow-up: 10 weeks [MID +/- 6.76] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 2 lower (9.63 lower to 5.63 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder internal rotation in degrees (change from baseline) - Follow-up: 12 weeks [MID +/- 3.77] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 0.93 higher (2.65 lower to 4.51 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 2 days [MID +/- 5.37] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 6.03 higher (0.81 to 11.25 higher)	⊕⊕OO LOW	CRITICAL

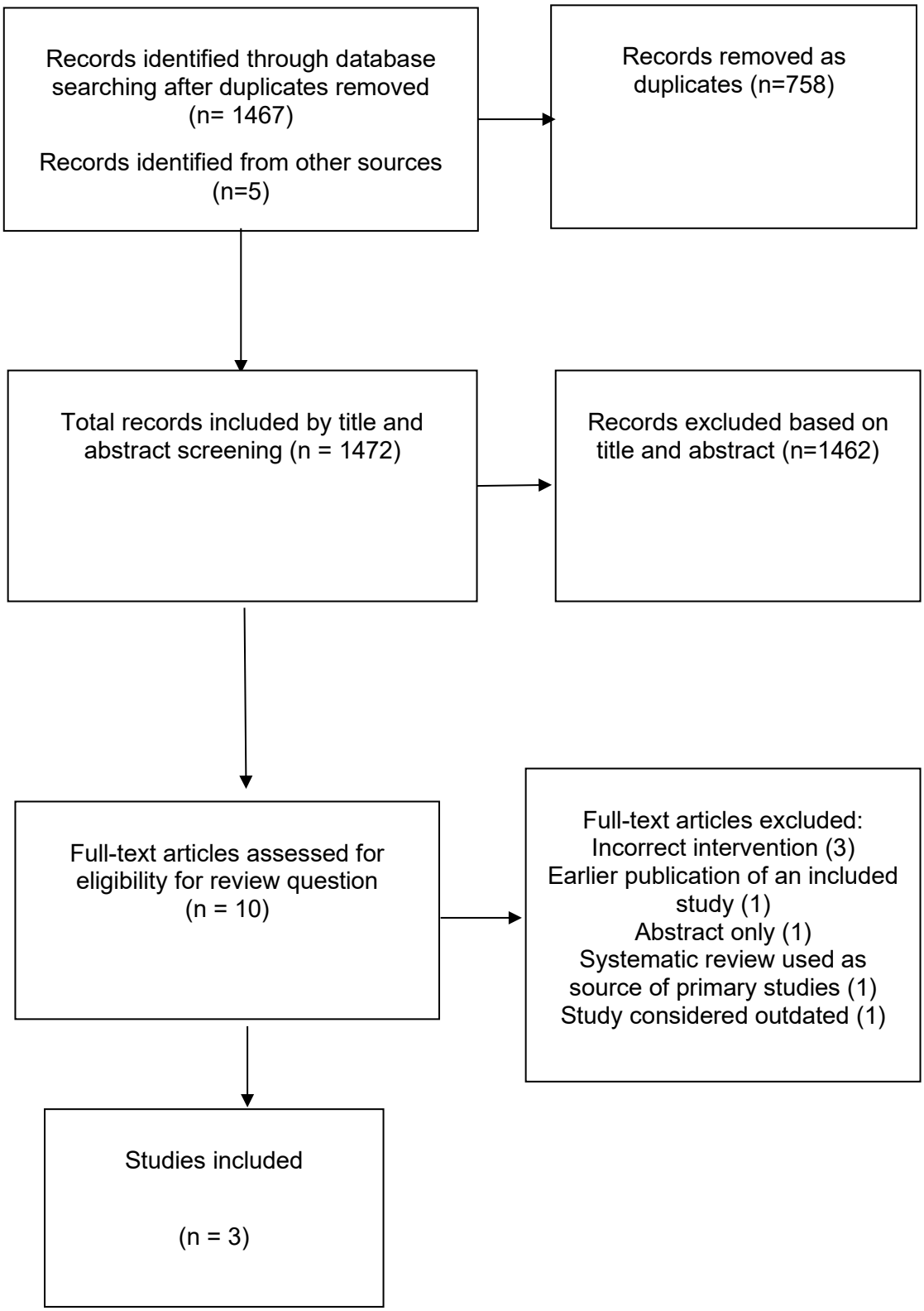
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 5 weeks [MID +/- 5.50] (Better indicated by higher values)												
1	randomised trials[8]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	35	-	MD 9.97 higher (4.1 to 15.84 higher)	⊕⊕OO LOW	CRITICAL
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 10 weeks [MID +/- 5.40] (Better indicated by higher values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 3 lower (9.39 lower to 3.39 higher)	⊕OOO VERY LOW	CRITICAL
Range of movement: shoulder external rotation in degrees (change from baseline) - Follow-up: 12 weeks [MID +/- 4.38] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 0.41 higher (3.96 lower to 4.78 higher)	⊕OOO VERY LOW	CRITICAL
Upper limb muscle strength: shoulder internal rotation at 43 degrees (maximal voluntary isometric contraction) - Follow-up: 13 weeks [MID +/- 0.06] (Better indicated by higher values)												
1	randomised trials[13]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73	72	-	MD 0.02 higher (0.01 lower to 0.05 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper limb muscle strength of affected side in kg - Follow-up: 12 weeks [MID +/- 2.98] (Better indicated by higher values)												
1	randomised trials[10]	serious[6]	no serious inconsistency	serious[3]	serious[4]	none	34	34	-	MD 0.8 lower (3.32 lower to 1.72 higher)	⊕OOO VERY LOW	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 6 months [MID +/- 1.45] (Better indicated by higher values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	67	-	MD 0.3 higher (0.65 lower to 1.25 higher)	⊕⊕⊕O MODERATE	CRITICAL
Upper body function (strength and endurance test) - Follow-up: 12 months [MID +/- 1.30] (Better indicated by higher values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	67	-	MD 0.4 higher (0.46 lower to 1.26 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain: VAS (0 to 100) at FU - Follow-up: after radiotherapy [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[7]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	17	20	-	MD 5.4 lower (19.16 lower to 8.36 higher)[8]	⊕⊕OO LOW	CRITICAL
Pain: VAS 0 to 10 (change from baseline) - Follow-up: 10 weeks [MID reduction of 2 points] (Better indicated by lower values)												
1	randomised trials[1]	very serious[2]	no serious inconsistency	serious[3]	serious[4]	none	24	24	-	MD 1.70 lower (2.89 to 0.51 lower)	⊕OOO VERY LOW	CRITICAL
Pain: EORTC-C30 pain scale 0 to 100 (change from baseline) - Follow-up: 3 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	36	37	-	MD 9.10 lower (19.22 lower to 1.02 higher)	⊕⊕OO LOW	CRITICAL
Pain: EORTC-C30 pain scale 0 to 100 (change from baseline) - Follow-up: 6 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	33	32	-	MD 7.10 lower (17.36 lower to 3.16 higher)	⊕⊕OO LOW	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 6 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	67	-	MD 6.1 higher (0.09 to 12.11 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neuropathic pain (0 to 100) - Follow-up: 12 months [MID +/- 13] (Better indicated by lower values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	67	-	MD 3.2 higher (2.7 lower to 9.1 higher)	⊕⊕⊕O MODERATE	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 6 months [MID 0.8 to 1.25; RR less than 1 favours face to face exercise]												

1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	very serious[12]	none	4/67 (6%)	4/67 (6%)	RR 1 (0.26 to 3.83)	0 fewer per 1000 (from 44 fewer to 169 more)	⊕OOO VERY LOW	CRITICAL
Incidence of lymphoedema (measured by bioimpedance spectroscopy) - Follow-up: 12 months [MID 0.8 to 1.25; RR less than 1 favours face to face exercise]												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	very serious[12]	none	8/67 (11.9%)	8/67 (11.9%)	RR 1 (0.4 to 2.51)	0 fewer per 1000 (from 72 fewer to 180 more)	⊕OOO VERY LOW	CRITICAL
Quality of life: EQ-5D VAS (0 to 100) - Follow-up: 3 months [MID +/-0.08] (Better indicated by higher values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	37	-	MD 11.4 higher (3.94 to 18.86 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life: EQ-5D VAS (0 to 100) - Follow-up: 6 months [MID +/-0.08] (Better indicated by higher values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	34	34	-	MD 6 higher (0.7 lower to 12.7 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 6 months [MID +/- 9.75] (Better indicated by higher values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	67	67	-	MD 5.5 lower (12.22 lower to 1.22 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT B+4 - Follow-up: 12 months [MID +/- 9.65] (Better indicated by higher values)												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	67	67	-	MD 4 lower (10.4 lower to 2.4 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: FACT-G (0 to 108) - Follow-up: 6 weeks [MID +/- 5.82] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	12	17	-	MD 4.8 lower (14.7 lower to 5.1 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACT-G (0 to 108) - Follow-up: 12 weeks [MID +/- 5.94] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	12	17	-	MD 3.6 higher (5.17 lower to 12.37 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACIT-F - Follow-up: 6 weeks [MID +/- 9.96] (Better indicated by higher values)												
1	randomised trials[10]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[12]	none	12	17	-	MD 4.7 lower (20.81 lower to 11.41 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: FACIT-F - Follow-up: 12 weeks [MID +/- 9.52] (Better indicated by higher values)												
1	randomised trials[10]	very serious[12]	no serious inconsistency	no serious indirectness	serious[4]	none	12	17	-	MD 8.9 higher (5.92 lower to 23.72 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: EORTC C30 - Follow-up: 3 months [MID -8 to +12] (Better indicated by higher values)												
2	randomised trials[14,15]	serious[16]	no serious inconsistency	serious[17]	serious[4]	none	70	71	-	MD 11.65 higher (6.7 to 16.61 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: EORTC C30 - Follow-up: 6 months [MID -8 to +12] (Better indicated by higher values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	33	32	-	MD 9 higher (1.61 to 16.39 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC BR23 - Arm symptoms at 3 months [MID +/- 9.01] (Better indicated by lower values)												
2	randomised trials[14,15]	serious[16]	no serious inconsistency	serious[17]	serious[4]	none	68	68	-	MD 4.51 lower (10.21 lower to 1.19 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life: EORTC BR23 - Arm symptoms at 6 months [MID +/- 9.83] (Better indicated by lower values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	36	34	-	MD 2.4 lower (11.17 lower to 6.37 higher)	⊕⊕OO LOW	CRITICAL

Quality of life: EORTC BR23 - Breast symptoms at 3 months [MID +/- 8.79] (Better indicated by lower values)												
2	randomised trials[14,15]	serious[16]	no serious inconsistency	serious[17]	no serious imprecision	none	67	71	-	MD 2.88 lower (8.55 lower to 2.8 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: EORTC BR23 - Breast symptoms at 6 months [MID +/- 8.53] (Better indicated by lower values)												
1	randomised trials[14]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	35	34	-	MD 3.7 higher (3.8 lower to 11.2 higher)	⊕⊕OO LOW	CRITICAL
Quality of life: WHOQOL (1 to 5) - Follow-up: after radiotherapy [MID +/- 0.35] (Better indicated by higher values)												
1	randomised trials[7]	serious[6]	no serious inconsistency	no serious indirectness	serious[4]	none	17	20	-	MD 0.42 higher (0.05 to 0.79 higher)	⊕⊕OO LOW	CRITICAL
Patient adherence to exercise (at 6 or 12 months) [MID 0.8 to 1.25; RR greater than 1 favours face to face exercise]												
1	randomised trials[5]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50/67 (74.6%)	50/67 (74.6%)	RR 1.00 (0.82 to 1.22)	0 fewer per 1000 (from 134 fewer to 164 more)	⊕⊕⊕O MODERATE	IMPORTANT
Patient adherence: number of days engaged in aerobic exercise - Follow-up: 6 weeks [MID +/- 6.50] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 6 lower (12.86 lower to 0.86 higher)	⊕OOO VERY LOW	CRITICAL
Patient adherence: number of days engaged in aerobic exercise - Follow-up: 12 weeks [MID +/- 6.45] (Better indicated by higher values)												
1	randomised trials[9]	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	22	19	-	MD 6 lower (12.63 lower to 0.63 higher)	⊕OOO VERY LOW	CRITICAL

[1] Giron 2016
[2] Study at high risk of bias. Quality of the outcome downgraded twice.
[3] Partially applicable study. Quality of the outcome downgraded once.
[4] 95% confidence interval crosses one end of a defined MID interval. Quality of the outcome downgraded once.
[5] Hayes 2013
[6] Study at moderate risk of bias. Quality of the outcome downgraded once.
[7] Hwang 2008
[8] Data for Hwang 2008 was taken from McNeely 2010.
[9] Charati 2022
[10] Reis 2013
[11] Odynets 2019a
[12] Xie 2010
[13] 95% confidence interval crosses both ends of a defined MID interval. Quality of the outcome downgraded twice.
[14] Wiskemann 2017
[15] Haines 2010
[16] Odynets 2019a (reported by Odynets 2018a)
[17] >33.3% of weighted data from studies at moderate risk of bias. Quality of the outcome downgraded once.
[18] >33.3% of weighted data from partially applicable studies. Quality of the outcome downgraded once.

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Study	Bruce J, Mazuquin B, Mistry P, Rees S, Canaway A, Hossain A, Williamson E, Padfield EJ, Lall R, Richmond H, Chowdhury L. Exercise to prevent shoulder problems after breast cancer surgery: the PROSPER RCT. Health Technology Assessment. 2022 Feb 1;26(15).			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis **Study design:** Within-trial economic evaluation **Approach to analysis:** Costs and QALYs were calculated for each trial participant, and total costs and QALYs were then calculated for each arm of the trial. These results were then used to perform an incremental analysis. **Perspective:** UK NHS and Personal Social Services (PSS) **Time horizon:** 12-months **Discounting:** No discounting due to 12-month time horizon	**Population:** Women undergoing breast cancer surgery, at risk of postoperative upper limb morbidity **Intervention:** Usual care plus a physiotherapist-led exercise programme **Comparator:** Usual care	**Cost difference:** -£386.78 (95% CI -£2,491.18, £1717.62) **Currency and cost year:** British Pound Sterling 2015 **Costs included:** Primary analysis – direct intervention costs and broader health-care/PSS costs. Secondary analysis – wider costs and set-up costs.	**QALY difference:** 0.029 (95% CI 0.001, 0.056)	**Incremental analysis:** Dominant **Analysis of uncertainty:** Physiotherapist-led exercise programmes had lower costs and greater QALYs in most one-way sensitivity analyses. At the cost effectiveness threshold values of £20,000 and £30,000 per QALY, the probability was 78% and 84%, respectively, that exercise was the more cost effective of the two arms. The probability of cost effectiveness at a willingness to pay threshold of £20,000 per QALY increased to 97% when the high-cost cancer treatment were excluded.
Data sources				
Outcomes: Data on inpatient hospital spells and outpatient attendances during the trial were sourced from HES. **Quality of life:** Health states were measured prospectively using the EQ-5D-5L at three times during the trial, baseline, 6-months and 12-months. **Costs:** Resource use was captured prospectively alongside the trial and used to calculate costs. Direct intervention costs including physiotherapy time and patient materials, and broader health-care/PSS costs such as attendance at a pain clinic were calculated by the trial team, or were obtained from the PSSRU, NHS reference costs, NHS supply chain and from an NHS prescription cost analysis.				
Comments				
Source of funding: This project was funded by the National Institute for Health Research (NIHR) Health Technology Assessment programme and was published in full in Health Technology Assessment; Vol. 26, No. 15.				
Overall applicability				
Directly applicable (**Table 5**)				
Overall quality				
Potentially serious limitations (**Table 6**)				

Study	Haines TP, Sinnamon P, Wetzig NG, Lehman M, Walpole E, Pratt T, Smith A. Multimodal exercise improves quality of life of women being treated for breast cancer, but at what cost? Randomized trial with economic evaluation. Breast cancer research and treatment. 2010 Nov;124(1):163-75.			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis **Study design:** Within-trial economic evaluation **Approach to analysis:** Costs and QALYs were	**Population:** Newly diagnosed breast cancer undergoing adjuvant therapy	**Cost difference:** $270 (95% CI $134, $2,084) [£138.53 (95% CI £68.75,	**QALY difference:** -0.01 (95% CI -0.09, 0.11)	**Incremental analysis:** Dominated **Analysis of uncertainty:** Calculated through 2,000 bootstrap replications of the dataset. There was

Study	Haines TP, Sinnamon P, Wetzig NG, Lehman M, Walpole E, Pratt T, Smith A. Multimodal exercise improves quality of life of women being treated for breast cancer, but at what cost? Randomized trial with economic evaluation. Breast cancer research and treatment. 2010 Nov;124(1):163-75.			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
calculated for each trial participant, and total costs and QALYs were then calculated for each arm of the trial. These results were then used to perform an incremental analysis. **Perspective:** Australian Societal **Time horizon:** 6-months **Discounting:** Discounting is not mentioned – it is likely it was not done given the 6-month time horizon.	following surgery **Intervention:** Multimodal exercise program comprising strength, balance and endurance training elements **Comparator:** sham flexibility and relaxation program	£1,069.28) British Pound Sterling 2006] **Currency and cost year:** Australian Dollar 2006 **Costs included:** Cost of program provision, direct health care costs (Medicare subsidized hospitalization, pharmaceutical costs and other direct health care costs) and productivity costs (paid and unpaid employment)		low probability that the intervention would be both less costly and more effective than the control condition over a 6-month time horizon. For the full dataset the likelihood the intervention would be cost-effective was 0.05%. When outliers were excluded the likelihood the intervention would be cost-effective was 25.55%.
Data sources				
Outcomes: Other outcomes collected as part of the trial include EORTC with BR23 supplement, upper limb swelling, body composition, cancer-related fatigue, general physical capacity and shoulder range of motion. Adverse events were documented prospectively in a log book by participants. **Quality of life:** Health-related quality of life was the primary study outcome and was measured using the EQ-5D instrument with visual analogue scale (VAS), which were then converted to utility scores. Analyses were done at baseline, 3, 6 and 12 months follow-up. **Costs:** Cost of the program provision and direct health costs were valued using market prices. Hospitalisations costs calculated using Australian Diagnosis Related Grouping cost weights, and productivity costs through paid employment by multiplying loss or gain in work-time over the follow-up period relative to baseline assessment using individual wage rates or the study median wage rate if participant had not provided their individual wage rate. Resource use data were extracted from the Medicare Australia Medical Benefit Scheme and Pharmaceutical Benefits Scheme databases. Participants prospectively captured indirect/productivity losses using the Health and Labour Questionnaire.				
Comments				
Source of funding: Not declared, however no conflicts of interest were declared				
Overall applicability				
Partially applicable (**Table 5**)				
Overall quality				
Potentially serious limitations (**Table 6**)				

Study	Gordon LG, DiSipio T, Battistutta D, Yates P, Bashford J, Pyke C, Eakin E, Hayes SC. Cost-effectiveness of a pragmatic exercise intervention for women with breast cancer: results from a randomized controlled trial. Psycho-Oncology. 2017 May;26(5):649-55.			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis **Study design:** Within-	**Population:** Women who have undergone	**Cost difference:**	**QALY difference:** 0.009	**Incremental analysis:** Service provider model: $105,231 [£50,577.83

Study	Gordon LG, DiSipio T, Battistutta D, Yates P, Bashford J, Pyke C, Eakin E, Hayes SC. Cost-effectiveness of a pragmatic exercise intervention for women with breast cancer: results from a randomized controlled trial. Psycho-Oncology. 2017 May;26(5):649-55.			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
trial economic evaluation **Approach to analysis:** Costs and QALYs were calculated for each trial participant, and total costs and QALYs were then calculated for each arm of the trial. These results were then used to perform an incremental analysis. **Perspective:** Australian 'broad' perspective covering 'health providers, patients and government'. Two models were considered, a service provider model where the intervention is implemented by a community organization and a private model where exercise physiologists working privately integrate the intervention into their practice. **Time horizon:** 12-months **Discounting:** Discounting is not mentioned – it is likely it was not done given the 12-month time horizon.	surgery for primary breast cancer **Intervention:** 8-month exercise intervention (involving regular contact with an exercise physiologist over the phone, or home delivered face to face) **Comparator:** Usual care	Service provider model: $947 [£455.16 British Pound Sterling 2014] Private model: $818 [£393.16 British Pound Sterling 2014] **Currency and cost year:** Australian Dollar 2014 **Costs included:** Exercise physiologist and administrative salaries, participant education booklets and supportive materials, a range of exercise measurement devices and hand weights, telephone expenses, office consumables and rental and marketing expenses.		British Pound Sterling 2014] Private model: $90,842 [£43,661.96 British Pound Sterling 2014] **Analysis of uncertainty:** One-way sensitivity analyses were performed for the calculated QALYs, and different cost scenarios. The model was sensitive to variations in the EQ-5D-3L weights used – with results ranging from $16,685 per QALY gained to usual care being dominant (cheaper and more effective) for the private model. Under a service provider model the results for variations in the EQ-5D-3L ranged from $19,328 per QALY to usual care being dominant (cheaper and more effective). In probabilistic sensitivity analysis, the likelihood of being cost effective was 44.4% and 46.3% for the service provider model and private model respectively.
Data sources				
Outcomes: Fact-B+4 questionnaire multi-dimensional tool used to assess quality of life – this was the primary outcome of the study. **Quality of life:** Australian algorithm used to obtain a EuroQol-5D-3L weight, which was then used to derive QALYs for each participant. QALYs were a secondary outcome of the study. **Costs:** Project records were used to calculate the cost of the intervention resources in the service provider model. In the private model costs were calculated using the Australian Government's Medicare Benefits Schedule.				
Comments				
Source of funding: Funded by the National Breast Cancer Foundation, Australia.				
Overall applicability				
Partially applicable (**Table 5**)				
Overall quality				
Potentially serious limitations (**Table 6**)				

Table 5: Applicability checklist

Study	1.1 Is the study population appropriate for the review question?	1.2 Are the interventions appropriate for the review question?	1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	1.4 Is the perspective for costs appropriate for the review question?	1.5 Is the perspective for outcomes appropriate for the review question?	1.6 Are all future costs and outcomes discounted appropriately?	1.7 Are QALYs derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome?	1.8 Overall judgement
Bruce et al. (2022)	Yes	Yes	Yes (UK based study)	Yes (NHS and PSS perspective)	Yes	No – No discounting due to 12-month time horizon	Partly – EQ-5D-5L utility values used and were not mapped on to 3L	Directly applicable
Haines et al. (2010)	Yes	Yes	Partly (Australian based study)	Partly – Australian societal perspective	Partly – Australian societal perspective	Not clear – Discounting is not mentioned, but as the time horizon is 6-months it is assumed discounting was not performed.	Yes – EQ-5D (assumed to be 3L given the study is from 2010)	Partially applicable
Gordon et al. (2017)	Yes	Yes	Partly (Australian based study)	Partly – Australian 'broad' perspective	Partly – Australian 'broad' perspective	Not clear – Discounting is not mentioned, but as the time horizon is 12-months it is assumed discounting was not performed.	Yes – EQ-5D-3L	Partially applicable

Table 6: Limitations checklist

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
Bruce et al. (2022)	Yes	No – 12 month time horizon	Yes	Yes	Partly – Imputation used to handle missing data. Approximately 30-35% of data was missing. Imputations were doing using chained equations and predictive mean matching. Imputation is generally recommended as what should be chosen in the base case, and thus the authors inclusion here is in line with that. Additionally, imputation is reasonable given the amount of missing data and the need to try to account for this in some way.	Partly – broader health-care costs (such as informal care and the intervention training costs) were only considered as part of a secondary analysis. Also, imputation used to handle missing cost data.	Yes	Yes – UK study	Yes	Yes	Yes	Potentially serious limitations – unclear the generalizability to a longer time horizon.

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
Haines et al. (2010)	Yes	No – 6 month time horizon	Yes	Yes	Yes	Yes	Yes – extracted from the Medicare Australia Medical Benefit Scheme and Pharmaceutical Benefits Scheme databases.	Yes	Partly – Information is presented in different parts of the paper making it difficult to locate	Yes	Yes	Potentially serious limitations – unclear the generalizability to a longer time horizon.
Gordon et al. (2017)	Yes	No – 12 month time horizon	Yes	Yes	Yes	Yes	Partly – broad perspective for costs used in this paper may not be suitable for decision making for a narrower NHS perspective	Yes	Yes	Yes	Yes	Potentially serious limitations – unclear the generalizability to a longer time horizon.

Appendix I – Health economic model

This question was not prioritised for original economic analysis.

Appendix J – Excluded studies

Clinical Studies

Study	Reason for exclusion
Baima, J., Reynolds, S.-G., Edmiston, K. et al. (2017) Teaching of Independent Exercises for Prehabilitation in Breast Cancer. Journal of cancer education : the official journal of the American Association for Cancer Education 32(2): 252-256	- Data not reported in an extractable format *Data was not reported by group (intervention vs comparator)*
Boing, L., Do Bem Fretta, T., De Carvalho Souza Vieira, M. et al. (2020) Pilates and dance to patients with breast cancer undergoing treatment: Study protocol for a randomized clinical trial - MoveMama study. Trials 21(1): 35	- study protocol
Bu, Xiaofan, Ng, Peter Hf, Xu, Wenjing et al. (2022) The Effectiveness of Virtual Reality-Based Interventions in Rehabilitation Management of Breast Cancer Survivors: Systematic Review and Meta-analysis. JMIR serious games 10(1): e31395	- Not a relevant study design *Meta-analysis combines data from RCTs and non-RCTs*
Cantarero-Villanueva, I., Fernandez-Lao, C., Diaz-Rodriguez, L. et al. (2011) A multimodal exercise program and multimedia support reduce cancer-related fatigue in breast cancer survivors: A randomised controlled clinical trial. European Journal of Integrative Medicine 3(3): e189-e200	- Does not contain a population of people meeting the inclusion criteria in the protocol *More than 12 months since treatment (surgery or radiotherapy) in 31.3% of participants in the intervention group*
Castro-Martin, E., Ortiz-Comino, L., Gallart-Aragon, T. et al. (2017) Myofascial Induction Effects on Neck-Shoulder Pain in Breast Cancer Survivors: Randomized, Single-Blind, Placebo-Controlled Crossover Design. Archives of Physical Medicine and Rehabilitation 98(5): 832-840	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery at baseline was >12 months for 38.1% of participants*
Cave, Judith and Jones, Alison (2006) Physiotherapy improves shoulder function after treatment in women with early breast cancer. Cancer treatment reviews 32(5): 398-401	- Not a relevant study design *Commentary on Lauridsen 2005*
Chan, D.N.S.; Lui, L.Y.; So, W.K. (2010) Effectiveness of exercise programmes on shoulder mobility and lymphoedema after axillary lymph node dissection for breast cancer: systematic review. Journal of Advanced Nursing 66(9): 1902-1914	- Systematic review excluded studies meeting inclusion criteria in the protocol *Kilbreath 2006; Laurisden 2005*

Study	Reason for exclusion
Cheema, B., Gaul, C.A., Lane, K. et al. (2008) Progressive resistance training in breast cancer: A systematic review of clinical trials. Breast Cancer Research and Treatment 109(1): 9-26	- Not a relevant study design *Systematic review included RCTs and non-RCTs; time interval between surgery and the start of exercise was not reported*
Cho, O.-H.; Yoo, Y.-S.; Kim, N.-C. (2006) Efficacy of comprehensive group rehabilitation for women with early breast cancer in South Korea. Nursing and Health Sciences 8(3): 140-146	- Not a relevant study design *Quasi-experimental design*
Courneya, Kerry S, Segal, Roanne J, Mackey, John R et al. (2007) Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 25(28): 4396-4404	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery was not reported*
D'Egidio, V., Sestili, C., Mancino, M. et al. (2017) Counseling interventions delivered in women with breast cancer to improve health-related quality of life: a systematic review. Quality of Life Research 26(10): 2573-2592	- Not a relevant study design *Systematic review included RTCs and non-RTCs; no information about time since surgery/radiotherapy*
De Groef, A., Van Kampen, M., Verlvoesem, N. et al. (2017) Effect of myofascial techniques for treatment of upper limb dysfunctions in breast cancer survivors: randomized controlled trial. Supportive Care in Cancer 25(7): 2119-2127	- Does not contain a population of people meeting the inclusion criteria in the protocol *Not all participants had radiotherapy; the time since radiotherapy was not reported*
de la Rosa Diaz, Irene, Torres Lacomba, Maria, Cerezo Tellez, Ester et al. (2017) Accessory Joint and Neural Mobilizations for Shoulder Range of Motion Restriction After Breast Cancer Surgery: A Pilot Randomized Clinical Trial. Journal of chiropractic medicine 16(1): 31-40	- Study does not contain a relevant intervention *Co-intervention was manual lymphatic drainage for postoperative oedema*
Demirci, P.Y.; Tasci, S.; Oztunc, G. (2022) Effect of foot massage on upper extremity pain level and quality of life in women who had a mastectomy operation: A mixed-method study. European Journal of Integrative Medicine 54: 102160	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery was more than 2 years in 70% of participants*
Dincer, U, Kaya, E, Cakar, E et al. (2007) Effectiveness of comprehensive rehabilitation program and home-based exercise in middle and long term mastectomy related disability.	- Study not reported in English

Study	Reason for exclusion
Turkiye fiziksel tip ve rehabilitasyon dergisi 53(4): 138-143	
Dong-Suk, L., Hyeun-Sil, K., Seung-Ok, C. et al. (2021) The effects of exercise intervention for post-operative breast cancer patients in Korea: A systemic review and meta-analysis of randomized controlled trials. Asian Oncology Nursing 21(2): 74-87	- Study does not contain a relevant intervention *Systematic review included studies managing lymphoedema*
Dong, X., Yi, X., Gao, D. et al. (2019) The effects of the combined exercise intervention based on internet and social media software (CEIBISMS) on quality of life, muscle strength and cardiorespiratory capacity in Chinese postoperative breast cancer patients:a randomized controlled trial. Health and Quality of Life Outcomes 17(1): 109	- Does not contain a population of people meeting the inclusion criteria in the protocol
Dos Santos, S., Hill, N., Morgan, A. et al. (2010) Acupuncture for treating common side effects associated with breast cancer treatment: A systematic review. Medical Acupuncture 22(2): 81-97	- Systematic review included studies not meeting inclusion criteria in the protocol
Espindula, R.C., Nadas, G.B., Da Rosa, M.I. et al. (2017) Pilates for breast cancer: A systematic review and meta-analysis. Revista da Associacao Medica Brasileira 63(11): 1006-1011	- Study does not contain a relevant outcome
Eyigor, S., Uslu, R., Apaydin, S. et al. (2018) Can yoga have any effect on shoulder and arm pain and quality of life in patients with breast cancer? A randomized, controlled, single-blind trial. Complementary therapies in clinical practice 32: 40-45	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery/radiotherapy was not reported*
Eyigor, S, Karapolat, H, Yesil, H et al. (2010) Effects of pilates exercises on functional capacity, flexibility, fatigue, depression and quality of life in female breast cancer patients: a randomized controlled study. European journal of physical and rehabilitation medicine 46(4): 481-7	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery/radiotherapy was not reported. Time since diagnosis was 38 and 37 months in the intervention and control groups respectively*
Forchuk, C., Baruth, P., Prendergast, M. et al. (2004) Postoperative Arm Massage: A Support for Women with Lymph Node Dissection. Cancer Nursing 27(1): 25-33	- Data not reported in an extractable format

Study	Reason for exclusion
Gajbhiye, Poonam P. and Deshpande, Leena (2013) To compare the effects of Pilates exercises and Conventional therapy on Upper Extremity Function and Quality of Life in women with breast cancer. Indian Journal of Occupational Therapy (Indian Journal of Occupational Therapy) 45(1): 3-9	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery/radiotherapy was not reported*
Galantino, M.L. and Stout, N.L. (2013) Exercise interventions for upper limb dysfunction due to breast cancer treatment. Physical therapy 93(10): 1291-1297	- Review article but not a systematic review
Galantino, Mary Lou and Stout, Nicole L (2013) Exercise interventions for upper limb dysfunction due to breast cancer treatment. Physical therapy 93(10): 1291-7	- Duplicate reference
Galiano-Castillo, N., Cantarero-Villanueva, I., Fernandez-Lao, C. et al. (2016) Telehealth system: A randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. Cancer 122(20): 3166-3174	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery at baseline was >12 months in 27.5% in the intervention group and 46.3% in the control group*
Giacalone, Andrea; Alessandria, Paola; Ruberti, Enzo (2019) The Physiotherapy Intervention for Shoulder Pain in Patients Treated for Breast Cancer: Systematic Review. Cureus 11(12): e6416	- Review article but not a systematic review
Gordon, LG, Battistutta, D, Scuffham, P et al. (2005) The impact of rehabilitation support services on health-related quality of life for women with breast cancer. Breast cancer research and treatment 93(3): 217-226	- Does not contain a population of people meeting the inclusion criteria in the protocol
Hanssens, S, Fontaine, C, Decoster, L et al. (2012) The effect of a varied exercise program (VEP) on shoulder function and lymphedema (LE) in breast cancer survivors (BCs): a pilot study. Journal of clinical oncology 30: doi101200jco20123027suppl82	- Conference abstract
Hu, C. and Zhou, L. (2011) Exercise interventions for upper-Limb dysfunction caused by breast cancer treatment. Clinical Journal of Oncology Nursing 15(5): 569-570	- Review article but not a systematic review

Study	Reason for exclusion
Huo, H, Wang, Q, Zhou, S et al. (2021) The application of personalized rehabilitation exercises in the postoperative rehabilitation of breast cancer patients. Annals of palliative medicine 10(4): 4486-4492	- Not a relevant study design *Non-randomised controlled trial*
Joo, O.Y., Moon, S.J., Lee, D.W. et al. (2021) The effect of early arm exercise on drainage volume after total mastectomy and tissue expander insertion in breast cancer patients: a prospective study. Archives of Plastic Surgery 48(6): 583-589	- Study does not contain a relevant outcome
Kim, M, Lee, M, Kim, M et al. (2019) Effectiveness of therapeutic inflatable ball self-exercises for improving shoulder function and quality of life in breast cancer survivors after sentinel lymph node dissection. Supportive care in cancer	- Not a relevant study design *Quasi-experimental design*
Kneis, S., Wehrle, A., Ilaender, A. et al. (2018) Results From a Pilot Study of Handheld Vibration: Exercise Intervention Reduces Upper-Limb Dysfunction and Fatigue in Breast Cancer Patients Undergoing Radiotherapy: VibBRa Study. Integrative Cancer Therapies 17(3): 717-727	- Not a relevant study design *Non-randomised controlled trial*
Lara-Palomo, I.C., Castro-Sanchez, A.M., Cordoba-Pelaez, M.M. et al. (2021) Effect of myofascial therapy on pain and functionality of the upper extremities in breast cancer survivors: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health 18(9): 4420	- Systematic review included studies not meeting inclusion criteria in the protocol
Le Vu, B, Dumortier, A, Guillaume, M et al. (1997) Efficacy of massage and mobilization of the upper limb after surgical treatment of breast cancer. Bulletin du cancer 84(10): 957-961	- Study not reported in English
Le, VB, Dumortier, A, Guillaume, M-V et al. (1997) Physiotherapy after surgery for breast cancer. EFFICACITE DU MASSAGE ET DE LA MOBILISATION DU MEMBRE SUPERIEUR APRES TRAITEMENT CHIRURGICAL DU CANCER DU SEIN. Bulletin du cancer 84(10): 957-961	- Study not reported in English
Lee, S.A., Kang, J.Y., Kim, Y.D. et al. (2010) Effects of a scapula-oriented shoulder exercise	- Does not contain a population of people meeting the inclusion criteria in the protocol

Study	Reason for exclusion
programme on upper limb dysfunction in breast cancer survivors: a randomized controlled pilot trial. Clinical rehabilitation 24(7): 600-613	*Mean time since breast cancer surgery to participation in study was 350.2 (SD 236.6) days*
Liu, L., Petrich, S., McLaren, B. et al. (2018) An integrative Tai Chi program for patients with breast cancer undergoing cancer therapy: study protocol for a randomized controlled feasibility study. Journal of Integrative Medicine 16(2): 99-105	- study protocol
Liu, Xuepu; Li, Qiuping; Zhao, Xingzhen (2015) Study on influence of super early zero docking upper limb rehabilitation gymnastics on shoulder joint function rehabilitation of breast cancer patients after modified radical mastectomy. Chinese nursing research 29(5b): 1706-1709	- Study not reported in English
Lotze, M.T., Duncan, M.A., Gerber, L.H. et al. (1981) Early versus delayed shoulder motion following axillary dissection. A randomized prospective study. Annals of Surgery 193(3): 288-295	- Data not reported in an extractable format *Data was combined from participants with melanoma and participants with breast cancer*
Loubani, K, Kizony, R, Milman, U et al. (2021) Hybrid Tele and In-Clinic Occupation Based Intervention to Improve Women's Daily Participation after Breast Cancer: a Pilot Randomized Controlled Trial. International journal of environmental research and public health 18(11)	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery at baseline was not reported*
Luo, X.-C., Liu, J., Fu, J. et al. (2020) Effect of Tai Chi Chuan in breast cancer patients: A systematic review and meta-analysis. Frontiers in Oncology 10: 607	- Systematic review included studies not meeting inclusion criteria in the protocol
Malicka, I, Stefańska, M, Rudziak, M et al. (2011) The influence of Nordic walking exercise on upper extremity strength and the volume of lymphoedema in women following breast cancer treatment. Isokinetics and exercise science 19(4): 295-304	- Does not contain a population of people meeting the inclusion criteria in the protocol *Average time since surgical treatment was 7.6 ±6.5 years*
Mariano, KOP, De Fatima Pinheiro Pessanha Diniz, M, Silva, AT et al. (2015) Effect of exercises with swiss ball previously applied to radiation therapy for breast cancer. Revista neurociencias 23(1): 55-61	- Study not reported in English

Study	Reason for exclusion
Massingill, Jeanne, Jorgensen, Cara, Dolata, Jacqueline et al. (2018) Myofascial Massage for Chronic Pain and Decreased Upper Extremity Mobility After Breast Cancer Surgery. International journal of therapeutic massage & bodywork 11(3): 4-9	- Does not contain a population of people meeting the inclusion criteria in the protocol *Interventions did not started within a year of the end of surgery in around half of participants*
Mayo, N (2006) Reducing Arm morbidity Through Physical Therapy Provided Pre- and Post- Breast Cancer Surgery. Physician Data Query (PDQ)	- Not a peer-reviewed publication *Clinical trials registry without published results*
McNeely, Margaret L, Campbell, Kristin, Ospina, Maria et al. (2010) Exercise interventions for upper-limb dysfunction due to breast cancer treatment. The Cochrane database of systematic reviews: cd005211	- Systematic review used as source of primary studies
Meneses, K., McNees, P., Azuero, A. et al. (2009) Preliminary evaluation of psychoeducational support interventions on quality of life in rural breast cancer survivors after primary treatment. Cancer Nursing 32(5): 385-397	- Study does not contain a relevant intervention *The intervention (psychoeducation) was not about unsupervised post-surgical or post-radiotherapy arm/shoulder exercises*
Mulero Portela, A.L., Colon Santaella, C.L., Cruz Gomez, C. et al. (2008) Feasibility of an exercise program for Puerto Rican women who are breast cancer survivors. Rehabilitation Oncology 26(2): 20-31	- Does not contain a population of people meeting the inclusion criteria in the protocol *All participants received surgical treatment for breast cancer within the past 5 years*
Mur-Gimeno, E., Postigo-Martin, P., Cantarero-Villanueva, I. et al. (2022) Systematic review of the effect of aquatic therapeutic exercise in breast cancer survivors. European journal of cancer care 31(1): e13535	- Systematic review used as source of primary studies *Included study not found in search: Odynets, T., Briskin, Y., & Todorova, V. (2019). Effects of different exercise interventions on quality of life in breast cancer patients: A randomized controlled trial. Integrative Cancer Therapies, 18,*
Mustian, Karen M; Katula, Jeffrey A; Zhao, Hongwei (2006) A pilot study to assess the influence of tai chi chuan on functional capacity among breast cancer survivors. The journal of supportive oncology 4(3): 139-145	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since breast cancer surgery or radiotherapy was not reported; one of the inclusion criteria was 1 week to 30 months post breast cancer treatment*
Naczk, Alicja, Huzarski, Tomasz, Dos, Janusz et al. (2022) Impact of Inertial Training on Muscle	- Does not contain a population of people meeting the inclusion criteria in the protocol

Study	Reason for exclusion
Strength and Quality of Life in Breast Cancer Survivors. International journal of environmental research and public health 19(6)	*Participants with mastectomy (average time from surgery: 12.1 years)*
Odynets, T.; Briskin, Y.; Pityn, M. (2019) Effectiveness of individualized physical rehabilitation programs for upper extremity disorders in women with post-mastectomy syndrome. Revista Andaluza de Medicina del Deporte 12(4): 372-375	- Full text paper not available
Oliveira, MM, Souza, GA, Miranda Mde, S et al. (2010) Upper limbs exercises during radiotherapy for breast cancer and quality of life. Revista brasileira de ginecologia e obstetricia 32(3): 133-138	- Study not reported in English
Pan, Y., Yang, K., Shi, X. et al. (2015) Tai Chi Chuan exercise for patients with breast cancer: A systematic review and meta-analysis. Evidence-based Complementary and Alternative Medicine 2015: 535237	- Systematic review included studies not meeting inclusion criteria in the protocol
Pan, Y.Q., Yang, K.H., Wang, Y.L. et al. (2014) Massage interventions and treatment-related side effects of breast cancer: a systematic review and meta-analysis. International Journal of Clinical Oncology 19(5): 829-841	- Study does not contain a relevant intervention *Intervention is not aimed at improving arm/shoulder problems*
Paolucci, T., Bernetti, A., Paoloni, M. et al. (2019) Therapeutic Alliance in a Single Versus Group Rehabilitative Setting After Breast Cancer Surgery: Psychological Profile and Performance Rehabilitation. BioResearch Open Access 8(1): 101-110	- Primary study *Study does not contain extractable data*
Paolucci, T., Bernetti, A., Bai, A.V. et al. (2021) The recovery of reaching movement in breast cancer survivors: two different rehabilitative protocols in comparison. European journal of physical and rehabilitation medicine 57(1): 137-147	- Does not contain a population of people meeting the inclusion criteria in the protocol *Time since surgery was more than 12 months*
Park, H.-Y., Nam, K.E., Lim, J.-Y. et al. (2021) Real-time interactive digital healthcare system for post-operative breast cancer patients: study protocol for a randomized controlled trial. Trials 22(1): 549	- study protocol
Pinto-Carral, A., Molina, A.J., de Pedro, A. et al. (2018) Pilates for women with breast cancer: A	- Systematic review used as source of primary studies

Study	Reason for exclusion
systematic review and meta-analysis. Complementary Therapies in Medicine 41: 130-140	*Gajbhiye 2013 met inclusion criteria in our protocol*
Redemski, T., Hamilton, D.G., Schuler, S. et al. (2022) Rehabilitation for Women Undergoing Breast Cancer Surgery: A Systematic Review and Meta-Analysis of the Effectiveness of Early, Unrestricted Exercise Programs on Upper Limb Function. Clinical Breast Cancer	- Not a relevant study design *Systematic review included studies which did not meet the inclusion criteria in the protocol (for example, Wingate 1989 was excluded because the combination of data from a non-randomised study and a randomised controlled trial)*
Reger, M., Kutschan, S., Freuding, M. et al. (2022) Water therapies (hydrotherapy, balneotherapy or aqua therapy) for patients with cancer: a systematic review. Journal of Cancer Research and Clinical Oncology 148(6): 1277-1297	- Study does not contain a relevant intervention *Intervention focused on lymphoedema*
Rekha, K and Reshma Rihana, SM (2020) Effects of swiss ball exercise and stretching exercise in chest wall mobility and shoulder range of motion among post-operative breast cancer women. Asian journal of pharmaceutical and clinical research 13(4): 137-141	- Not a relevant study design *Quasi-experimental study*
Ribeiro, I.L., Moreira, R.F.C., Ferrari, A.V. et al. (2019) Effectiveness of early rehabilitation on range of motion, muscle strength and arm function after breast cancer surgery: a systematic review of randomized controlled trials. Clinical rehabilitation 33(12): 1876-1886	- Systematic review included studies not meeting inclusion criteria in the protocol
Richmond, H., Lait, C., Srikesavan, C. et al. (2018) Development of an exercise intervention for the prevention of musculoskeletal shoulder problems after breast cancer treatment: the prevention of shoulder problems trial (UK PROSPER). BMC health services research 18(1): 463	- Secondary publication of an included study that does not provide any additional relevant information
Rizzi, S.K.L.A., Haddad, C.A.S., Giron, P.S. et al. (2021) Exercise protocol with limited shoulder range of motion for 15 or 30 days after conservative surgery for breast cancer with oncoplastic technique a randomized clinical trial. American Journal of Clinical Oncology: Cancer Clinical Trials 44(6): 283-290	- Data not reported in an extractable format *Mean differences between time points were not reported; measures of dispersion (standard deviation, standard error, confidence intervals) were not reported which could be used to calculate mean differences*
Rosner, M. (2011) Evaluation of a nordic walking program on shoulder joint mobility and isometric force in breast cancer patients.	- Study not reported in English

Study	Reason for exclusion
Deutsche Zeitschrift fur Sportmedizin 62(5): 120-124	
Sandel, S.L., Judge, J.O., Landry, N. et al. (2005) Dance and movement program improves quality-of-life measures in breast cancer survivors. Cancer Nursing 28(4): 301-309	- Does not contain a population of people meeting the inclusion criteria in the protocol *Not all participants received the intervention within 12 months of their breast cancer surgery*
Sato, F, Arinaga, Y, Sato, N et al. (2016) The Perioperative Educational Program for Improving Upper Arm Dysfunction in Patients with Breast Cancer at 1-Year Follow-Up: a Prospective, Controlled Trial. Tohoku journal of experimental medicine 238(3): 229-236	- Not a relevant study design *Non-randomised controlled trial*
Sato, F; Ishida, T; Ohuchi, N (2014) The perioperative educational program for improving upper arm dysfunction in patients with breast cancer: a controlled trial. Tohoku journal of experimental medicine 232(2): 115-122	- Not a relevant study design *Non-randomised controlled trial*
Seung Ah, Lee, Kang, Ji-Young, Yong Duck, Kim et al. (2010) Effects of a scapula-oriented shoulder exercise programme on upper limb dysfunction in breast cancer survivors: a randomized controlled pilot trial. Clinical Rehabilitation 24(7): 600-613	- Does not contain a population of people meeting the inclusion criteria in the protocol
Shah, M. and Shah, B. (2015) Randomized controlled trial study of functional impairment in post mastectomy patients of G.C.R.I. Indian Journal of Physiotherapy and Occupational Therapy 9(2): 188-192	- Not a relevant study design *Observational study*
Shamley, D.R., Barker, K., Simonite, V. et al. (2005) Delayed versus immediate exercises following surgery for breast cancer: A systematic review. Breast Cancer Research and Treatment 90(3): 263-271	- Study does not contain a relevant outcome
Shao, Y.-W., Shu, Q., Xu, D. et al. (2021) Effect of different rehabilitation training timelines to prevent shoulder dysfunction among postoperative breast cancer patients: study protocol for a randomized controlled trial. Trials 22(1): 16	- study protocol
So, HS, Kim, IS, Yoon, JH et al. (2006) Effects of aerobic exercise using a flex-band on physical functions & body image in women	- Study not reported in English

Study	Reason for exclusion
undergoing radiation therapy after a mastectomy. Taehan Kanho Hakhoe chi 36(7): 1111-1122	
Sprod, L.K., Drum, S.N., Bentz, A.T. et al. (2005) The effects of walking poles on shoulder function in breast cancer survivors. Integrative Cancer Therapies 4(4): 287-293	- Does not contain a population of people meeting the inclusion criteria in the protocol *Participants did not start intervention within 12 months of their breast cancer surgery*
Sweeney, F.C., Demark-Wahnefried, W., Courneya, K.S. et al. (2019) Aerobic and Resistance Exercise Improves Shoulder Function in Women Who Are Overweight or Obese and Have Breast Cancer: A Randomized Controlled Trial. Physical therapy 99(10): 1334-1345	- Does not contain a population of people meeting the inclusion criteria in the protocol *13% of participants did not have radiotherapy*
Tatham, Barbara, Smith, Jenna, Cheifetz, Oren et al. (2013) The efficacy of exercise therapy in reducing shoulder pain related to breast cancer: a systematic review. Physiotherapy Canada. Physiotherapie Canada 65(4): 321-30	- Systematic review included studies not meeting inclusion criteria in the protocol
Wang, B-G, Yuan, X-Y, Wang, Q-T et al. (2005) Functional rehabilitation gymnastics for the edema of upper limbs and the activity of shoulder joint in postoperative patients with breast cancer. Chinese journal of clinical rehabilitation 9(30): 16-19	- Study not reported in English
Wang, YL, Sun, XY, Wang, YB et al. (2012) The effect of different exercise forms on upper extremity function and life quality in the patients after breast cancer surgery. Chinese journal of physical medicine and rehabilitation [zhong huo wu li yi xue yu kang fu za zhi] 34(1): 64-66	- Study not reported in English
Wingate, L., Croghan, I., Natarajan, N. et al. (1989) Rehabilitation of the mastectomy patient: A randomized, blind, prospective study. Archives of Physical Medicine and Rehabilitation 70(1): 21-24	- Not a relevant study design *Data was combined from a non-randomised pilot study and a randomised controlled trial*
Yang, Y., Gu, D., Qian, Y. et al. (2021) Effectiveness of aerobic exercise on upper limb function following breast cancer treatment: a systematic review and meta-analysis. Annals of palliative medicine 10(3): 3396-3403	- Does not contain a population of people meeting the inclusion criteria in the protocol *Unclear how long after surgery or radiotherapy participants received interventions*

Study	Reason for exclusion
Yuan, R.-Z., Li, K.-P., Wei, X.-L. et al. (2021) Effects of free range-of-motion upper limb exercise based on mirror therapy on shoulder function in patients after breast cancer surgery: study protocol for a randomized controlled trial. Trials 22(1): 815	- study protocol
Yuste Sanchez, M.J., Lacomba, M.T., Sanchez, B.S. et al. (2015) Health related quality of life improvement in breast cancer patients: Secondary outcome from a simple blinded, randomised clinical trial. Breast 24(1): 75-81	- Study does not contain a relevant intervention *Intervention included manual lymphatic drainage*

Economic studies

Study	Reason for exclusion
Perrier L, Foucaut A, Touillaud M, Kempf-Lepine AS, Morelle M, Heinz D, Gomez F, Meyrand R, Baudinet C, Berthouze S, Carretier J. A cost-effectiveness analysis of a 6-month physical activity program versus usual dietary care during adjuvant chemotherapy in breast cancer patients. Value in Health. 2016 May 1;19(3):A149-50.	- Abstract only
Gordon LG, Scuffham P, Battistutta D, Graves N, Tweeddale M, Newman B. A cost-effectiveness analysis of two rehabilitation support services for women with breast cancer. Breast cancer research and treatment. 2005 Nov;94(2):123-33.	- Study too old for economic evaluation results to be considered useful for decision making
Khan KA, Mazuquin B, Canaway A, Petrou S, Bruce J. Systematic review of economic evaluations of exercise and physiotherapy for patients treated for breast cancer. Breast cancer research and treatment. 2019 Jul;176(1):37-52.	- Systematic review included studies not meeting inclusion criteria in the protocol
Bruce J, Mazuquin B, Canaway A, Hossain A, Williamson E, Mistry P, Lall R, Petrou S, Lamb SE, Rees S, Padfield E. Exercise versus usual care after non-reconstructive breast cancer surgery (UK PROSPER): multicentre randomised controlled trial and economic evaluation. bmj. 2021 Nov 11;375.	- Initial publication of an included Health Technology Assessment (HTA). This publication is substantially shorter, therefore we excluded it and instead only included the substantially more comprehensive HTA report.
May AM, Bosch MJ, Velthuis MJ, Van Der Wall E, Bisschop CN, Los M, Erdkamp F, Bloemendal HJ, De Roos MA, Verhaar M, ten	- Inappropriate intervention (exercise intervention for cancer-related fatigue)

Study	Reason for exclusion
Bokkel Huinink D. Cost-effectiveness analysis of an 18-week exercise programme for patients with breast and colon cancer undergoing adjuvant chemotherapy: the randomised PACT study. BMJ open. 2017 Mar 1;7(3):e012187.	
van Waart H, van Dongen JM, van Harten WH, Stuiver MM, Huijsmans R, Hellendoorn-van Vreeswijk JA, Sonke GS, Aaronson NK. Cost–utility and cost-effectiveness of physical exercise during adjuvant chemotherapy. The European Journal of Health Economics. 2018 Jul;19(6):893-904.	Inappropriate intervention (exercise intervention aimed to improve overall physical function and cancer-related fatigue, and not specific to improving arm or shoulder mobility)
Mewes JC, Steuten LM, Duijts SF, Oldenburg HS, van Beurden M, Stuiver MM, Hunter MS, Kieffer JM, van Harten WH, Aaronson NK. Cost-effectiveness of cognitive behavioral therapy and physical exercise for alleviating treatment-induced menopausal symptoms in breast cancer patients. Journal of cancer survivorship. 2015 Mar;9(1):126-35.	- Inappropriate intervention (cognitive behavioural therapy and physical exercise for alleviating treatment-induced menopausal symptoms)

Appendix K – Research recommendations – full details

K.1.1 Research recommendation

What is the most effective and cost-effective way of delivering the intervention (for example type of physiotherapy or exercise, mode of delivery, number of sessions) to reduce arm and shoulder problems after breast cancer surgery or radiotherapy, and what is the acceptability of the intervention for different groups, such as:

- women, men, trans people and non-binary people
- people from minority ethnic family backgrounds
- people with learning disabilities or cognitive impairment, or physical disabilities, or both
- neurodiverse people?

K.1.2 Why this is important

The committee highlighted that there was a lack of long-term evidence (only 4 studies reported more than 12 months follow-up [Bendz 2002, Box 2002a, Ibrahim 2017, Mutrie 2012, Pace do Amaral 2012]). They also noted that lower quality evidence compared interventions to each other and showed that there were significant results at short term (6 months or less) and medium term (more than 6 months and up to 12 months) in most of the outcomes but without a clear effect of a particular intervention. They discussed the importance of investigating outcomes at longer follow-up times (beyond 12 months) to understand how each intervention benefits people in the long term, such as the ability to remain independent and to carry out activities of daily living effectively and without pain. The committee also highlighted that it was important to have feedback on the impact of different ways of delivering interventions to assess patients' acceptability. Therefore, a research recommendation was developed to cover this gap in the evidence and to find the most effective and cost effective way of delivering the intervention (type of physiotherapy or exercise, mode of delivery, number of sessions).

K.1.3 Rationale for research recommendation

Importance to 'patients' or the population	Little is known about the best way of delivering interventions to reduce arm and shoulder problems after breast cancer surgery or radiotherapy. The best way of delivering the intervention may depend on the type of physiotherapy or exercise, on the mode of delivery (for example face to face or virtual, individual or in group), and on the number of sessions. A greater understanding on the best way of delivering interventions will help to provide the best intervention to reduce the number of people who experience arm and shoulder problems after breast cancer surgery or radiotherapy. Patients' acceptability is important to increase the uptake of interventions.
Relevance to NICE guidance	Different types of interventions to reduce arm and shoulder problems have been considered in this guideline and there is limited data on the best way to deliver the intervention and in the short and medium term effects, and very little

	data on longer term effects of these interventions. There was no evidence on patients' acceptability.
Relevance to the NHS	The outcome would affect the ways of delivering interventions to treat arm and shoulder problems by the NHS. More knowledge on this can also reduce the number of people who experience persistent problems, and the costs associated with additional treatment for those people.
National priorities	Moderate
Current evidence base	4 RCTs reporting outcomes beyond 12 months. No UK-based RCTs. No data on the best way to deliver the interventions or on patients' acceptability.
Equality considerations	None known

K.1.4 Modified PICO table

Population	Adults with early or locally advanced breast cancer (18 and over) who have undergone any of the following treatments alone or in combination: • surgery for breast cancer alone or with: axillary clearance, sentinel lymph node biopsy, or node sampling • radiotherapy for breast cancer alone or with regional lymph node radiotherapy
Intervention	Post-surgery or post-radiotherapy: • Physiotherapy aimed at maximising people's ability to move and function • Exercise or rehabilitation classes for people who have undergone surgery or radiotherapy
Comparator	Different ways of delivering the interventions (for example type of physiotherapy or exercise, mode of delivery, number of sessions, frequency, intensity of interventions) compared to each other
Outcome	• Upper limb function: ○ Disabilities of the Arm, Shoulder and Hand scale (DASH; activity limitations domain should be reported separately) ○ Range of movement (ROM), for example: shoulder flexion and abduction ○ Upper limb muscle strength • Pain (validated scales for example: numerical rating scale [NRS], Oxford Shoulder Score) • Incidence of lymphoedema • Quality of life (EQ-5D, FACT-B+4, EORTC-QoL-C30) • Resource use and cost • Patient adherence • Patient acceptability

Study design	Mixed methods (Randomised controlled trial and qualitative to measure patient acceptability)
Timeframe	• Short term: 6 months • Medium term: 12 months • Long term: 2 years or longer (or until the condition is stable)
Additional information	Subgroups: • women, men, trans people and non-binary people • people from minority ethnic family backgrounds • people with mental or health disabilities • neurodiverse people • age (indications for radiotherapy may vary depending on age) • pre-existing shoulder conditions (osteoarthritis, frozen shoulder, post traumatic conditions. This would have an impact on study participation) • comorbidities (for example, osteoporosis) • side effects of cancer treatment (for example, fatigue, lymphoedema, axillary web syndrome)

K.1.5 Research recommendation

What is the adherence to, and satisfaction with, different intervention formats (for example individual, group, virtual, and face to face) to reduce arm and shoulder problems after breast cancer surgery or radiotherapy and what is the impact of greater adherence on effectiveness for different groups, such as:

- women, men, trans people and non-binary people
- people from minority ethnic family backgrounds
- people with learning disabilities or cognitive impairment, or physical disabilities, or both
- neurodiverse people?

K.1.6 Why this is important

The evidence showed that there was no difference between interventions and comparators for patients' adherence in the long term (beyond 12 months). Only 2 RCTs found a significant difference in patients' adherence between comparisons at short and medium term but none of the RCTs provided data showing that patients' adherence had an effect on effectiveness. There was no evidence on factors affecting adherence, but the committee highlighted that lack of adherence is likely to be linked to lack of confidence of people to do the exercises given to them in written materials (for example leaflets) or because instructions were not clear (for example, instructions about how long intervention should be continued for). They made a research recommendation on whether adherence and satisfaction were different depending on the format of the intervention (individual, group, virtual, and face to face) because they expect that people who regularly take part in the interventions are more likely to experience the benefits.

K.1.7 Rationale for research recommendation

Importance to 'patients' or the population	Little is known about adherence and satisfaction to different formats (individual, group, virtual, and face to face) of interventions to reduce arm and shoulder problems after breast cancer surgery or radiotherapy.
Relevance to NICE guidance	Adherence to interventions to reduce arm and shoulder problems have been considered in this guideline and there is a lack of data on adherence and satisfaction to different formats (individual, group, virtual, and face to face) of these interventions. There is also a lack of evidence on the impact of greater adherence on effectiveness.
Relevance to the NHS	The outcome would affect the types of treatment for arm and shoulder problems provided by the NHS. More knowledge on which interventions are preferred by patients, and which they are more likely to adhere, to can help choose the most effective interventions and reduce the number of people who need further treatment.
National priorities	Moderate
Current evidence base	Minimal RCT data on adherence to different formats of interventions, mostly non-UK based. No data on satisfaction. No data on the impact of adherence on effectiveness.
Equality considerations	None known

K.1.8 Modified PICO table

Population	Adults with early or locally advanced breast cancer (18 and over) who have undergone any of the following treatments alone or in combination: • surgery for breast cancer alone or with: axillary clearance, sentinel lymph node biopsy, or node sampling • radiotherapy for breast cancer alone or with regional lymph node radiotherapy
Intervention	Post-surgery or post-radiotherapy: • Physiotherapy aimed at maximising people's ability to move and function (in different formats: individual, group, virtual, and face to face) • Exercise or rehabilitation classes for people who have undergone surgery or radiotherapy (in different formats: individual, group, virtual, and face to face)
Comparator	Different ways of delivering the interventions (type of physiotherapy or exercise, mode of

	delivery, number of sessions) compared to each other
Outcome	• Patient adherence • Patient satisfaction (validated questionnaires or scales) • Patient adherence impact on effectiveness
Study design	Randomised controlled trial
Timeframe	• Short term: 6 months • Medium term: 12 months • Long term: 2 years or longer (or until the condition is stable)
Additional information	Subgroups: • women, men, trans people and non-binary people • people from minority ethnic family backgrounds • people with mental or health disabilities • neurodiverse people • age as some age groups may be more adherent than others (for example, access to virtual technology might be a possible issue in this population) • pre-existing shoulder conditions (osteoarthritis, frozen shoulder, post traumatic conditions. This would have an impact on study participation) • comorbidities (for example, osteoporosis) • side effects of cancer treatment (for example, fatigue, lymphoedema, axillary web syndrome)

Appendix L – Methods

Reviewing research evidence

Review protocols

Review protocols were developed with the guideline committee to outline the inclusion and exclusion criteria used to select studies for each evidence review.

Searching for evidence

Evidence was searched for each review question using the methods specified in the 2023 NICE guidelines manual.

Selecting studies for inclusion

All references identified by the literature searches and from other sources (for example, previous versions of the guideline or studies identified by committee members) were uploaded into EPPI reviewer software (version 5) and de-duplicated. Titles and abstracts were assessed for possible inclusion using the criteria specified in the review protocol. 10% of the abstracts were reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.

The full text of potentially eligible studies was retrieved and assessed according to the criteria specified in the review protocol. A standardised form was used to extract data from included studies. Study investigators were contacted for missing data when time and resources allowed (when this occurred, this was noted in the evidence table and relevant data was included).

Methods of combining evidence

Data synthesis for intervention studies

Where possible, meta-analyses were conducted to combine the results of quantitative studies for each outcome.

Pairwise meta-analysis

Pairwise meta-analyses were performed in Cochrane Review Manager V5.3, with the exception of incidence rate ratio analyses which were carried out in R version 4.1.0. using the package ‘metafor’. A pooled relative risk was calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event, and a pooled incidence rate ratio was calculated for dichotomous outcomes reporting total numbers of events. Both relative and absolute risks were presented, with absolute risks calculated by applying the relative risk to the risk in the comparator arm of the meta-analysis (calculated as

the total number events in the comparator arms of studies in the meta-analysis divided by the total number of participants in the comparator arms of studies in the meta-analysis).

A pooled mean difference was calculated for continuous outcomes (using the inverse variance method) when the same scale was used to measure an outcome across different studies. Where different studies presented continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes were all converted to the same scale before meta-analysis was conducted on the mean differences.

For continuous outcomes analysed as mean differences, change from baseline values were used in the meta-analysis if they were accompanied by a measure of spread (for example standard deviation). Where change from baseline (accompanied by a measure of spread) were not reported, the corresponding values at the timepoint of interest were used. If some studies only reported data as a change from baseline, analysis was done on these data, and for studies where only baseline and final time point values were available, change from baseline standard deviations were estimated, assuming a correlation of 0.5 as a conservative estimate (Follman et al., 1992; Fu et al., 2013).

For all syntheses, fixed- and random-effects models were fitted, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met, even after appropriate pre-specified subgroup analyses were conducted, random-effects results are presented. Fixed-effects models were deemed to be inappropriate if there was significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

In cases where subgroup analyses were performed, it was planned that pooled results would be reported in the GRADE tables, but the results from each subgroup would only reported if there was evidence suggesting between subgroup heterogeneity. This is defined as a statistically significant test for subgroup interactions (at the 95% confidence level). Where no such evidence was identified, only pooled results were presented.

Appraising the quality of evidence

Intervention studies (relative effect estimates)

RCTs and quasi-randomised controlled trials were quality assessed using the Cochrane Risk of Bias Tool. Evidence on each outcome for each individual study was classified into one of the following groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.

Each individual study was also classified into one of three groups for directness, based on if there were concerns about the population, intervention, comparator and/or outcomes in the study and how directly these variables could address the specified review question. Studies were rated as follows:

- Direct – No important deviations from the protocol in population, intervention, comparator and/or outcomes.

- Partially indirect – Important deviations from the protocol in one of the following areas: population, intervention, comparator and/or outcomes.
- Indirect – Important deviations from the protocol in at least two of the following areas: population, intervention, comparator and/or outcomes.

Minimally important differences (MIDs) and clinical decision thresholds

The Core Outcome Measures in Effectiveness Trials (COMET) database was searched to identify published minimal clinically important difference thresholds relevant to this guideline that might aid the committee in identifying clinical decision thresholds for the purpose of GRADE. Identified MIDs were assessed to ensure they had been developed and validated in a methodologically rigorous way, and were applicable to the populations, interventions and outcomes specified in this guideline. In addition, the Guideline Committee were asked to prospectively specify any outcomes where they felt a consensus clinical decision threshold could be defined from their experience. In particular, any questions looking to evaluate non-inferiority (that one treatment is not meaningfully worse than another) required a clinical decision threshold to be defined to act as a non-inferiority margin.

Clinical decision thresholds were used to assess imprecision using GRADE and aid interpretation of the size of effects for different outcomes. Clinical decision threshold that were used in the guideline are given in Table 7 and also reported in the relevant evidence reviews.

Table 7: Identified Clinical decision thresholds

Outcome	Clinical decision threshold	Source
DASH scale	7-point difference: MD –7 to +7 points	Bruce J, Mazuquin B, Mistry P, Rees S, Canaway A, Hossain A, et al. Exercise to prevent shoulder problems after breast cancer surgery: the PROSPER RCT. Health Technol Assess 2022;26(15).
QuickDASH scale	8-point difference: MD –8 to +8 points	Mintken PE, Glynn P, Cleland JA. Psychometric properties of the shortened disabilities of the Arm, Shoulder, and Hand Questionnaire (QuickDASH) and Numeric Pain Rating Scale in patients with shoulder pain. J Shoulder Elbow Surg. 2009 Nov-Dec;18(6):920-6.
Pain 11-point numerical rating scale	Reduction of 2 points or 30% pain intensity	Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001 Nov;94(2):149-158.
Pain 100-mm VAS	More or less pain: 13-mm change in score	Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Ann Emerg Med. 2001 Dec;38(6):633-8.
Pain Oxford Shoulder Score	6-point difference: MD –6 to +6 points	van Kampen DA, Willems WJ, van Beers LW, Castelein RM, Scholtes VA, Terwee CB. Determination and comparison of the smallest detectable change (SDC) and the minimal important change (MIC) of four-shoulder patient-reported outcome measures (PROMs). J Orthop Surg Res. 2013 Nov 14;8:40.
Quality of life EQ-5D-5L + VAS	EQ-5D-5L: -0.08 to +0.08 VAS: -0.07 to +0.07	Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. Health Qual Life Outcomes. 2007 Dec 21;5:70.

Outcome	Clinical decision threshold	Source
Quality of life EORTC QLQ-C30	Global quality of life: -8 to 12	Musoro JZ, Coens C, Fiteni F, Katarzyna P, Cardoso F, Russell NS, King MT, Cocks K, Sprangers MA, Groenvold M, Velikova G, Flechtner HH, Bottomley A; EORTC Breast and Quality of Life Groups. Minimally Important Differences for Interpreting EORTC QLQ-C30 Scores in Patients With Advanced Breast Cancer. JNCI Cancer Spectr. 2019 Jun 4;3(3):pkz037.

For continuous outcomes expressed as a mean difference where no other clinical decision threshold was available, a clinical decision threshold of 0.5 of the median standard deviations of the comparison group arms was used (Norman et al. 2003). For continuous outcomes expressed as a standardised mean difference where no other clinical decision threshold was available, a clinical decision threshold of 0.5 standard deviations was used. For SMDs that were back converted to one of the original scales to aid interpretation, rating of imprecision was carried out before back calculation. For relative risks and hazard ratios, where no other clinical decision threshold was available, a default clinical decision threshold for dichotomous outcomes of 0.8 to 1.25 was used. Odds ratios were converted to risk ratios before presentation to the committee to aid interpretation.

GRADE for intervention studies analysed using pairwise analysis

GRADE was used to assess the quality of evidence for the outcomes specified in the review protocol. Data from randomised controlled trials were initially rated as high quality. The quality of the evidence for each outcome was downgraded or not from this initial point, based on the criteria given in Table 8. These criteria were used to apply preliminary ratings, but were overridden in cases where, in the view of the analyst or committee the uncertainty identified was unlikely to have a meaningful impact on decision making.

Table 8: Rationale for downgrading quality of evidence for intervention studies

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels. Extremely serious: If greater than 33.3% of the weight in a meta-analysis came from studies at critical risk of bias, the outcome was downgraded three levels
Indirectness	Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels.
Inconsistency	Concerns about inconsistency of effects across studies, occurring when there is unexplained variability in the treatment effect demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic. N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study. Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded.

GRADE criteria	Reasons for downgrading quality
	Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level. Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels.
Imprecision	If an MID other than the line of no effect was defined for the outcome, the outcome was downgraded once if the 95% confidence interval for the effect size crossed one line of the MID, and twice if it crosses both lines of the MID. If the line of no effect was defined as an MID for the outcome, it was downgraded once if the 95% confidence interval for the effect size crossed the line of no effect (i.e. the outcome was not statistically significant), and twice if the sample size of the study was sufficiently small that it is not plausible any realistic effect size could have been detected. Outcomes meeting the criteria for downgrading above were not downgraded if the confidence interval was sufficiently narrow that the upper and lower bounds would correspond to clinically equivalent scenarios.
Publication bias	Where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias. When a funnel plot showed convincing evidence of publication bias, or the review team became aware of other evidence of publication bias (for example, evidence of unpublished trials where there was evidence that the effect estimate differed in published and unpublished data), the outcome was downgraded once. If no evidence of publication bias was found for any outcomes in a review (as was often the case), this domain was excluded from GRADE profiles to improve readability.

References

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Norman G., Sloan JA., Wyrwich KW. (2003) Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care 41(5):582-92.