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Report

Delayed versus immediate exercises following surgery for breast cancer: a systematic review

Delva R. Shamley[1], Karen Barker[2], Vanessa Simonite[3], and Anna Beardshaw[4]
[1]*Oxford Brookes University, Physiotherapy, Oxford, UK;* [2]*Physiotherapy Research Unit, Nuffield Orthopaedic Centre NHS Trust, Oxford, UK;* [3]*Department of Mathematical Sciences, Oxford Brookes University, Oxford, UK;* [4]*Physiotherapy Department, John Radcliffe Hospital, Oxford, UK*

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Summary

Background. Seroma formation, wound healing and fluid drainage are a concern for both surgeons and patients. Excessive fluid production can result in seroma formation, and inadequate drainage of seromas is known to cause infection, pain, discomfort and longer periods of hospitalisation. Postoperative exercises given to maintain movement of the arm are believed to increase the amount of fluid production following surgery. This review aimed to determine whether a program of delayed exercises reduces the risk of seroma formation, fluid loss and hospital stay, without loss of arm movement.

Method. A systematic review. RCTs of early versus delayed shoulder mobilisation after surgery in females with breast cancer were included in the review. *Outcomes*. One or more measurements of shoulder range of motion, wound complications, fluid drainage volumes and incidence of seroma formation. *Design*. Randomised controlled trials, control group of delayed exercise/mobilisation. *Validity assessment* was carried out using a data extraction form based on the CONSORT statement. *Study characteristics* recorded include sample size, intervention, control, period of exercise delay, surgical procedure and conclusions drawn. *Data synthesis* was carried out using random effects and weighted mean differences to test for heterogeneity and combined effects.

Results. 12 RCTs were included in the review of which 6 were included for meta-analysis. Delaying exercises significantly decreases seroma formation (OR = 0.4; 95%CI 0.2–0.5; $p = 0.00001$). No significant differences were found for drainage volume or hospital stay.

Conclusion. Current evidence from RCTs supports the use of a delayed program of arm exercises to reduce seroma formation. Clinical and statistical inconsistencies between studies did not allow any conclusions to be drawn regarding the effects of delayed exercises on fluid drainage, hospital stay and immediate or long term ability to move the arm.

Introduction

Seroma formation, wound healing and fluid drainage are a major concern for both the surgeon and the patient after surgery for breast cancer. Poor fluid drainage is associated with seroma formation and the potential for infection during aspiration [1]. Factors such as type of incision, extent of axillary dissection, tumour size and number of positive nodes are reported to have no effect on drainage [2]. Strategies for reducing seroma formation and improving wound healing include delaying arm exercises postoperatively. However, the significance of exercise in this immediate postoperative period on fluid drainage and seroma formation is not clear. Concern remains that delaying exercises causes limited movement of the ipsilateral arm and may potentially lead to residual shoulder dysfunction. The effect of early versus delayed mobilisation postoperatively, on immediate and residual shoulder function, has been extensively studied since the debate began in 1948 [3]. A number of trials have tested the two exercise options with respect to several outcomes, notably, seroma formation, wound healing, fluid drainage volumes and shoulder mobility [3–14]. However, heterogeneity of surgical techniques, patient groups and clinical outcomes measured have resulted in conflicting conclusions been drawn regarding the effects of early versus delayed exercises. This review aims to determine whether a programme of delayed exercises, achieved by a variety of means, reduces the risk of seroma formation, fluid loss and hospital stay without loss of arm movement.

Method

Search strategies for identification of studies

Studies were identified searching the Cochrane Controlled Trial Register and the main bibliographic and

specialised databases, MEDLINE, EMBASE, CINAHL, AMED, PEDRO, REHABDATA and PROQUEST MEDICAL LIBRARY. The years 1960–June 2002 were searched.

In addition the reference lists of relevant articles were hand searched to identify missing studies. No language restrictions were applied, where necessary arrangements for translation of articles were made.

Search terms

MeSH terms were breast cancer, mastectomy, wide local excision (WLE) shoulder morbidity, physiotherapy and exercise. Combinations of keywords and wildcards were used to carry out database searches.

Searches were limited to randomised controlled trials.

Inclusion criteria

Articles identified by the database search were checked for the following inclusion criteria:

Population: Females who had received surgery for primary breast cancer.
Intervention: Comparative trials of early versus delayed shoulder mobilisation after surgery.
Outcomes: One or more measurements of shoulder range of motion, wound complications, fluid drainage volumes and incidence of seroma formation.
Design: Randomised controlled trials, control group of delayed exercise/mobilisation.

Data extraction and quality assessment

Study eligibility was independently assessed by three reviewers (DS, KB, AB) and any disagreement was solved by consensus. Assessors were blind to authors and publications.

In order to compare the quality of the studies a standard set of data was abstracted from each paper using a standardised protocol and data collection form. The data collection form assessed the quality of the trials based on the CONSORT statement [15].

The data was extracted independently and in duplicate by 2 of the reviewers (DS, KB).

In cases where agreement was not reached this was resolved through discussion until a consensual position was reached. In cases where details were absent from articles an attempt to contact the authors was made to clarify points or to obtain missing data. Clarification of the distinction between the two arms of the trial was received via email contact from Knight [13]. The criteria used for quality assessment are detailed in Table 1.

Study characteristics

Details of the study characteristics of each paper are summated in Table 2, showing sample size, date of study and conclusion reached by the authors of the papers.

Data analysis

The results for the incidence of seroma and shoulder restriction are expressed as combined odds ratios based on a fixed effects model and tested for heterogeneity [16]. Data on the duration of hospital stay and drainage volume are expressed as combined differences in means [17]. Random effects methods were applied for comparison, and as the most appropriate method of analysis where significant heterogeneity had been identified [18]. The software used to perform these analyses were the Cochrane Collaboration's review manager software (RevMan version 4.1). Funnel plots, used to check for publication bias were produced using SPSS version 10.0.

Results

A total of 12 RCTs were included in the final review, of which six were included in the meta-analysis. Figure 1 represents the trial flow and provides exclusion details.

The small number of trials available for all of the outcomes studied limited the extent to which publication bias could be assessed. Funnel plots could not be interpreted conclusively and no statistical tests for publication bias have been applied, as these have low power in meta-analyses of less than 20 trials [19].

Incidence of seroma

Data on the incidence of seroma were available in five studies: there was no statistically significant evidence of heterogeneity. Seroma occurred in 56 out of 207 patients (27%) for whom exercise was delayed and 110 out of 237 patients (46%) who started exercise immediately. Using the fixed effects method, the combined odds ratio for the effect of delaying exercise is 0.41 (95% CI 0.20–0.95, $p = 0.00001$). A similar estimate of effect size was obtained using random effects methods: combined odds ratio 0.40, (95% CI 0.22–0.73, $p = 0.003$) (Table 3).

Drainage volume

Six studies contributed data on drainage volumes in the form of means and standard deviations: in one study [7], standard deviations were estimated from the range of values for drainage volume in each group. There was statistically significant evidence of heterogeneity between studies ($p < 0.00001$). When results vary greatly between studies, it may not be appropriate to combine the results, but there is no clear procedure for deciding whether the results should be combined [16]. Heterogeneity needs to be explored to determine why the effect of delaying exercise varied from one study to another [18] where heterogeneity exists, then a random effects model, in which the effect size is assumed to vary from one study to another, is more appropriate (Table 4).

Table 1. Characteristics of selected studies

Study	Sample size Exs/delay	Intervention	Control	Period of exercise delay	Dx/surgical procedure	Conclusion
Flew, 1979 [5]	29/35	Undefined PT	Protocol of delayed mvt	7 days	Early BC/radical mastectomy	Advised delay shoulder movement
Lotze et al., 1981 [6]	21/19	Protocol of PT with progressive ROM	Protocol of delayed movement	Flex – 8 days Abd – 12 days	Melanoma/MRM and axillary dissection	Recommends delaying early shoulder ROM beyond 40° until day 7 post-op
Horst et al., 1985 [7]	31/28	Protocol of PT	Protocol of delayed movement with progressive increase in ROM	6 days	Mastectomy & axillary dissection	No conclusion drawn
Rodier et al., 1987 [8]	47/53	Undefined PT	Undefined ltd movement	Unstated. 6.3 days on calculation using time of D/C after drain removal	1. MRM & axillary dissection 2. Tumorectomy/ quadrandectomy & axillary dissection	Advocates early PT post-op
Dawson et al., 1989 [9]	51/49	Undefined exercises	Immobilisation	5 days	MRM	Recommends abandoning routine shoulder exercises before day 5 post-op
Wingate et al., 1989 [10]	61/54	Protocol of PT	Undefined ltd movement	Unstated	MRM & axillary dissection	Advocates early and intensive PT post-op
Jansen et al., 1990 [11]	78/66	Protocol of PT	Immobilisation	8 days	1. MRM 2. Wide lumpectomy & axillary dissection 3. Only axillary dissection.	Advocates period of rest post-op despite lack of significance in results
Petrek et al., 1990 [12]	27/30	Graduated ROM PT	Protocol of delayed movement	5 days	Stage 1/11 BC. 1. MRM 2. Limted dissection of breast and axillary dissection	Advocates early rehabilitation post-op
Knight et al., 1995 [13]	19/19	Undefined exercises	Undefined ltd movement	12 days	MRM & axillary dissection	Recommends postmastectomy period of shoulder immobilisation for 12 days

Table 1. Continued

Study	Sample size Exs/delay	Intervention	Control	Period of exercise delay	Dx/surgical procedure	Conclusion
Schutz et al., 1997 [14]	89/74	Undefined except by pain	Undefined ltd movement	7 days	MRM & axillary dissection	Recommends delaying PT 1 week post-op
Chen and Chen 1999 [2]	116/115	Protocol of exs	Undefined	3/6/14 days	MRM & axillary dissection	Delay exercises till drains removed (up to 14 d)
Abe et al., 1998 [4]	58/58	Undefined	Undefined	7 days	MRM/standard Mastectomy/breast conserving	Delay exs for 7d but allow unrestricted mvt

Key: PT, Physiotherapy; ROM, Range of movement; BC, Breast cancer; MRM, Modified radical mastectomy.

The results of the random effects method are shown in Table 4. This shows that when exercise was delayed, the combined mean drainage volume was 175 ml lower than when exercise began immediately, however, this was not a statistically significant result (95% CI −397–47 ml, $p = 0.12$).

Hospital stay

Five studies provided data on the length of hospital stay: there was statistically significant evidence of heterogeneity. Using the random effects method, the combined mean difference was not statistically significant (Estimated mean reduction 0.63 days, 95% CI −1.91–0.66, $p = 0.3$) (Table 5).

Discussion

The results of this review do not provide evidence to support the view that delaying exercises following surgery for breast cancer reduces fluid drainage and hospital stay. Neither does it supports the view that delay results in long-term damage to arm movements. Whilst statistically significant heterogeneity was found between studies, no significant differences were found for either fluid drainage or hospital stay between the two groups. There is some support for the beneficial effect of delayed exercise on the incidence of seroma, as for this outcome there was no evidence of heterogeneity and the combined results showed that for a patient whose exercises are delayed, the odds of developing a seroma were reduced by a factor of 40%.

Clinical and statistical heterogeneity

The extreme values obtained from an overall test of heterogeneity, shown in Tables 3 and 4, indicate that combining the results of studies provides data that is less meaningful than determining the reasons for the variations in the trials reviewed. Further statistical evaluations were not feasible owing to the paucity of studies. The most notable clinical inconsistencies were the timing of mobilisations and the description of the two arms of the trials. Study designs varied particularly in what was ascribed to the delayed exercise group. Descriptions of the protocol used in these groups was inadequate and varied from complete immobilisation [9, 11] to freedom to move within the limits of pain [13]. Similarly, full descriptions of the protocols for the immediate exercise group were absent in 6 of the 12 trials (Table 2). Group descriptions varied from clearly prescribed, graded exercise regimes through to unlimited movement of the arm. It is clear that the definitions of 'exercise' has been blurred in several studies and varies across studies. This threatens internal validity and presents difficulties for between study comparisons. On the whole, exercises given to this

Table 2. Data extraction sheet

	Petrek	Lotze	Rodier	Jansen	Schutz	Wingate	Dawson	Knight	Horst	Flew	Chen	Abe
Power calculation	N	N	N	N	N	N	N	N	N	N	N	N
Sample size	57	37	100	144	163	115	100	38	57	64	344	116
Specific objectives stated	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Hypothesis stated	N	N	N	N	N	Y	N	Y	N	N	N	N
Inclusion criteria clearly stated	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Exclusion criteria clearly stated	Y	Y	N	Y	N	N	N	Y	N	N	Y	N
Randomised	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Randomisation process stated	N	N	N	N	Y	N	N	N	N	N	N	N
Concealed allocation	?	?	?	?	?	N	?	?	?	Y	N	?
Stratified *a priori*	Y	Y	N	N	N	N	N	N	N	N	N	N
Blinding of outcome assessor	?	?	?	?	?	Y	?	?	Y	?	?	N
Validated questionnaire	N	N	N	N	N	N	N	N	N	N	N	N
Validated objective shoulder Measurement	Y	?	N	?	?	Y	N	N	N	N	N	N
Reliability/repeatability measures	N	N	N	N	N	N	N	N	N	N	N	N
Stats test stated	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Correct rationale for selection of stats	Y	N	N	N	N	N	N	N	N	N	Y	N
Correct use of parametric non par	Y	N	?	?	Y	?	?	?	?	?	?	?
Sub-grp analysis surg, RT + A52	N	N	Y	N	Y	N	N	N	N	N	Y	Y
Correction/adjustment – e.g. age, RT	N	N	N	N	N	N	N	N	N	?	?	N
p-value	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Grps equal at baseline-stated	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y
Grps equal at baseline-stats incl.					Y							
Age clearly stated	Y	Y	?	N	Y	Y	Y					
Surgery type clearly stated	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Other med Rx stated e.g. RT + A59	N	Y	Y	N	N	N	N	N	Y	Y	N	Y
Grade of Ca/node involvement	Y	Y	Y	N	Y	Y	Y	?	N	Y	Y	Y
Full description of exercise/PT	Y	Y	N	N	Y	Y	N	N	Y	N	Y	N
Complete immobils versus exercise	N	N	N	Y	N	N	Y	N	N	N	N	N

Table 2. Continued

	Petrek	Lotze	Rodier	Jansen	Schutz	Wingate	Dawson	Knight	Horst	Flew	Chen	Abe
Undefined ltd mvmt versus exercise	N	N	Y	N	Y	Y	N	Y	N	N	Y	Y
Defined ltd mvmt versus exercise	Y	Y	N	N	N	N	N	N	Y	Y	N	N
No. of appropriate outcome measures	3	7	2	5	3	5	5	3	3	6	4	6
Length of stay	Y	Y	N	N	N	Y	Y	N	N	Y	N	N
Circumferential arm measures	N	N	N	N	N	Y	N	N	N	Y	N	N
>2 GH measures	N	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y
2 or more GH measures	N	Y	N	Y	N	Y	N	N	Y	Y	Y	N
Objective functional Ax	N	N	N	N	N	Y	N	N	N	N	N	N
Subjective functional Ax	N	N	N	N	N	N	N	N	N	N	N	N
Drainage volume stated	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Wound healing monitored	N	Y	N	Y	Y	?	Y	Y	Y	Y	N	Y
Seroma nos reported	N	Y	Y	Y	Y	N	Y	Y	N	N	N	Y
Aspiration vol	Y			Y	N		Y	Y		Y	Y	Y
Loss to follow up stated	N	Y	N	Y	Y	N	N	Y	Y	Y	N	N
Numbers equal between groups	?	?	?	?	?	?	?	N	Y	N	?	Y
Reasons given for losses	N	Y	?	Y	Y	N	N	Y	N	N	?	n/a
Adequate recognition of confounding Variables	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	N
Follow up period stated	N	Y	N	Y	Y	Y	N	N	Y	Y	Y	Y
OM taken on hosp IP d/c	?	N	?	Y	Y	Y	?	?	?	Y	Y	Y
F/u to 3 months	N	Y	N	Y	Y	Y	?	?	?	Y	Y	N
F/u to 6 months	N	Y	N	Y	Y	N	?	?	Y	N	Y	N

Key: Y, yes; N, no; ?, not reported; RT, radiotherapy; Ca, cancer; PT, physiotherapy; exs, exercise; ltd mvmt, limited movement; GH, glenohumeral; AX, assessment; OM, outcome measures; IP d/c, inpatient discharge; F/u, follow up.

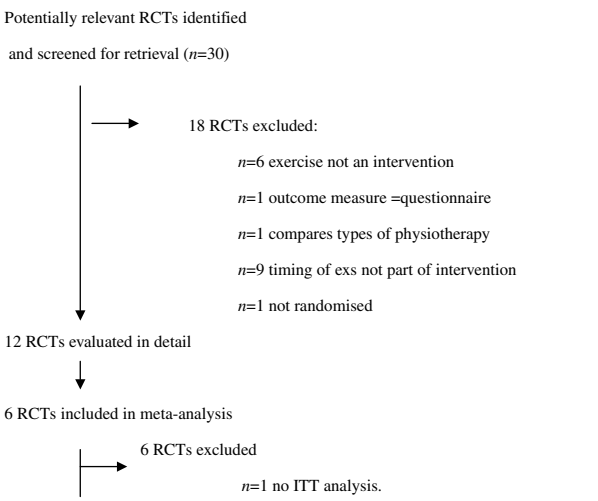


Figure 1. Trial flow diagram.

group of patients by either physiotherapists or breast care nurses mimic normal active movements. A clear distinction must therefore be made between the protocols for each arm of the trial, to enable the effect of exercise, if there is one, to be seen.

Meta-analysis of the small number of studies included in the analyses appears to indicate that delaying exercises for a week reduces the incidence of seroma. This is a key finding for the patient and the surgeon, as seromas mean discomfort for the patient and increased hospital costs. Caution is required in interpreting this result, as available data was utilised for analyses, not individual patient data, and tests for heterogeneity have low power [20]. The extreme level of heterogeneity found for drainage volume may be due to the variation in the way drainage fluid was recorded, sometimes including aspirations and fluid drained at the first outpatient appointment.

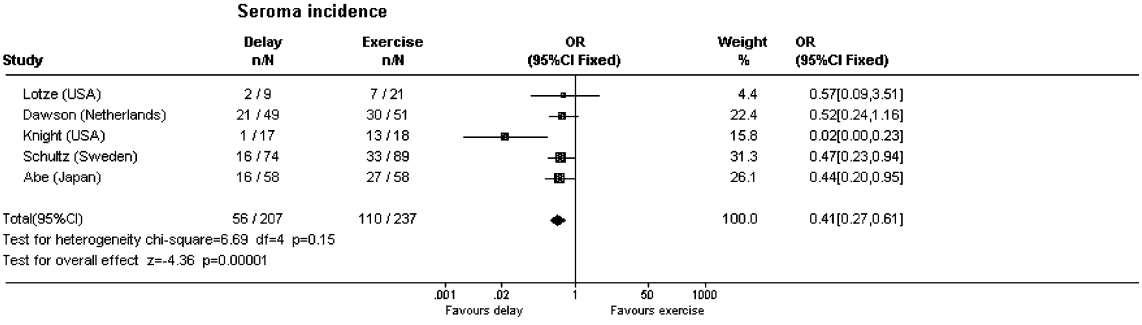
What delay means for the patient in terms of arm movement is less clear. None of the studies reviewed stated either the type of instrument used to assess range of shoulder movement, or the anatomical landmarks used to measure range of motion. Both of these exclusions pose a threat to the internal validity of this outcome for all of the trials reviewed. The assumption has been made by the reviewers that a universal goniometer was used. There is ample evidence supporting the need for clear, standardised measurement protocols and the need for inter- and intra-tester reliability to be part of the measurement protocol [21].

Meta-analysis of range of movement was not possible, as measures varied from recording the incidence of dysfunction, to the time taken to reach a specified range, with only two studies providing absolute ranges of movement. One study included a functional questionnaire for patients, but did not report the results or link them to any objective measures. This review is unable to draw any conclusions with respect to the effects of delaying exercises on the range of movement of the shoulder. As most trials stopped short of enforcing complete immobilisation (10 studies included arm movement of some description in the delayed group) the research question seems to have become whether to start ADL movements or graded mobilisations immediately after surgery.

General study quality

Most of the trials failed to include statements regarding power calculations, concealed allocation, reliability and repeatability measures, randomisation process (with the exception of Schutz et al. [14] and Flew [5]), or blinding of outcome assessor (with the exception of Wingate et al. [10] and Horst et al. [7]). The collective absence of these criteria point to the potential for bias in these trials. Furthermore, statistical rationale and evidence supporting the correct use of parametric tests was missing in 8 of 12 studies which is particularly concerning in the absence of power calculations and small sample sizes. Two studies did not provide evidence of group comparability at baseline, while only 3 provided statistical evidence to support their homogeneity (Table 2). However, between studies baseline data collected was relatively homogenous. Chen and Chen [2] was the only study to explore the relationship of baseline measures to trial outcomes. They found that patient age, weight, body mass index and length of wound incision were highly correlated to the volume of fluid drained. These parameters were not included in the other trials, yet seem to indicate the need to document potentially influential variables, and ensure their equal distribution across groups at baseline. All studies

Table 3. Weighted mean difference for seroma incidence



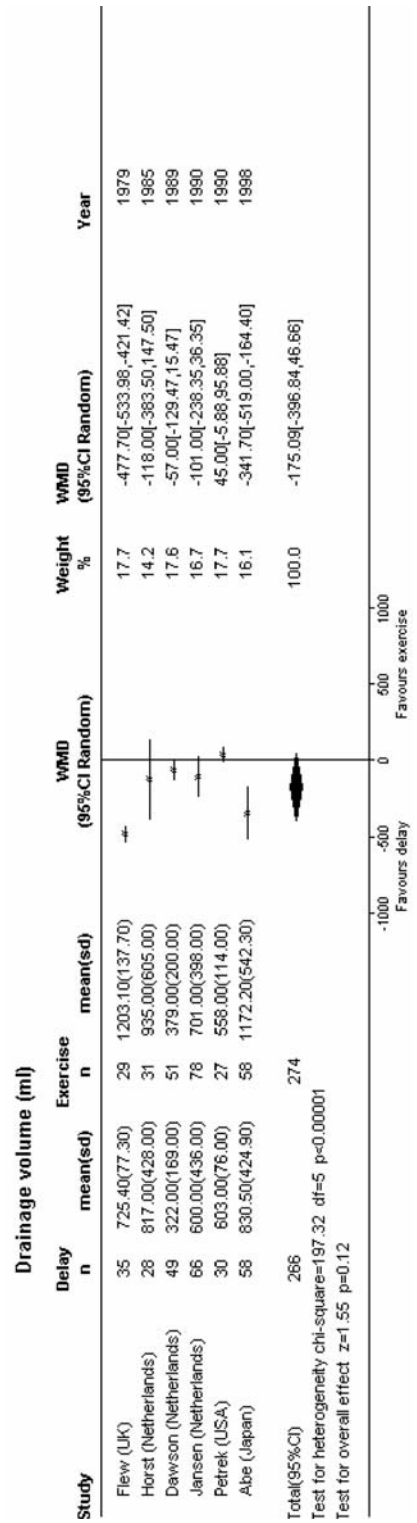


Table 4. Weighted mean difference for drainage volume

gave details of the inclusion criteria but only five stated the exclusion criteria. This clearly has implications for the assessment of shoulder joint range of movement as any prior injury or surgery may influence this outcome, most notably in small samples. Reporting of surgical intervention was generally detailed and again demonstrated heterogeneity within groups and between studies. Flew [5] reported more radical surgery including the removal of pectoralis minor and sternal head of pectoralis major while Lotze et al. [6] reported 'sometimes' removing pectoralis minor; Lotze included melanoma and breast cancer; Abe et al. [4] and Rodier et al. [8] included modified radical mastectomy and breast conserving surgery; and Rodier et al. [8] included patients who had preoperative chemotherapy and radiotherapy.

None of the trials included randomisation for subgroups to account for different treatment protocols such as surgery and radiotherapy (important for follow up arm measurements) with information regarding the distribution of these protocols across groups at baseline being largely absent. Two trials [4, 8] did, however, carry out *post hoc* sub-group analyses demonstrating significant differences in fluid volume between surgical protocols. Once again these represent variables that could influence the outcomes of a trial and yet were not considered in the majority of the trials reviewed. The reporting of trial procedures was very poor in most trials reviewed. Four of the 12 trials included in this review appeared after the development of the first CONSORT statement (consolidated statement on reporting trials) published in 1995. Despite this, these four trials suffered from the same poor reporting as the others. The extent to which word count restrictions from journals contribute to the absence of information in articles, is unknown.

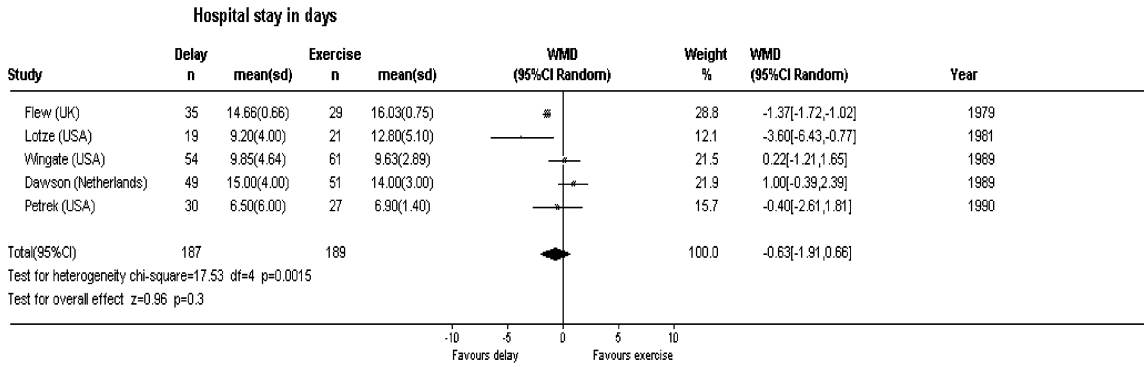
Conclusions

This review has identified support for delaying exercises to reduce seroma formation. However, incomplete reporting of trials and faults in study designs resulting in poor internal and external validity have been identified. The lack of clinical and statistical consistency between the studies included in this review do not allow any conclusions to be drawn regarding the effects of delayed exercises on fluid drainage, hospital stay and either immediate or long term ability to move the arm.

Future research

This patient group represent a challenge to researchers, owing to the complexity and multiplicity of presentations and management strategies. Research designs need to reflect this if they are to answer clinical

Table 5. Weighted mean difference for hospital stay



questions to the satisfaction of clinicians and patients alike. Future studies should therefore:

- Make a clear distinction between the protocols for each arm of the trial. Protocols to include defined graded exercises implemented at defined times, clear defined follow up periods and validated outcome measures.
- Determine the variables known to influence the outcomes to be measured and account for these in the design to avoid bias.
- Determine the sample size (including for sub-group analysis) needed to be able to detect a difference should one exists.
- Adhere to the standards of trial procedure and reporting outlined in the CONSORT statement to allow a full interpretation of results to be made.

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Address for offprints and correspondence: Dr D.R. Shamley, Research Fellow, Oxford Radcliffe Hospitals Trust Charity Programme Lead, Physiotherapy, Oxford Brookes University, School of Health and Social Care, Jack Straws Lane, Marston, OX3 OFL, UK; *Tel.:* 01865 485287; *Fax:* 01865 769679; *E-mail:* drshamley@brookes.ac.uk