Multidisciplinary rehabilitation for follow-up of women treated for breast cancer (Review)

Khan F, Amatya B, Ng L, Demetrios M, Zhang NY, Turner-Stokes L

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[Intervention Review]

Multidisciplinary rehabilitation for follow-up of women treated for breast cancer

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ABSTRACT

Background

Breast cancer is the most common malignancy in women worldwide. Multidisciplinary rehabilitation aims to improve outcomes for women but the evidence base for its effectiveness is yet to be established.

Objectives

To assess the effects of organised multidisciplinary rehabilitation during follow-up in women treated for breast cancer.

Search methods

We searched the Cochrane Breast Cancer Group Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*), MEDLINE, EMBASE, CINAHL, AMED, PEDro and LILACS in December 2011.

Selection criteria

Randomised and controlled clinical trials (RCTs, CCTs, respectively) that compared multidisciplinary rehabilitation with some form of control intervention (such as a lower level or different type of intervention, minimal intervention, waiting list controls or no treatment, interventions given in different settings).

Data collection and analysis

The type of data retrieved did not allow for quantitative synthesis and therefore a narrative synthesis was provided. The methodological quality of the included studies was evaluated by three authors using the risk of bias tool.

Main results

Two RCTs, including 262 participants, met the inclusion criteria. Both trials scored poorly for methodological quality. There was 'low level' evidence that multidisciplinary rehabilitation produced short-term gains at the levels of impairment (that is range of shoulder movement), psychosocial adjustment and quality of life after breast cancer treatment (up to 12 months). No evidence was available for the longer-term functional outcomes for caregivers or the cost effectiveness of these programmes. It was not possible to suggest the most appropriate frequency and duration of therapy or choice of one type of intervention over another.

Authors' conclusions

There was 'low level' evidence that multidisciplinary rehabilitation can improve the outcomes of people with breast cancer in terms of functional ability, psychosocial adjustment and participation in social activities. There was no evidence available on functional gain at the level of activity. This review highlights the limitations of RCTs in rehabilitation settings and the need for high-quality trial-based research in this area. Regular evaluation and assessment of breast cancer survivors for rehabilitation is recommended.

PLAIN LANGUAGE SUMMARY

Multidisciplinary rehabilitation for follow-up of women treated for breast cancer

Breast cancer is the most common cancer in women worldwide. The majority of women diagnosed with breast cancer undergo treatment involving surgery and radiotherapy or chemotherapy, or both. With these major advances in breast cancer management, many patients still have to deal with short or long-term side effects and psychological distress related to the disease and treatment, which have a substantial impact on their quality of life. Multidisciplinary rehabilitation aims to improve outcomes for women but the evidence base for its effectiveness is yet to be established. Multidisciplinary rehabilitation programmes vary and include more than one intervention, usually selected from medical, exercise, education, and psychological counselling and support interventions. This review evaluated trials that assessed the effects of organised multidisciplinary rehabilitation during follow-up in women treated for breast cancer.

The review identified only two randomised controlled trials, involving 262 patients with breast cancer. The data from these studies provide low-grade evidence for multidisciplinary rehabilitation in producing short-term gains at the levels of impairment (range of shoulder movement), psychosocial adjustment and quality of life after breast cancer treatment. None of the studies reported the longer-term functional outcomes of such care, the impact on caregivers or cost effectiveness of these programmes.

Overall, the results of this review suggest that multidisciplinary rehabilitation is not harmful and may improve functional ability and quality of life in the short term. This review highlights the lack of robust trials in the field and the need for further high-quality trial-based research.

BACKGROUND

Description of the condition

Breast cancer is the most common malignancy in women worldwide, comprising up to 16% of all cancers in women (WHO 2008). In 2004, approximately 520,000 women died of breast cancer in both developed and developing countries. The worldwide incidence of breast cancer, however, is on the rise (WHO 2008). The estimated incidence rates of breast cancer vary worldwide. The incidence rate in Australia is approximately 83 new cases per 100,000 women, which is lower than rates estimated for North American women (99 per 100,000) and New Zealand (92 per 100,000), but generally the same level is estimated for Western European and Northern European regions (85 and 83 per 100,000 women, respectively). The rates estimated for women in regions such as Southern Europe (62 per 100,000 women) and Central and Eastern Europe (43 per 100,000) are lower than those in Australia (WHO 2008). Many factors can account for these international variations in incidence rates, including differences in genetic susceptibility, reproductive patterns, lifestyle (diet and physical activity), obesity levels, screening intensity, use of hormonal contraceptives and hormone replacement therapy (CCS 2007; Hulka 2008), environmental factors such as proximity to carcinogenic pollution (Wolff 1995), as well as differences in diagnostic procedures and completeness of cancer registration.

Owing to the ageing population, the number of women diagnosed with breast cancer is expected to increase in the future, globally. For example, in Australia, by 2015 the number of new breast cancer cases among women is projected to be 22% higher than in 2006, with an estimated 15,409 women expected to be newly diagnosed (AIHW 2009). This equates to an estimated 42 women in Australia being diagnosed with breast cancer every day in 2015. The projected increase in women diagnosed with breast cancer has implications for these women and their families, the wider community and the health system capacity to provide the services required (AIHW 2009).

Data on the breast cancer death rates for women from the Globocan database (Ferlay 2004) report estimates for 2002 based on data two to five years earlier. The estimates suggest that age-standardised mortality rates for women with breast cancer were significantly lower in Australia (18 deaths per 100,000 women) than in New Zealand (25 per 100,000), Northern Europe (23 per 100,000), Western Europe (22 per 100,000) and Western Africa (20 per 100,000), whilst estimates for women in regions such as South America (15 per 100,000) and many Asian regions are lower. These differences in mortality rates may be due to factors including differences in incidence rates, features at diagnosis (for example stage, histology), availability and quality of treatment (CCS 2008). The five-year relative survival rate for breast cancer varies from 80% in developed countries and 60% in middle-income countries to 40% in low-income countries, the latter indicating a lack of early detection, diagnosis and treatment programmes (Coleman 2008). Several risk factors for breast cancer have been documented (IARC 2002; IARC 2008; Lacey 2009). These include familial history of breast cancer, exposure to endogenous oestrogens (early menarche, late age first childbirth, late menopause) and exogenous hormones (hormone replacement therapy, contraception). Approximately 21% of deaths from breast cancer worldwide are linked to modifiable risk factors (such as physical inactivity, obesity and alcohol use) (Danaei 2005). The World Health Organization (WHO) promotes comprehensive breast cancer management and control by targeting prevention, early detection (WHO 2007), diagnosis and treatment (Yip 2009), rehabilitation and palliative care (WHO 2008).

The majority of women diagnosed with breast cancer undergo multidisciplinary treatment involving surgical intervention and radiotherapy or chemotherapy, or both, based upon clinical presentation, tumour characteristics and stage (American Joint Committee on Cancer Staging, AJCC 2002). Besides these major advances in breast cancer management, many patients still have to deal with severe short or long-term side effects and psychological distress related to the disease and its treatment, which have a substantial impact on their quality of life (QoL). Common complications of surgical procedures can include wound breakdown, sepsis, seroma formation, pain (post-surgical pain, phantom pain, post-mastectomy pain syndrome and musculoskeletal pain), decreased range of shoulder movement, lymphoedema and psychosocial dysfunction (McDonald 2005). The triad of fatigue, mood disorders and cognitive complaints are not uncommon in breast cancer survivors and need further evaluation (Carpenter 1998). Radiotherapy can be associated with shoulder joint contractures, radiation-induced brachial plexopathy, upper-limb oedema, chest wall pain and wound breakdown; whilst chemotherapy is associated with short-term side effects (such as emesis, nausea, stomatitis, alopecia, myalgias, neuropathy, fatigue) and long-term side effects (such as menopause, weight gain, fatigue, cardiac dysfunction and cognitive dysfunction) (Markes 2006; Pattridge 2001). However, other studies report varying degrees of severity of these issues (Lee 2007; Lee 2008a; Lee 2008b). Even anti-oestrogen therapy (for example tamoxifen) can cause problems, such as endometrial, visual and voice changes (NICE 2006). A range of neuropsychological sequelae can occur in many women following treatment for breast cancer (such as anxiety, depression, sexual dysfunction and body dysmorphism, or both). As disease progresses various other concerns may arise, which include bone metastases, tumour infiltration causing plexopathy (acutely painful, involving lower brachial plexus trunks), radiation-induced plexopathy (paraesthesias that is less painful), or both (Franklin 2007; Silver 2007).

Although patient mortality has reduced owing to improved education, screening and advanced therapy (surgery, radiotherapy and drug treatments), many breast cancer survivors may experience ongoing limitations in their everyday activities and restrictions in participation due to many factors. Moreover, a higher level of emotional distress was reported in women treated for breast cancer than in the general population (Spiegel 1997). Patients discharged to the community continue to improve over many months, however in this transition period various adjustment issues may surface, such as the patients' perceptions of self worth, self image and role reversal within the family. Families often struggle to cope with new demands associated with increased care needs, inability to drive and return to work, financial constraints, marital stress and general limitation in women's participation in social activities. Ongoing monitoring, education and counselling of the patient (and family) are important. There are significant costs and socioeconomic implications, with an increased demand for health care and social and vocational services, and caregiver burden. At present, there are few studies that address long-term outcomes in breast cancer survivors or that compare different treatment methods in these women. Further research is needed to understand the long-term needs, the psychosocial impact, and 'ageing' with disabilities for women who have been treated for breast cancer.

Description of the intervention

For this review, multidisciplinary rehabilitation was defined as the coordinated delivery of an intervention by two or more disciplines (that is, physiotherapy, occupational therapy, social work, psychology and other allied healthcare disciplines, and nursing) that is referred by a medical specialist (surgeon, oncologist, rehabilitation physician). Multidisciplinary rehabilitation is designed to be patient-centred, time-limited and functionally oriented, and aims to maximise activity and participation (social integration) using a bio-psychosocial model.

Rehabilitation is defined as "a problem-solving educational process aimed at reducing disability and handicap (participation in social activities) experienced by someone as a result of disease or injury" (Wade 1992).

Women after breast cancer treatment can present to rehabilitation settings with a range of difficulties which may be physical, emotional, psychosocial or environmental. Multidisciplinary re-

habilitation encompasses the framework and common language for describing the impact of disease at different levels, advocated by WHO, using the International Classification of Functioning, Disability and Health (ICF) (WHO 2001). For example, in women after breast cancer treatment:

- 'impairments' are problems with body (anatomical) structures or function (physiological, such as lymphoedema, pain, decreased range of shoulder movement);
- 'activity limitation' (disability) is a difficulty faced by a person in executing everyday tasks (mobility or self-care);
- 'restriction in participation' relates to problems experienced by a person which limit involvement in societal participation and life situations (that is, employment, family life, social reintegration);
- 'contextual factors' are:
    - 'environmental', which make up the physical, social and attitudinal environment in which a person lives their life (construction the same as above), and
    - 'personal' (such as gender, race, coping style, social and educational background), which may affect the person's experience of living with their condition.

The ICF provides a framework to account for contextual factors when measuring disability and participation. For example, lymphoedema (incidence 10% to 30%) (Kligman 2004) or post-mastectomy pain (incidence 4% to 27%) may lead to difficulty lifting, carrying or reaching due to axillary scarring and oedema and neck or shoulder pain (Silver 2007), impacting mobility and self-care. These disabilities can have a cumulative effect over time and cause considerable distress to the cancer survivors and their families, and reduce their QoL (Gordon 2005). These can limit participation, which means they may have an impact on returning to work, driving, family and intimate relationships.

The rehabilitation intervention for women with breast cancer includes all time periods, that is, the early post-operative period, whilst going through all adjuvant therapies since the definitive treatment, and late phases of care.

How the intervention might work

Multidisciplinary rehabilitation for women after breast cancer treatment can utilise various categories within the structured framework outlined by the ICF for targeted intervention and therapy. The framework provides clinicians with specific categories within relevant domains as interventions, for example, 'activity and participation' (which relate to mobility, self-care, domestic life etc) and environmental factors (transport and access to places, relationships and attitudes etc).

A number of systematic reviews have been conducted to support uni-disciplinary rehabilitation input for women with breast cancer. These include exercise therapy to reduce upper-limb dysfunction (that is, to improve range of shoulder movement) due to breast cancer treatment (McNeely 2010); exercise on treatment-related physical changes during adjuvant treatment (Markes 2006); and physical therapy in managing lymphoedema (Preston 2004). There is strong evidence that exercise enhances physiological and functional outcomes and improves QoL in breast cancer survivors (Markes 2006; McNeely 2010) and other cancer survivors (MacVicar 1986; MacVicar 1989). The optimum timing for physical exercises of the upper limbs after surgery in breast cancer survivors is unclear, however treatment initiated at six weeks post-operatively had similar outcomes to programmes that commenced at six months (Laurideson 2005). Therapy is aimed at increasing upper extremity strength and joint range of motion (especially the shoulder joint), decreasing pain and managing lymphoedema. Women after breast cancer treatment may also have a number of sources of pain (such as adhesive capsulitis, brachial plexopathy, fibrosis, complex regional pain, phantom breast pain). Post-mastectomy pain (rate 4% to 27%) is unrelated to the type of surgery or the usual risk factors (Stevens 1995). Treatment of pain should be similar to treatment of other chronic pain conditions in rehabilitation, addressing physical and emotional issues as well as using a cognitive behavioural approach. Psychological interventions that involve both group and individual therapy (psychotherapy, cognitive behaviour training) in women with metastatic breast cancer are not supported by existing evidence (Edwards 2008). The multidisciplinary rehabilitation focus is on reviewing treatment regimens (surgical, radiotherapy, chemotherapy), minimising complications (seromas), managing pain and promoting exercise to maximise function. Multidisciplinary rehabilitation has been found to be effective in neurological conditions such as multiple sclerosis (Khan 2011) and acquired brain injury (Turner Stokes 2005); and in musculoskeletal populations such as in persons following hip and knee arthroplasty procedures (Khan 2008).

Why it is important to do this review

There are no systematic reviews for multidisciplinary rehabilitation in breast cancer survivors to date. Other reasons for doing this review include the following.

The management of breast cancer has transformed the condition from a 'death sentence' to that of a 'chronic' disease. The emphasis has shifted to a greater awareness of functional and participatory issues in these patients (Franklin 2007). New models of cancer rehabilitation aim to preserve and promote function during all disease and treatment phases. These phases include I. staging, pre-treatment; II. primary treatment; III. after treatment; IV. recurrence; and V. end of life (Gerber 2005). This multidisciplinary model identifies symptoms and functional deficits that occur most frequently at each stage, establishing a framework for provision of rehabilitative care over time. The identified symptoms and functional deficits assist in establishing cancer rehabilitation programmes and highlight the rehabilitative interventions that can be introduced into clinical settings (Reitman 2004).

Therefore, a systematic review on this topic is required to summarise the best available evidence to date. This review aimed to identify the existing evidence for multidisciplinary rehabilitation care in women after breast cancer treatment and gaps in current knowledge. As expected, the number of studies identified for this review are limited, therefore issues for future expansion of the evidence base by traditional research and other methods are discussed.

OBJECTIVES

To assess the effects of multidisciplinary rehabilitation in persons after breast cancer treatment, and specifically to explore the following areas.

- Does organised multidisciplinary rehabilitation achieve better outcomes than the absence of such services in women after breast cancer treatment and for their caregivers?
- Which types of programmes are effective and in which setting?
- Does a greater intensity (time and expertise, or both) of rehabilitation lead to greater gains?
- Which specific outcomes are influenced (survival, dependency, social integration, mood, quality of life)?
- Are there demonstrable cost benefits for multidisciplinary rehabilitation in breast cancer survivors?

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) and clinical controlled trials (CCTs), which included quasi-randomised and quasi-experimental designs with comparative controls (controlled before-and-after studies), that assessed the effectiveness of organised multidisciplinary rehabilitation for women treated for breast cancer with either routinely available local services or lower levels of intervention (such as medical or nursing care only).
We included studies that compared multidisciplinary rehabilitation in different settings or at different levels of intensity.

Types of participants

- Adult women 18 years and older
- Confirmed diagnosis of breast cancer, regardless of time of onset or disease stage
- Surgical removal of breast tumour: lumpectomy, local wide excision, modified radical mastectomy, radical mastectomy
- Axillary lymph node dissection (AND) or sentinel node biopsy or dissection (SNB)

No studies were identified that involved participants with other types of cancers or other diagnoses where data were specifically provided for women with breast cancer.

Types of interventions

Multidisciplinary rehabilitation was defined as any intervention delivered by two or more disciplines (for example nursing, physiotherapy (PT), occupational therapy (OT), dietetics and nutrition, social work (SW), psychology or neuropsychology) and referred by a medical specialist (surgeon, oncologist, rehabilitation physician). The aim of multidisciplinary rehabilitation was to maximise activity and participation as defined by the ICF (WHO 2001).
Multidisciplinary rehabilitation interventions and programmes have no definite classification and can be broadly described in terms of settings and content (Turner Stokes 2011).
In this review, multidisciplinary rehabilitation settings may include:

- inpatient settings, where care is delivered 24 hours a day in a hospital ward or specialist rehabilitation unit;
- ambulatory and outpatient settings, which may be within a hospital or in the community;
- home-based settings, which are set within the patient's own home and local community.

Multidisciplinary rehabilitation varies in its content, intensity and frequency of therapy, and these are often tailored to the needs of an individual patient. The common terms used in the literature regarding programme content include:

- physical rehabilitation;
- cognitive and behavioural therapy;
- vocational and recreational rehabilitation;
- psychological and counselling input.

However, the actual content of any two programmes within the same category may vary greatly, and similar programmes may have been given different labels (Turner Stokes 2011).
We considered for inclusion in this review all studies that stated or implied multidisciplinary rehabilitation, provided they satisfied the definitions above, and compared them to some form of control condition. Control conditions included:

- lower level or different types of intervention, such as 'routinely available local services' (e.g., medical and nursing care);
- minimal intervention (such as 'information only');
- waiting list controls or no treatment;

- interventions given in different settings and a lower intensity of the intervention.

We categorised the multidisciplinary rehabilitation interventions for analysis based on:

- the type of multidisciplinary rehabilitation received;
- the intensity of multidisciplinary rehabilitation; and
- the time from definitive treatment to commencement of the multidisciplinary rehabilitation programme (see Subgroup analysis and investigation of heterogeneity section for more details).

We excluded those studies that assessed the effect of therapy from a single discipline (for example, physiotherapy only) or any unidisciplinary intervention or modality (for example, physical exercise, gym, stretching programme).

Types of outcome measures

Primary outcomes

Primary outcomes aimed to reflect the burden of disease on patients and their caregivers and on the services provided for them. They were categorised according to the ICF (WHO 2001) into:

- impairment or disability (limitation in activity), or both, e.g., limitation in range of shoulder movement, arm weakness, lymphoedema, pain measured by validated tools such as the Functional Independence Measure (FIM) (Granger 1998), Barthel index (BI) (Mahoney 1965), Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B) (Brady 1997), Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) (Ganz 1992; Schag 1991), Cancer Survivor Unmet Needs (CaSUN) measure (Hodgkinson 2007a) and Perceived Impact of Problem Profile (PIPP) (Pallant 2006);

- restriction in participation (environmental or personal context), e.g., QoL using the SF-36 (Ware 1993) or European Organization for Research and Treatment Quality of Life Questionnaire (EORTC-QLQ) (Aaronson 1993), fatigue (Fatigue Impact Scale) (Fisk 1994), carer burden (Caregiver Strain Index) (Robinson 1983), The Cancer Survivors' Partners Unmet Needs (CaSPUN; Hodgkinson 2007b), psychological (Depression Anxiety Stress Scale) (Lovibond 1995) and vocational outcomes (Work Instability Scale) (Gilworth 2003) and patient satisfaction measures.

Secondary outcomes

These included:

- outcomes that reflected service utilisation, such as

- the duration of hospital stay in both the acute and subacute settings,
- readmission,
- cost of care,
- extent of services used at the time of discharge;

- any adverse events that may have resulted from the intervention, defined as those events that were life-threatening or required prolonged hospitalisation.

Search methods for identification of studies

See: Breast Cancer Group methods used in reviews.
We considered articles in all languages with a view to translate the articles, if necessary.

Electronic searches

We searched the following sources.
(a) The Cochrane Breast Cancer Group Specialised Register. Details of the search strategies used by the Group for the identification of studies and the procedure used to code references are outlined in the Group's module (www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html). We extracted and considered trials coded with the key words 'breast cancer', 'advanced breast cancer', 'early breast cancer', 'locally advanced breast cancer', 'breast cancer history', 'palliative care', 'psychosocial intervention/supportive care', 'exercise', 'diet', 'follow up', 'multidisciplinary care', 'ambulatory care', 'rehabilitation', 'physical therapy modalities', 'home care services', 'interdisciplinary care', 'integrated care', 'multimodal care', 'cognitive therapy', 'behaviour therapy' and 'counselling' for inclusion in the review.
(b) MEDLINE (via PubMed) (from January 2008 to December 2011). See Appendix 1.
(c) EMBASE (via Ovid) (from January 2008 to December 2011). See Appendix 2.
(d) CINAHL (from January 2008 to December 2011). See Appendix 3.
(e) AMED (January 1985 to December 2011). See Appendix 4.
(f) PEDro (January 1985 to December 2011). See Appendix 5.
(g) Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, current issue). See Appendix 6.
(h) LILACS (January 1982 to December 2011). See Appendix 7.
(i) WHO International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/Default.aspx) for all prospectively registered and ongoing trials (7 December 2011). See Appendix 8.

Searching other resources

We checked the bibliographies of identified trials and contacted their authors and known experts in the field seeking published and unpublished trials. We handsearched the most relevant journals (Breast Cancer Research and Treatment, Breast Cancer, Breast Cancer Research, Supportive Care in Cancer, Journal of Cancer

Therapy, American Journal of Clinical Oncology: Cancer Clinical Trials, Annals of Cancer Research and Therapy, Journal of Surgical Oncology, Journal of Oncology, European Journal of Cancer and Clinical Oncology, Journal of the Cancer Institute, Physical Therapy, Archives of Physical Medicine and Rehabilitation, Clinical Rehabilitation).

We also undertook an expanded search by using the related articles feature (via PubMed), searching key authors (via Web of Science) and searching SIGLE (System for Information on Grey Literature in Europe).

Data collection and analysis

Selection of studies

Three authors (FK, BA, LN) independently screened and shortlisted all abstracts and titles of studies identified by the search strategy for appropriateness based on the selection criteria. Authors (FK, BA, LN) independently evaluated each study from the shortlist of potentially appropriate studies for inclusion or exclusion. The full text of the article was obtained, when necessary, for further assessment to determine if the trial met the inclusion or exclusion criteria. When no consensus was met about the possible inclusion or exclusion of any individual study, we made a final consensus decision by discussion amongst all the authors. If there was still no consensus, we had planned to submit the full article to the editorial board for arbitration. However, these further steps were not necessary. Authors were not masked to the name(s) of the author(s), institution(s) or publication source at any level of the review.

We included only trials with sufficient details about the multidisciplinary rehabilitation programme. We had intended to contact the trialists of the eligible studies to seek further information about the method of randomisation or the complete description of the multidisciplinary rehabilitation interventions if necessary, however this was not required.

Data extraction and management

Three authors (BA, MD, NZ) independently extracted the data from each study that met the inclusion criteria. We summarised all studies that met the inclusion criteria in the 'Characteristics of included studies' table provided in the Review Manager 5 software developed by The Cochrane Collaboration (RevMan 5) to include details on design, participants, interventions and outcomes. We included the following information:

- publication details;
- study design, study setting, inclusion and exclusion criteria, method of allocation, risk of bias;
- patient population, e.g., age, type of surgical procedure, type of tumour;
- details of the intervention;
- outcome measures;
- withdrawals, length and method of follow-up and the number of participants followed up.

Assessment of risk of bias in included studies

We used the GRADE approach to grading the quality of evidence, as described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The GRADE approach is applicable to all types of studies. The four levels of quality using the GRADE approach and the five factors that impact the quality level of the included studies are shown in Table 1 and Table 2.

Three authors (BA, NZ, MD) independently assessed the methodological quality of the included studies using the Cochrane Collaboration 'Risk of bias' tool (Chapter 8.5) (Higgins 2011). We assessed the sequence generation; allocation concealment; blinding of participants, therapists and outcome assessors; incomplete outcome data and selective outcome reporting. A judgement of 'low' indicated a low risk of bias, 'yes' indicated a high risk of bias, and 'unclear' indicated either unclear or unknown risk of bias. See Table 1.

We considered studies to be of high methodological quality if the risk of bias for all domains was low. We termed these studies 'high-quality studies'. We rated studies to be of low methodological quality if there were unclear or high risk of bias for one or more domains and termed them 'low-quality studies' (see Table 2). Any disagreement or lack of consensus was resolved by a fourth author (FK).

Measures of treatment effect

It was not possible to obtain measures of treatment effect or to pool the data using meta-analysis owing to insufficient data, the type of data available, and the diversity of methods used in the studies. If studies had been available, we would have calculated risk ratios (RR) with 95% CIs for dichotomous data and differences in means or standardised differences in means (SMD) with 95% confidence intervals (CIs) for continuous data. We would also have calculated for each outcome of interest, summary estimates of treatment effect (with 95% CIs for each comparison). As data aggregation was not possible, we have presented the results of individual studies in the Characteristics of included studies table and described the results in the discussion section.

Dealing with missing data

We would have attempted to contact the primary authors of potentially eligible studies to provide clarification of the data if necessary, however, this was not required.

In addition, we excluded studies with fatal flaws (for instance, withdrawals by more than 40% of the patients or nearly total non-

adherence to the protocol or very poor or non-adjusted comparability in the baseline criteria).

Assessment of heterogeneity

We followed statistical analysis method as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). However, it was not possible to conduct a comprehensive quantitative analysis owing to the variability of methods used and the type of available data reported in each study.

Assessment of reporting biases

Publication bias (Egger 1998) was minimised by sourcing unpublished data. We would have contacted authors for the full data set or the reason for not publishing the data, however, this was not required in this review.

Data synthesis

As mentioned above, we were unable to conduct a quantitative analysis owing to lack of studies identified, clinical heterogeneity and the variation in methods and available data in included studies. If sufficient studies had been available, we would have attempted a quantitative analysis provided there was clinical homogeneity and the data in each study allowed for such an analysis. We would also have calculated a weighted treatment effect across trials using the Cochrane statistical package Review Manager 5 (Revman 5) and expressed the results as risk ratios (RRs) and risk differences (RDs) with 95% confidence intervals (CIs) for dichotomous outcomes and mean differences (MDs) and 95% CIs for continuous outcomes. We would have initially used a fixed-effect model and Chi ^{2} tests for heterogeneity to assess outcome data for compatibility with the assumption of a uniform risk ratio ($P > 0.10$). In the presence of significant heterogeneity ($P < 0.10$), random-effects model meta-analysis would have been used instead.
We have highlighted the strength of study findings, discussed gaps in current literature and identified future research directions in the Discussion section.

Subgroup analysis and investigation of heterogeneity

We were unable to perform subgroup analysis for the following subgroups owing to the lack of available data:

- type of surgery (breast conserving versus mastectomy), axillary dissection, chemotherapy or radiotherapy, or both. The participants in the included studies were post-surgical in a subacute setting and had completed chemotherapy or radiotherapy, or both;
- age (< 50 years of age versus > 50 years of age). All participants in the eligible studies were > 49 years (except 2 women in one study (Hartmann 2007) and details were not provided);
- type of rehabilitation programme (inpatient, ambulatory care) and intensity of treatment (high-intensity, low-intensity multidisciplinary rehabilitation). The two included studies were conducted in an inpatient rehabilitation setting and compared high-intensity rehabilitation with a control group (a low-intensity group and a wait-list group);
- time from definitive treatment (surgery, radiotherapy and chemotherapy) to commencement of multidisciplinary rehabilitation (acute: < six weeks, intermediate: six weeks to six months, and longer-term: > six months). All participants in the included studies were in the later phase after completing treatment for breast cancer (12 and 24 months later). Those in the acute stage after treatment (six weeks or less following surgery or definitive treatment) could therefore not be compared to participants randomised or recruited in the convalescent stages after breast cancer treatment (more than six weeks following definitive breast cancer treatment) to commencement of multidisciplinary rehabilitation.

Factors that contributed to a heterogeneous set of studies included: the type and intensity of multidisciplinary rehabilitation care, the primary outcome, and the duration of patient follow-up.

Sensitivity analysis

No sensitivity analysis was performed. If studies had been available, and heterogeneity existed across trials, sensitivity analyses would have been conducted by omitting trials with a high risk of bias.

RESULTS

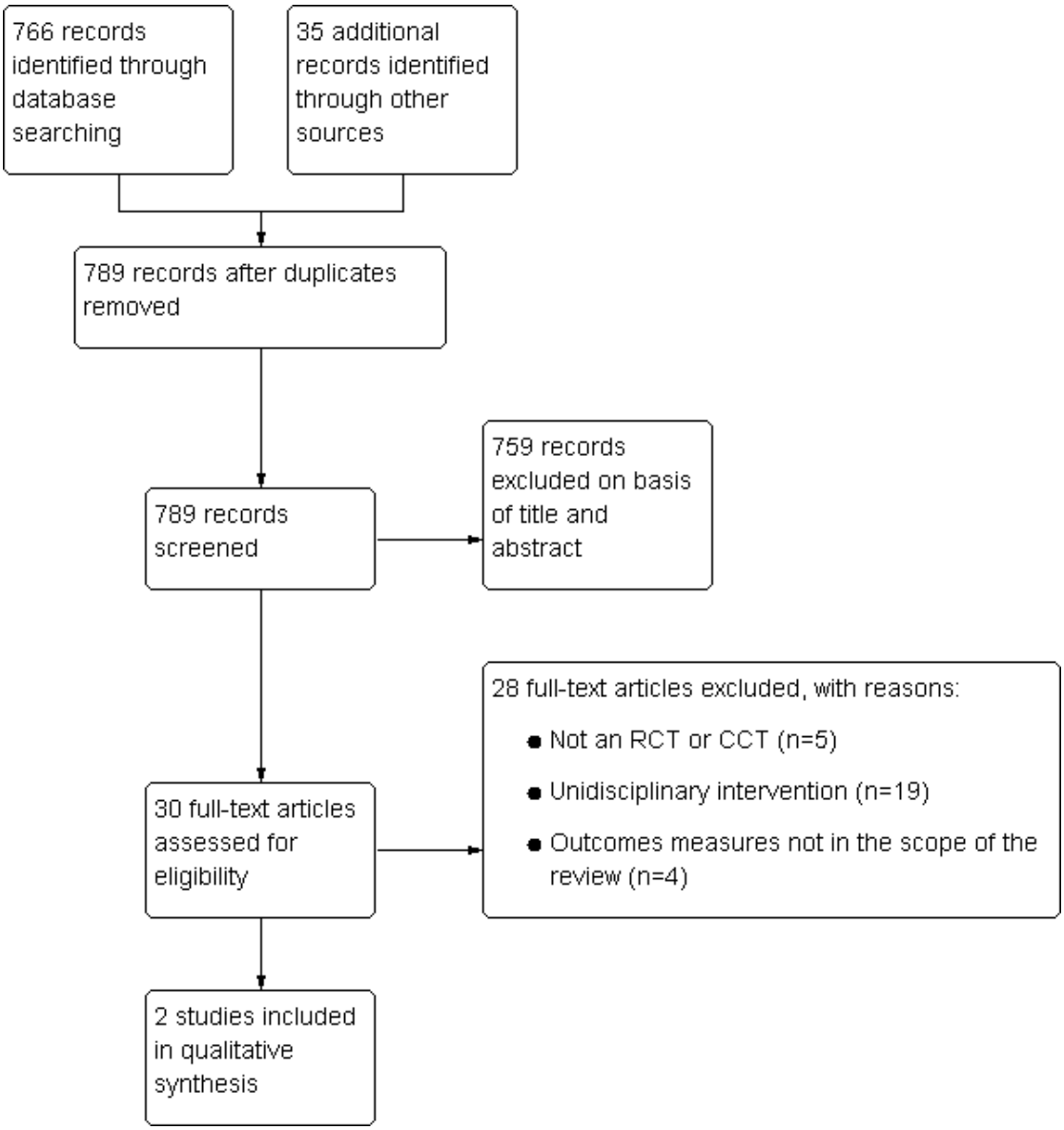
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.
See: Characteristics of included studies and Characteristics of excluded studies.

Results of the search

The electronic and manual searches yielded a total of 789 titles. Of these, 30 passed the first screening review and were selected for closer scrutiny (see Figure 1 for the study flow chart).

Figure 1. Study flow diagram.



Included studies

Two RCTs (Cho 2006; Hartmann 2007) involving a total of 262 participants fulfilled the inclusion criteria for this review (see Characteristics of included studies table). Both trials compared higher-intensity models of rehabilitation with control groups, which were either a lower-intensity rehabilitation group (Hartmann 2007) or a wait-list control (Cho 2006). The included studies were conducted in two different countries: Germany and South Korea. The multidisciplinary rehabilitation interventions in both studies consisted of physical activity and psycho-educational interventions. Both studies assessed QoL as one of their primary outcomes. Impairment, in the form of range of shoulder movement of the affected arm, was addressed in one study (Cho 2006).

Ongoing studies

One RCT was identified evaluating a multidisciplinary ambulatory rehabilitation programme for women following definitive breast cancer (BC) treatment, however the study has just commenced recruitment and no data are available at this stage. (This study is being conducted by the Author group of this review.)

Excluded studies

We excluded 28 studies (and abstracts) for the reasons shown in the Characteristics of excluded studies table. The primary reasons for exclusion were:

- not an RCT or CCT (n = 5);
- uni-disciplinary intervention (n = 19);
- outcome measures not within the scope of this review (n = 4).

Risk of bias in included studies

See: Characteristics of included studies table.

In general, the methodological quality of the two trials on multidisciplinary rehabilitation for follow-up of women treated for breast cancer appeared to be poor. Both trials (Cho 2006; Hartmann 2007) had substantial flaws in their methodological design with a high risk of bias related to their randomisation procedure; blinding of patients, therapists and outcome assessors; reporting of co-interventions; and outcome analysis.

The randomisation procedure was unclear in Hartman et al (Hartmann 2007). The study was initially designed as an RCT but was redefined midway through the study as a prospective exploratory feasibility study due to 'missing knowledge'. The RCT by Cho et al (Cho 2006) showed methodological issues in a small convenience sample of women with breast cancer, limited to a single Korean facility. Similarity of baseline characteristics was satisfactory in Cho et al (Cho 2006) but in Hartmann et al (Hartmann 2007) the participants in the intervention group were more impaired in social function compared to the control group participants (67 versus 74.8, P = 0.073). There was no mention of concealed allocation or blinding of patients, therapists and outcome assessors in either studies. Owing to the nature of the intervention, blinding of the patients and therapists is usually not possible. A feasible alternative is to evaluate expectations for the rehabilitation response in the intervention and control groups, in advance, among both patients and therapists (Karjalainen 2003). Both studies failed to report avoidance of co-interventions or their equal distribution throughout the study groups. Reporting of co-interventions could have helped judgement of their division among study groups and whether they affected the outcome. Outcome measurements used in Cho 2006 were not validated in the breast cancer population. Both studies were under powered with inadequate sample size. The duration of follow-up was unclear in Cho 2006. The dropout rates were moderate (15%) in both studies. However, in Hartmann 2007 5% withdrew consent with no reasons provided while Cho 2006 did not report the time points of dropouts.

Effects of interventions

Participant characteristics

The participants of the included studies in this review included 262 women (223 completers) with breast cancer. These women had confirmed diagnosis of breast cancer and had undergone mastectomies followed by chemotherapy or radiotherapy, or both. The details of the surgical procedure and adjuvant treatments were not provided. All participants were recruited in the subacute stage at least 12 months after completion of their definitive breast cancer treatment. All women were older than 49 years except for two women who were less than 35 years old in the study by Hartmann et al (Hartmann 2007); see Characteristics of included studies.

Intervention characteristics

The type and structure of the multidisciplinary rehabilitation intervention used in the two studies varied.

Hartmann et al (Hartmann 2007) compared a 'step-by-step' model with a 'single burst' model (both inpatient rehabilitation) to determine whether a more prolonged intervention delivered over a period of several months could produce a more sustained improvement in QoL at one year. Their active arm consisted of an initial three-week inpatient multidisciplinary rehabilitation programme

(incorporating medical input, psychology and physiotherapy) followed by two subsequent inpatient breaks of one week at four and eight months. The control group received only one episode of a four-week 'step-by-step' inpatient multidisciplinary rehabilitation programme.

Cho et al (Cho 2006) reported an ambulatory multidisciplinary intervention including a group-based programme at a tertiary care centre in Korea (three episodes per week for 10 weeks) together with a home-based exercise programme. The intervention included: psychology-based education; exercise; peer support group activity; medical, dietician and image consultant input; and a fitness instructor. The control group were participants allocated to the wait-list with no treatment (they were offered treatment post-study).

Neither study provided details of the type of rehabilitation modalities used (stretching, gym, task reacquisition) or the actual duration or intensity of specific therapy interventions.

Study characteristics

Effectiveness of multidisciplinary rehabilitation on impairment

Hartmann et al (Hartmann 2007) did not report changes in the level of impairment.

Cho et al (Cho 2006) reported increased range of shoulder movement of the affected shoulder joint in the intervention group (11.5 ± 7.8%) compared with the control group (1.3 ± 4.8%) (P < 0.001). The differences in improvement in shoulder extension, abduction, external rotation and internal rotation after the intervention were significant in the intervention group compared with the controls (P < 0.001, P = 0.011, P = 0.006, P < 0.001, respectively). Shoulder flexion significantly improved in both the intervention (from 90.7% pre-test to 95.0% post-test, P = 0.003) and control groups (from 91.2% to 94.8%, P = 0.004). The difference between groups was not statistically significant (P = 0.667).

Effectiveness of multidisciplinary rehabilitation on disability (activity)

Hartmann et al (Hartmann 2007) reported no changes (mean) in physical function between the treatment and control groups (1.5 versus 1.2, P = 0.743). Cho et al (Cho 2006) did not report changes at the level of disability.

Effectiveness of multidisciplinary rehabilitation on psychosocial outcomes and QoL

Both included studies addressed psychological outcomes and QoL. In the study by Hartmann et al (Hartmann 2007) the treatment group showed improved QoL, emotional and cognitive function after four weeks of receiving therapy compared with the control group. However, this was not statistically significant (general QoL (gQoL) 16 versus 12.6, P = 0.098; emotional function 30.7 versus 23.7, P = 0.066; cognitive function 11 versus 4.5, P = 0.127). In a subgroup analysis of patients with impaired cognitive function at baseline, the authors reported a significant difference between groups in QoL. The authors reported that at the 12-month follow-up, the intervention group improved their cognitive function by 2.3 points, whereas it decreased in the control group by -5.5 (P = 0.010). They concluded that although not generally superior to conventional inpatient rehabilitation programmes, the 'step-by-step' programme had marked benefits for patients with cognitive impairment.

Cho et al (Cho 2006) reported that after the rehabilitation programme, psychosocial adjustment improved in the intervention group by 2.9 ± 6.3 points while it decreased in the control group by 3.0 ± 6.3 points (P < 0.001). Similarly, QoL improved in the intervention group by 0.9 ± 1.3 points while it decreased in the control group by 0.1 ± 1.0 points (P = 0.002). The authors indicated that an alleviation of physical symptoms or impaired function might have contributed to the enhancement in QoL in the intervention group.

Study quality

Both studies (Cho 2006; Hartmann 2007) were of poor methodological design with high risk of bias (see Characteristics of included studies table). These studies provide 'low level' evidence for inpatient and ambulatory multidisciplinary rehabilitation programmes in producing short-term gains (up to 12 months) at the levels of impairment (range of shoulder movement) (Cho 2006), psychosocial adjustment (emotional and cognitive function) (Cho 2006; Hartmann 2007) and participation (improved QoL) (Cho 2006; Hartmann 2007) for patients after breast cancer treatment compared with controls.

DISCUSSION

Summary of main results

Two RCTs (Cho 2006; Hartmann 2007) fulfilled the inclusion criteria for this review to address the effects of multidisciplinary rehabilitation in women after breast cancer treatment. There was 'low level' evidence that inpatient and ambulatory multidisciplinary rehabilitation programmes can produce short-term gains (up to 12 months) in terms of impairment, psychosocial adjustment and participation in social activities for patients after breast cancer treatment. There was no evidence available on functional gain at the level of activity, longer-term outcomes on caregivers or the cost effectiveness of these programmes. It was not possible to suggest the most appropriate frequency and duration of therapy or the

choice of one type of intervention over another (Characteristics of included studies).

A limited number of robust studies were expected in this field owing to the difficulties in trial design in multidisciplinary rehabilitation settings; hence issues for future expansion of the evidence base by traditional research and other methods are also discussed below.

Overall completeness and applicability of evidence

This review highlighted a number of limitations in breast cancer rehabilitation studies. The two RCTs identified were methodologically weak and therefore it was not possible to address some of the questions posed in the original objectives outlined in the protocol. Within these studies there were problems that confounded comparisons or the assimilation of data. These were as follows:

- minimal information regarding the content of multidisciplinary rehabilitation programmes (i.e., modalities, duration and intensity of therapy, and the spectrum of care targeted);
- diversity of outcome measures, which varied from functional ability, to 'handicap' (participation) and QoL;
- lack of longer-term follow-up (more than 12 months), lack of availability of longitudinal data;
- no information on the cost effectiveness of rehabilitative care;
- recognition of neuropsychological sequelae (mood, affect , work-related issues) as barriers to societal reintegration but no studies addressed participatory issues after breast cancer treatment;
- minimal data on caregivers' perspectives or their involvement in the multidisciplinary programmes.

The two studies, therefore, contributed in a very limited way to the synthesis of the evidence for multidisciplinary rehabilitation for women following breast cancer treatment. In addition, it was neither possible to determine conclusively which type of programme could be effective, and in which setting, nor whether a greater intensity (time or expertise, or both) or 'dose' of rehabilitation would lead to greater gains. Further studies are needed to suggest an optimum number, duration and intensity of treatment sessions, and also to identify other factors that may affect outcomes. It was not possible to determine which specific outcomes are influenced (dependency, social integration, mood) by multidisciplinary rehabilitation.

Multidisciplinary rehabilitation is a complex intervention, which is defined as 'complex' when the active ingredient in the intervention is not easily identifiable (MRC 2000). The outcome measures used in the breast cancer population need to reflect the complex constructs of multidisciplinary rehabilitation and focus on impairments, disability and restriction in participation, as advocated by the WHO ICF (WHO 2001). Generic measures used in breast cancer (and other cancer populations) in general rehabilitation settings (for example the Functional Independence Measure (FIM) or Barthel Index (B)I) may not be sufficiently sensitive to capture the relevant gains following intervention, and have floor or ceiling effects. In particular, QoL is difficult to measure given the many factors that influence it. Breast cancer specific measures can be comprehensive and varied (Campbell 2010; Hodgkinson 2007a; Schag 1991; te Velde 1996). For example, the Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) (Schag 1991) provides information about day to day problems and rehabilitation needs of these persons. With improved mortality rates following breast cancer treatment, more research is needed to gain consensus on a suitable battery of measures to capture changes in physical ability (at the level of impairment and disability) as well as the longer-term outcomes relating to psychosocial adjustment and QoL.

Quality of the evidence

In this review, our aim was to determine the effects of multidisciplinary rehabilitation for follow-up of women treated for breast cancer. The data synthesised from the two studies (Cho 2006; Hartmann 2007) provided 'low level' evidence for inpatient and ambulatory multidisciplinary rehabilitation programmes compared with controls in improving impairment and QoL in the short-term (up to 12 months) following rehabilitation. Both included studies were of poor methodological design with high risk of bias. Neither study provided detailed information on the specific type, duration, intensity and modality used in the rehabilitation therapy programme.

Drawing clinical conclusions about the magnitude and duration of the effectiveness of interventions for this indication was hampered by the limited number of studies and lack of high-quality studies that compared multidisciplinary rehabilitation to control interventions. However, the two included studies support multidisciplinary rehabilitation for women following breast cancer treatment.

Potential biases in the review process

The conclusions from this review are limited by the fact that there is only a small number of studies of poor methodological quality and with diverse approaches to multidisciplinary rehabilitation, as described above. In addition, the authors recognise a number of limitations in the methods of the review itself and the completeness of the retrieved literature.

1. There may have been a degree of selection bias from the literature search (van Tulder 2003) given that our search strategy principally encompassed the cited literature, despite the extended

range of terms that were used to capture the widest possible selection of the relevant literature.

2. Publication bias is well described in that trials with positive results tend to be published in favour of those with negative findings (Egger 1998). We cannot exclude the possibility that there have been negative trials that have not reached the published literature.

3. Similarly, although our search strategy included searching of reference lists within the relevant papers for other possible articles missed in our electronic searches, reference bias (Goetzsche 1987) is a further possible confounder in that authors too tend not to report findings that do not support their case for promoting the intervention in question.

We therefore welcome contact from any readers who are aware of important high-quality studies that would meet the criteria for this review but are so far not included.

Agreements and disagreements with other studies or reviews

The findings of this review highlight the existing gaps in the literature and emphasise the importance of finding some support for multidisciplinary rehabilitation for women after breast cancer treatment. These findings are consistent with existing guidelines (NBCC 2001; NCCC 2009).

AUTHORS' CONCLUSIONS

Implications for practice

Although conclusive trial-based evidence of the effectiveness of multidisciplinary rehabilitation for persons treated for breast cancer is currently lacking, the place for breast cancer rehabilitation is established at a clinical level. Treating clinicians generally accept the need to refer these patients early for physical interventions (lymphoedema programmes, improved range of shoulder movement) and for pain management. However, this review provides 'low level' evidence to support a broader multidisciplinary approach to optimise their function and psychosocial adjustment and to enhance participation and QoL. Those who require counselling or cognitive or behaviour therapy should also be screened for consideration for rehabilitation. To improve function and participation for these patients, more evidence is needed for specific modalities and therapies offered to build evidence-based practices in rehabilitation.

Implications for research

In breast cancer rehabilitation research there is a need for:

- well-designed research methods using both randomised and clinical controlled trials, and also using 'clinical practice trials' where data are routinely gathered without disrupting the natural milieu of treatment;
- information about specific rehabilitation modalities and interventions to improve evidence-based practices, the type, setting, intensity and duration of intervention;
- incorporation of patient (and caregiver) perspectives in rehabilitation programmes;
- more sensitive and appropriate outcome measurements that include various participatory domains relevant to this population (e.g., return to work);
- longitudinal data (functional and psychological), and ageing with disabilities over time;
- a consensus on a 'core set' of outcome measures in breast cancer trials using the WHO ICF domains.

The many challenges in rehabilitation for traditional research designs include: heterogeneous patient populations, interdependent components and contexts, multifaceted and multilayered treatments involving organisational restructure, individual interventions and ethical considerations (Khan 2010; Khan 2011). Some women following breast cancer treatment can present with diverse clinical presentations with varying levels of disability, requiring an individualised approach. Although RCTs are the gold standard for high level evidence, they are not always appropriate to answer all questions that need to be answered (Khan 2010a). Other alternatives include clinical practice trials that acquire prospective and retrospective data without disrupting the natural milieu of treatment (Gassaway 2005). Routine data obtained can give information about models and outcomes of rehabilitative care, what type of patients can benefit most, what intensity of rehabilitation input is required, and care pathways assessment (DeJong 2005; Gassaway 2005). This approach has been used in patients with chronic neurological disabilities (Khan 2010a).

Breast cancer registries exist in many countries and mainly contain survival, medical and treatment outcome data. However, subacute data in post-acute settings providing information about residual disability and restriction in participation after breast cancer treatment are not routinely available. This includes rehabilitation intervention and palliative care input, especially over a longer time. Furthermore, perspectives of patients or caregivers, or both, in multidisciplinary programmes, which is vital to facilitate communication and agreement amongst treating clinicians with respect to the clinical approach, may not always be incorporated in multidisciplinary care programmes. Ongoing development of a standard disability framework, such as the ICF 'core set' for breast cancer (lists of ICF categories selected by experts for targeted management which need to be addressed in multidisciplinary settings) (Brach

2004), can provide an opportunity to improve clinical agreement and communication amongst multidisciplinary teams.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cho 2006

Methods	Randomised Controlled Trial
Participants	South Korea. N = 65: treatment group = 34 and control = 31
Interventions	Treatment group - ambulatory multidisciplinary rehabilitation programme (psychology based education, exercise, peer- support group activity, medical input, dietician, image consultant, fitness instructor) for 3 episodes/sessions per week for 10 weeks Control group - wait-list no treatment (offered treatment post study)
Outcomes	Range of shoulder movement, Psychological Adjustment Scale, and a local quality-of-life measure
Notes	No report of adverse events

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants randomly allocated to treatment or control group
Allocation concealment (selection bias)	High risk	No allocation concealment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Overall 10 participants (15%) dropped out (6 in intervention, 4 in control group). Percentage of dropouts reported but not time points
Selective reporting (reporting bias)	Low risk	All pre-specified (primary and secondary) outcomes reported
Other bias	Unclear risk	Potential source of bias related to the study design No long-term follow-up Small sample size, not representative of all South Korean people - single hospital 10 week time point - no clear relationship to end of rehabilitation programme given Outcome measurement used not validated in breast cancer population Clinical and statistical significance for psychosocial adjustment and range of shoulder movement outcome measures not specified Control group- a convenience sample unmatched to treatment group

Cho 2006 (*Continued*)

		follow-up duration unclear
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors

Hartmann 2007

Methods	Randomised Controlled Trial (RCT). Designed as prospective RCT, but reclassified 'midway' as an 'explorative feasibility' study because of missing knowledge about effects
Participants	Germany. N = 197: treatment group = 98, control group= 99
Interventions	Treatment group - received 3 week step-by-step inpatient and outpatient multidisciplinary rehabilitation programme (physician input, psychology, physiotherapy), plus at 4 & 8 months later - a one week rehabilitation programme each time Control group - only a 4 week step-by-step inpatient and outpatient multidisciplinary rehabilitation programme
Outcomes	Quality Of Life - Questionnaires (QLQ-C30) of the European Organisation for Research and Treatment of Cancer (EORTC) for QoL
Notes	Length of follow-up 12 months. T0-beginning, T1-end of 3 or 4 week multidisciplinary rehabilitation programme, T2-12 months Breakdown of those treated as inpatients versus outpatients not specified No reports of adverse events

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Study design unclear: Participants randomly allocated to treatment or control group; randomisation procedures not specified
Allocation concealment (selection bias)	High risk	No information on allocation concealment
Incomplete outcome data (attrition bias) All outcomes	High risk	Overall, 29 (14.7%) dropouts (treatment group = 15, control = 14): in 19 cases exclusion criteria became evident, 10 withdrew consent with no reason Analyses performed as intention to treat. However, patient numbers did not add up,

		and dropouts overlap with excluded patients No demographic differences between dropouts and others, or between dropouts across treatment groups Percentage of dropouts reported but not time points
Selective reporting (reporting bias)	Unclear risk	Selective reporting Unclear if compliance was taken into account for the subgroup analysis Some domains of QoL not analysed at all time points even though reasons given as 'not appropriate social environment'
Other bias	Unclear risk	Adherence/ compliance with rehabilitation programme not discussed Incomplete attrition report Sample size inadequate (power required at 200 to detect overall effect of difference of15 points in quality of life (QoL)) Baseline characteristics dissimilar between groups (intervention group more impaired in social function 67 vs. 74.8, P = 0.073) Discrepancy between description of primary outcome: Quality Of Life - Questionnaires of European Organisation for Research and Treatment of Cancer (EORTC-QLQ) as primary and general quality of life (gQOL) and other outcomes (cognitive function, emotional function, physical function, social function, role function) as secondary
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of the participants and treating staff
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors

QoL = quality of life
RCT = randomised controlled trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bennett 2007	Uni-disciplinary intervention
Braden 1998	Uni-disciplinary intervention
Budin 2008	Uni-disciplinary intervention
Campbell 2005	Uni-disciplinary intervention
Demark-Wahenefried 2003	Outcome measures not within the scope of this review
Demark-Wahnefried 2007	Outcome measures not within the scope of this review
Demark-Wahnefried 2006	Not an RCT or CCT
Duijts 2009	Outcome measures not within the scope of this review
Gordon 2005	Not an RCT or CCT
Heim2007	Uni-disciplinary intervention
Kaltsatou 2011	Uni-disciplinary intervention
Kilgour 2008	Uni-disciplinary intervention
Koinberg 2006	Not an RCT or CCT
Lev 2001	Outcome measures not within the scope of this review
McClure 2010	Uni-disciplinary intervention
Milne 2008a	Uni-disciplinary intervention
Milne 2008b	Uni-disciplinary intervention
Mock 1994	Uni-disciplinary intervention
Na 1999	Uni-disciplinary intervention
Pinoto e Silva 2008	Not an RCT or CCT
Sandel 2005	Uni-disciplinary intervention
Schnur 2009	Uni-disciplinary intervention

(*Continued*)

Strauss-Blasche 2005	Not an RCT or CCT
Todd 2008	Uni-disciplinary intervention
Velthuis 2010	Uni-disciplinary intervention
Wengstrom 1999	Uni-disciplinary intervention
Wingate 1989	Uni-disciplinary intervention
Wonghongkul 2008	Uni-disciplinary intervention

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Levels of quality of individual studies

Judgement of risk of bias	Quality rating of study
Risk of bias of all domains low	High methodological quality = 'high-quality study'
Unclear or high risk of bias for one or more domains	Low methodological quality = 'low-quality study'
High risk of bias for most domains	Very low methodological quality = 'very low-quality study'

Table 2. Levels of evidence quality using the GRADE approach

Underlying methodology	Quality rating
Randomised trials; or double-upgraded observational studies	High
Downgraded randomised trials; or upgraded observational studies	Moderate
Double-downgraded randomised trials; or observational studies	Low
Triple-downgraded randomised trials; or downgraded observational studies; or case series/case reports	Very low

APPENDICES

Appendix 1. MEDLINE search strategy (January 2008 to 2011)

1. exp Breast Neoplasms/
2. (breast cancer$ or breast tumor$ or breast tumour$ or breast neoplasm$ or axillary dissection).tw.
3. (breast carcinoma$ or breast adenocarcinoma$ or breast sarcoma$).mp
4. exp mastectomy/
5. *Lymph node excision/
6. (axill$ adj3 lymph node dissection).mp
7. (sentinel node dissection).mp
8. or/1-7
9. exp Ambulatory Care/
10. exp Rehabilitation/
11. exp Hospitalization/
12. exp Physical Therapy Modalities/

13. exp Home Care Services, Hospital-Based/
14. Home Care Services/
15. exp Inpatients/
16. exp Outpatients/
17. exp Cognitive Therapy/
18. Behavior Therapy/
19. exp Social Work/
20. exp Dietetics/
21. exp Dietary Services/
22. exp Ocuupational therapy/
23. Counseling/
24. exp multidisciplinary/
25. exp interdisciplinary or integrated to multimodal
26. or/9-25
27. (rehabilitat$ or home health care or physiotherap$ or physical therap$ or speech or occupation$ or social work).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
28. (cognitive therap$ or behavio?r therap$ or counsel?ing or nutrition or diet$ or food).mp. [mp=title, original title, abstract, name of substance]
29. (outpatient$ or inpatient$ or hospital$ or home).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
30. or/27-29
31. 26 or 30
32. 8 and 31
33. randomized controlled trial.pt.
34. randomized controlled trials.sh.
35. controlled clinical trial.pt
36. random$.tw.
37. random allocation.sh
38. double-blind method.sh.
39. single-blind method.sh.
40. or/33-39
41. exp clinical trials/
42. (clin$ adj25 trial$).ti,ab.
43. clinical trial.pt
44. clinical trial$.tw.
45. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
46. placebos.sh.
47. placebo$.ti,ab.
48. random$.ti,ab.
49. research design.sh.
50. or/41-49
51. 40 or 50
52. 32 and 51
53. (animals not human).sh.
54. 52 not 53

Appendix 2. EMBASE search strategy (January 2008 to 2011)

1. exp Breast Tumor/
2. (breast cancer$ or breast tumor$ or breast tumour$ or breast neoplasm$).tw.
3. or/1-2
4. exp SHOULDER PAIN/ or exp SHOULDER/ or exp SHOULDER GIRDLE/
5. exp ARM/
6. (arm$ or shoulder$ or upper limb$ or upper extremit$).tw.
7. (chest pain$).tw.
8. adhesive capsulitis.mp. or exp Humeroscapular Periarthritis/
9. cording.mp.
10. or/4-9
11. 3 and 10
12. exp Cancer rehabilitation/ or exp Rehabilitation/ or exp Rehabilitation medicine/
13. physical therapy.mp. or exp Physiotherapy/
14. exp EXERCISE/
15. (rehabilitat$ or physiotherap$ or manual therap$ or exercise$ or mobili$).mp.
16. exp Daily Life Activity/
17. exp Occupational Therapy/
18. or/12-17
19. 11 and 18
20. Clinical Trial/
21. randomized controlled trial/
22. randomization/
23. single blind$.tw
24. double blind$.tw
25. Placebo$.tw
26. random?ised controlled trial$.tw
27. or/20-26
28. 19 and 27
29. Nonhuman/
30. 28 not 29

Appendix 3. EBSCOhost CINAHL search strategy (December 2011)

S31. S30, Limiters - Human; Publication Type: Clinical Trial
S30. S19 and S29
S29. S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28
S28. sentinel node dissect*
S27. axillary dissect*
S26. Lymph node excision*
S25. “mastectomy”
S24. (breast carcinoma* or breast adenocarcinoma* or breast sarcoma*).
S23. Breast tumor or breast tumour
S22. (Metastatic breast cancer or advance* breast cancer or recurrent* breast cancer)
S21. breast cancer
S20. (MH “Breast Neoplasms”) Search modes - Boolean/Phrase
S19. S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S18. (outpatient* or inpatient* or hospital* or home)
S17. (cognitive therap* or behavio?r therap* or counsel#ing or nutrition or diet* or food)
S16. (rehabilitat* or home health care or physiotherap* or physical therap* or speech or occupation*)
S15. (multidisciplinary or intergrated)
S14. (“Patient Care Team”) or (MH “Multidisciplinary Care Team”)

S13. (“Counseling”) or (MH “Counseling”)
S12. (“Dietary Services”) or (MH “Nutrition Services+”)
S11. (“Dietetics”) or (MH “Dietetics”)
S10. (“Social Work”) or (MH “Social Work+”)
S9. (“Behaviour Therapy”) or (MH “Behavior Therapy”)
S8. (“Cognitive Therapy”) or (MH “Cognitive Therapy”)
S7. (MH “Outpatients”)
S6. (MH “Inpatients”)
S5. (MH “Home Health Care+”)
S4. (MH “Physical Therapy+”)
S3. (MH “Hospitalization+”)
S2. (MH “Rehabilitation”)
S1. (MH “Ambulatory Care”)

Appendix 4. AMED search strategy (January 1985 to 2011)

1. exp Breast Neoplasms/
2. (breast cancer$ or breast tumor$ or breast tumour$ or breast neoplasm$ or axillary dissection).tw.
3. (breast carcinoma$ or breast adenocarcinoma$ or breast sarcoma$).mp
4. exp mastectomy/
5. *Lymph node excision/
6. (axill$ adj3 lymph node dissection).mp
7. (sentinel node dissection).mp
8. or/1-7
9. exp Ambulatory Care/
10. exp Rehabilitation/
11. exp Hospitalization/
12. exp Physical Therapy Modalities/
13. exp Home Care Services/
14. exp Inpatients/
15. exp Outpatients/
16. exp Cognitive Therapy/
17. Behavior Therapy/
18. exp Social Work/
19. exp diet therapy/
20. Counseling/
21. Patient Care Team/
22. (multidisciplinary or intergrated).tw.
23. (rehabilitat$ or physiotherap$ or physical therap$ or speech or occupation$ or social work).tw.
24. (cognitive therap$ or behavio?r therap$ or counsel?ing or nutrition or diet$ or food).tw.
25. (outpatient$ or inpatient$ or hospital$ or home).tw.
26. or/9-25
27. 8 and 26
28. limit 27 to (human and clinical trial)

Appendix 5. PEDro search strategy (January 1985 to 2011)

Abstract + Title = (breast cancer) OR (breast tumour) AND (rehabilitation) + Method = Clinical Trial

Appendix 6. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1. MeSH descriptor Breast neoplasms explode all trees
#2. breast cancer
#3. breast tumo*
#4. (#1 OR #2 OR #3)
#5. MeSH descriptor Ambulatory Care explode all trees
#6. MeSH descriptor Rehabilitation explode all trees
#7. MeSH descriptor Hospitalization explode all trees
#8. MeSH descriptor Physical Therapy Modalities explode all trees
#9. MeSH descriptor Home Care Services, Hospital-Based explode all trees
#10. MeSH descriptor Home Care Services explode all trees
#11. MeSH descriptor Inpatients explode all trees
#12. MeSH descriptor Outpatients explode all trees
#13. MeSH descriptor Cognitive Therapy explode all trees
#14. MeSH descriptor Behavior Therapy explode all trees
#15. MeSH descriptor Social Work explode all trees
#16. MeSH descriptor Dietetics explode all trees
#17. MeSH descriptor Dietary Services explode all trees
#18. MeSH descriptor Counseling explode all trees
#19. MeSH descriptor Patient Care Team explode all trees
#20. multidisciplinary or intergrated
#21. rehabilitat* or physiotherap* or physical therap* or speech or occupation* or social work
#22. (cognitive therap* or behavio?r therap* or counsel?ing or nutrition or diet* or food)
#23. (outpatient* or inpatient* or hospital* or home)
#24. (#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25. (#4 AND #24)
#26. (#25)

Appendix 7. LILACS search strategy (January 1982 to 2011)

(Mh Breast Neoplasms) OR (breast cancer$ or breast tumor$ or breast tumour$ or breast neoplasm$ or axillary dissection) OR (breast carcinoma$ or breast adenocarcinoma$ or breast sarcoma$) OR (Mh mastectomy) OR (Lymph node excision OR (axill$ adj3 lymph node dissection) OR (Mh sentinel node dissection)
AND (Mh Ambulatory Care) OR (Mh Rehabilitation) OR (Mh Hospitalization) OR (Mh Physical Therapy Modalities) OR (Mh Home Care Services, Hospital-Based) OR (Mh Home Care Services) OR (Mh Inpatients) OR (Mh Outpatients) OR (Mh Cognitive Therapy) OR (Mh Behavior Therapy) OR (Mh Social Work) OR (Mh Dietetics) OR (Mh Dietary Services) OR (Mh Counseling) OR (Mh Patient Care Team) OR (multidisciplinary) OR (intergrated) OR (rehabilitat$) OR (home health care) OR (physiotherap$) OR (physical therap$) OR (speech) OR (occupation$) OR (social work) OR (cognitive therap$) OR (behavior therap$) OR (counseling) OR (nutrition) OR (diet$) OR (food) OR (outpatient$) OR (inpatient$) OR (hospital$)
AND (((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal))

Appendix 8. WHO ICTRP search strategy

Advanced search:
1. Title: Multidisciplinary care for follow up of women treated for breast cancer
Recruitment Status: ALL
2. Condition: breast cancer%
Intervention: multidisciplinary care OR integrated care OR rehabilitative care OR multimodal care OR palliative care OR ambulatory care OR interdisciplinary care OR supportive care OR rehabilitation OR home care service%
Recruitment Status: ALL
3. Condition: breast cancer%
Intervention: (psychosocial OR physical OR cognitive OR behaviour OR behavior OR behavioural OR cognitive behavioural) AND (intervention% OR therap%)
Recruitment Status: ALL

WHAT'S NEW

Last assessed as up-to-date: 7 December 2011.

Date	Event	Description
23 November 2012	Amended	Edited copy (minor adjustments)

CONTRIBUTIONS OF AUTHORS

Fary Khan (FK) and Bhasker Amatya (BA) were involved in all aspects of the review. Louisa Ng (LN) assisted with the literature search, Marina Demetrios (MD) and Nina Zhang (NZ) conducted the study appraisals. Lynne Turner-Stokes (LTS) reviewed the manuscript. All authors contributed to the quality of the review.

DECLARATIONS OF INTEREST

The authors are clinicians in the field of Physical and Medical Rehabilitation who wish to provide the best possible service to their patients.

None have personal or financial conflicts of interest in the findings of this review.

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Internal sources

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None

INDEX TERMS

Medical Subject Headings (MeSH)

Breast Neoplasms [*rehabilitation; therapy]; Follow-Up Studies; Germany; Quality of Life; Randomized Controlled Trials as Topic; Range of Motion, Articular; Republic of Korea; Shoulder Joint [physiology]

MeSH check words

Female; Humans