Rehabilitation of breast cancer patients

Report from Kunnskapssenteret (Norwegian Knowledge Centre for the Health Services)
No 2–2009
Systematic Review

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Norwegian Knowledge Centre for the Health Services

Background: Breast cancer is the leading cause of cancer in women world wide. In 2007 in Norway 2761 new cases were diagnosed. Although recent advances in therapy have improved survival rates, they are associated with significant side effects. The Central Norway Regional Health Authority requested that the Norwegian Knowledge Centre for the Health Services perform a systematic review of the rehabilitation of breast cancer patients. **Objective:** The aim of this overview is to explore literature to assess the effect of single treatments and combination of treatments with respect to improvements in physical functionality and psychological well-being. **Methods:** Systematic searches in the databases: Cochrane Library, The Centre for Reviews and Dissemination databases, Medline, Embase, Cinahl, PsycINFO, AMED and PEDro until September 2008. **Results:** We included 46 randomized controlled trials. Investigated interventions were physiotherapy, different types of physical activity, different psychosocial interventions, nutrition, complementary interventions and complex rehabilitation programs. The studies on physical activity after primary cancer treatment showed

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(continued from page one) improved quality of life and reduced fatigue. It was difficult to conclude about the studies on physical activity during primary treatment due to inconsistency. Three studies showed that early physical activity was not associated with aggravated lymphedema. Four studies showed that cognitive behaviour therapy intervention after primary cancer treatment will increase overall quality of life. More documentation is needed for the interventions of physiotherapy, psychoeducation, social and emotional support, nutrition, complementary and complex interventions. **Conclusion:** •There is limited documentation for the effect of different rehabilitation interventions for breast cancer patients. •The documentation indicated that physical activity after primary cancer treatment may increase quality of life and reduce fatigue. •Patients might also have some benefits on quality of life from cognitive behaviour therapy interventions. •There is still a critical need for further research focusing on rehabilitation interventions throughout and after treatment among breast cancer patients.

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Nasjonalt kunnskapssenter for helsetjenesten
Oslo, mars 2009

Oppsummering

Rehabilitering av pasienter med brystkreft

Brystkreft rammer årlig i underkant av 3000 kvinner i Norge. Tidlig diagnostisering og behandling gjør at flere enn før overlever denne kreftformen, men også at flere opplever bivirkninger. Etter behandlingen kan pasienter oppleve kronisk tretthet (fatigue), konsentrasjonsproblemer, nedsatt skulderbevegelighet, vektøkning og lymfødem. Det er også rapportert om høyere forekomst av angst og depresjoner enn før. I denne rapporten vurderer vi hvor godt dokumentert effekten er av ulike tiltak for å rehabilitere pasienter med brystkreft.

Metode: Vi utførte et systematiske litteratursøk i åtte internasjonale databaser til og med september 2008. Vi inkluderte studier om kvinnelige pasienter med brystkreft uten metastase, som fikk et rehabiliteringsregime under eller etter gjennomgått primærbehandling.

Resultater: De fleste av de 46 randomiserte kontrollerte studiene som vi inkluderte, vurderte effekt av enkelttiltak (fysioterapi fysisk aktivitet, ulike psykososiale tiltak eller ernæring). Fem studier undersøkte tiltak fra komplementære tiltak mens tre studier undersøkte effekten av sammensatte tiltak. Studiene var svært forskjellige og resultatene kunne derfor ikke sammenstilles i meta-analyser. Studiene viste at:
- Det er fortsatt usikkert om manuell lymfedrenasje gir noen ytterligere effekt ut over generell behandling med kompresjonsbandasje.
- Fysisk aktivitet *etter* primær behandling ser ut til å motvirke fatigue og bedre livskvaliteten hos pasientene.
- Studiene som så på fysisk aktivitet *under* primær kreftbehandling var veldig forskjellige og ingen konklusjon kan trekkes.
- Fysisk aktivitet ser ikke ut til å påvirke utvikling av lymfødem.
- Kognitiv terapi etter brystkreftbehandling gir bedre livskvalitet.
- Det er for lite dokumentasjon ennå til å si noe om effekten av de andre psykososiale tiltakene.
-Det er behov for flere studier som ser på rehabiliteringsprogrammer innen ernæring, komplementære og sammensatte tiltak.

Konklusjon: Det er begrenset dokumentasjon om effekten av ulike rehabiliteringstiltak for brystkreftpasienter. Fysisk aktivitet og kognitiv behandlingsterapi ser ut til å bedre livskvaliteten. Fysisk aktivitet ser ut til å motvirke fatigue og ser ikke ut til å påvirke nivået av lymfødem. Det er behov for flere randomiserte studier om effekten av rehabiliteringstiltak for å minske fysiske og psykiske ettervirkninger av sykdom og behandling. Det er behov for å se på både hvilket innhold, tidspunkt i forløpet og lengde på tilbudet som brystkreftpasientene har best nytte av. Få av de inkluderte studiene har pasienter som har gjennomgått de nye behandlingsformene som gis til dagens brystkreftpasienter. Nye studier bør også utformes for å finne undergrupper av brystkreftpasienter som spesielt trenger fysisk og/eller psykisk oppfølging.

Sammendrag

Rehabilitering av pasienter med brystkreft

BAKGRUNN

Brystkreft er den kreftsykdommen flest kvinner i verden rammes av. I 2007 ble det diagnostisert 2761 nye tilfeller av brystkreft i Norge. Tidlig diagnostisering og behandling gjør at mange overlever denne kreftformen (5 års overlevelse er 86 %). Over 30 000 kvinner lever i dag etter å ha fått diagnosen brystkreft. Behandlingen innebærer operasjon og tilleggsbehandling (cellegiftbehandling og/eller strålebehandling og/eller hormonell behandling). De nye behandlingsformene for brystkreft har gitt bedre overlevelse, men også flere bivirkninger for pasientene. Flere pasienter opplever kronisk tretthet (fatigue), konsentrasjonsproblemer, nedsatt skulderbevegelighet, vektoppgang og lymfødem. Blant brystkreftpasienter er det også rapportert om en høyere forekomst av angst og depresjoner. En del av de langtidsoverlevende etter brystkreft lever med bivirkninger av sykdom og behandling flere år etter at de er ferdigbehandlet. Det er derfor viktig å vurdere hvordan ulike strategier best kan understøtte fysisk og psykisk rehabilitering.

MANDAT

Helse Midt-Norge ba i 2005 Nasjonalt kunnskapssenter for helsetjenesten om å bistå i utredningen av faggrunnlaget for rehabilitering av brystkreftpasienter. Bakgrunnen for forespørselen var at Helse Midt-Norge ønsket å bygge opp et rehabiliteringssenter som i størst mulig grad benytter metoder som er dokumentert virksomme. En utredningsgruppe ble opprettet med fagpersoner innen onkologi, fysioterapi, fysikalsk medisin, fysisk aktivitet og psykososiale tiltak.

For å studere om slike programmer er effektive trenger vi å vite:

- effekten av det enkelte rehabiliteringstiltaket
- om en kombinasjon av flere tiltak er bedre enn et enkelt rehabiliteringstiltak
- hvilke kombinasjoner av rehabiliteringstiltak som er de mest effektive

METODE

Vi har foretatt en systematisk gjennomgang av litteratur for å vurdere effekten av rehabiliteringstiltak som blir gitt etter brystkreftbehandling. Vi gjennomførte et litteratursøk for perioden til og med september 2008 i databasene Cochrane Library, The Centre for Reviews and Dissemination data bases, Medline, Embase, Cinahl, PsycINFO, AMED, og PEDro for å identifisere litteratur. To personer vurderte litteraturen uavhengig av hverandre for å vurdere relevans og kvalitet. Vi inkluderte bare randomiserte kontrollerte studier med høy eller moderat kvalitet vurdert etter en sjekkliste for randomiserte studier (Appendiks 4).

Inklusjonskriterier:
Studiedesign: Randomiserte kontrollerte studier.
Populasjon: Brystkreftpasienter som har gjennomgått kirurgi, og som kan ha fått tilleggsbehandling som stråling, cellegiftbehandling eller hormonell behandling.
Tiltak: Fysisk aktivitet, fysioterapi, psykososiale tiltak, ernæringstiltak, komplementær behandling og sammensatte rehabiliteringstiltak.
Utfall: somatiske, psykologiske og sosiale utfall.

RESULTATER

Vi oppsummerte resultater fra 46 randomiserte kontrollerte studier som undersøkte ulike tiltak for å rehabilitere brystkreftpasienter. Syv studier omhandlet fysioterapi, 11 studier fysisk aktivitet, 18 studier psykososiale tiltak, to studier ernæring, fem studier komplementære tiltak og tre studier vurderte effekten av sammensatte tiltak. Ti av de inkluderte studiene hadde høy kvalitet (flest innen fysisk aktivitet), mens de resterende 36 studiene hadde moderat kvalitet. Studiene var svært forskjellige og kunne ikke sammenstilles ved meta-analyser. Resultatene blir derfor oppsummert kvalitativt. Studiene ble inndelt på bakgrunn av om pasientene fikk rehabilitering under eller etter primær kreftbehandling.

Fysioterapi

Syv randomiserte kontrollerte studier med moderat kvalitet har sett på fysioterapi i rehabiliteringen av brystkreft. Tre studier viste liten effekt på lymfødem av manuell lymfedrenasje som tilleggsbehandling til kompresjonsbandasje. Én studie viste at multimodal fysioterapi (lymfedrenasje, kompresjonsbandasje, trening og evaluering) ga bedre effekt på lymfødem enn standard fysioterapi. Dokumentasjonen fra tre studier tilsier at det ikke er noen forskjell i skulderbevegelighet om fysioterapibehandling eller skuldertrening er gitt rett etter kirurgi eller flere uker etter kirurgi. Seks av studiene vurderte bare pasienter operert med aksille-glandel-toilette-kirurgi og ikke den mer skånsomme fjerningen av lymfeknuter som i dag blir gjort på over halvparten av pasientene i Norge ved biopsi av vaktpostlymfeknuter (Sentinel Node Biopsy). Kun én studie inkluderte en blandet populasjon.

Fysisk aktivitet

Elleve randomiserte kontrollerte studier har sett på fysisk aktivitet i rehabilitering av brystkreftpasienter. Ni av studiene hadde høy kvalitet. Seks av syv studier fant en bedring i livskvalitet når tiltaket ble gitt *etter* kreftbehandling. Fire studier viste at fysisk aktivitet etter kreftbehandling reduserte tretthet (fatigue). De fem studiene som så på fysisk aktivitet *under* primær kreftbehandling hadde ikke entydige resultater, og det er derfor vanskelig å konkludere om en sammenheng. Tre studier viste ingen endring i lymfødem etter tidlig trening (inkludert trening med vekter).

Psykososiale tiltak

De 18 inkluderte randomisertre kontrollererte studiene hadde begrenset dokumentasjon av hvilken effekt psykososiale tiltak hadde på brystkreftpasienter. Studiene har brukt mange ulike typer spørreskjemaer for å kartlegge pasientenes psykiske helsetilstand, noe som gjorde en sammenligning vanskelig. Seks studier med mode-

rat kvalitet studerte effekter av informasjon eller opplæring. Resultatene viste inkonsistente funn både på forbedring av livskvalitet, kreftrelatert engstelse og depresjon. Syv studier, hvorav én studie med høy kvalitet, undersøkte effekten av tiltak med en kognitiv[1] terapi. Fire av disse observerte en forbedring av livskvaliteten når tiltaket ble gitt *etter* kreftbehandlingen (flere av utfallene ble målt med forskjellige måleinstrumenter). Resultatene var inkonsistente for kognitive tiltak *under* kreftbehandlingen. Fem studier med moderat kvalitet hadde sosial eller emosjonell støtte som tiltak. Resultatene viste inkonsistente funn både på forbedring av livskvaliteten og på bedring av humørprofilen.

Ernæring
To randomisert kontrollerte studier så på ernæringstiltak, begge amerikanske. Noen korttidseffekter på vektreduksjon ble observert.

Komplementære tiltak
Fem randomisert kontrollerte studier så på komplementære tiltak i rehabilitering av brystkreft. De fire tiltakene var avspenning, akupunktur, yoga og kunst-terapi. Få studier på hvert av tiltakene og ulike utfall gjorde det vanskelig å konkludere noe fra disse komplementære tiltakene.

Sammensatte tiltak
Tre randomisert kontrollerte studier så på sammensatte rehabiliteringstiltak. To studier så på psykososiale tiltak sammen med fysisk aktivitet etter primær kreftbehandling; disse viste motstridende resultater på livskvalitet. Den tredje studien så på diett og fysisk aktivitet under primær kreftbehandling som sammensatte tiltak og viste effekt på nivået av kroppsfett, men ikke på livskvalitet.

KONKLUSJON

Det er begrenset dokumentasjon om effekt av rehabilitering for brystkreftpasienter. Inkluderte studier er små og ulike, noe som gjorde det vanskelig å sammenstille resultatene. Det er derfor fortsatt lite kunnskap som kan veilede valg av tiltak for rehabilitering av brystkreftpasienter. Det at vi ikke kan dokumentere effekten av tiltakene betyr ikke at vi ikke tror mange kan ha nytte av dem, men vi mangler god forskning som viser dette.

Dokumentasjonen indikerer at:

- Fysisk aktivitet som rehabiliteringstiltak hos brystkreftpasienter *etter* kreftbehandling ser ut til å bedre livskvaliteten og redusere fatigue.
- Kognitiv terapi som rehabiliteringstiltak hos brystkreftpasienter *etter* kreftbehandling ser ut til å bedre livskvaliteten.
- Tidlig fysisk aktivitet etter kirurgi ser ikke ut til å ha innvirkning på utviklingen av lymfødem.

Det trengs mer forskning som kan belyse både innhold, tidspunkt i forløpet og lengde på disse tiltakene.

[1] Kognitiv terapi er en psykoterapiform, der grunntanken i terapien er at emosjoner og atferd i høy grad blir bestemt av hvordan mennesker strukturerer sin verden ved hjelp av tenkning (http://www.kognitiv.no/)

Enkeltstudier i rapporten viste lovende, men utilstrekkelig dokumentert effekt om viktige spørsmål i rehabiliteringen av brystkreftpasienter. Det er usikkert om manuell lymfedrenasje (MLD) gir noen ytterligere effekt ut over generell fysioterapi og kompresjonsbandasje. Det er mulig at multimodal tilnærming med lymfedrenasje, trening og kompresjonsbandasje er bedre enn fysioterapi alene. Det var for lite samsvar mellom studiene som så på andre psykososiale tiltak enn CBT til å kunne konkludere på effekt av tiltakene. Det var også for lite samsvar mellom studiene som omhandlet ernæring eller komplementære tiltak til å kunne vise effekt av rehabiliteringstiltakene.

Behov for videre forskning

Det er behov for randomiserte kontrollerte studier for å undersøke effekten både av enkelttiltak og sammensatte tiltak i rehabiliteringen under og etter primær brystkreftbehandling. Alle studier er gjennomført i en periode der mer mutilerende kirurgi og fjerning av lymfeknuter i armhulen var vanlig.

Få av de inkluderte studiene har pasienter som har gjennomgått de nye og lange behandlingsformene som gis til dagens brystkreftpasienter. Det er derfor viktig å kartlegge hvilket rehabiliteringstilbud som er nyttig for denne gruppen. Studiene bør også utformes for å finne undergrupper av brystkreftpasienter som spesielt trenger fysisk og/eller psykisk oppfølging.

Key messages

Rehabilitation of breast cancer patients

Breast cancer is the leading cause of cancer in women world wide. Although recent advances in therapy have improved survival rates, they are associated with significant side effects. The Central Norway Regional Health Authority requested that the Norwegian Knowledge Centre for the Health Services (NOKC) perform a systematic review (SR) on rehabilitation of breast cancer patients.
The aim of this overview is to explore literature to assess the efficacy of single treatments and combination of treatments (e.g. rehabilitation programs) with respect to improvements in physical functionality and psychological well-being.

Results: We included 46 randomized controlled trials of moderate or high quality. Seven studies addressed physiotherapy, 11 studies investigated different types of physical activity, 18 studies examined different psychosocial interventions. Two studies addressed nutrition, and five studies address complementary interventions as rehabilitation. Three studies evaluated a complex rehabilitation program. Due to variation in interventions and outcomes it was not possible to perform meta-analyses. The studies on physical activity after primary cancer treatment showed effect on improving quality of life (QoL) and reducing fatigue. It was difficult to conclude about the studies on physical activity during primary treatment due to inconsistency. Three studies showed that early physical activity was not associated with aggravated lymphedema. Four studies showed that cognitive behaviour therapy (CBT) intervention after primary cancer treatment will increase overall QoL. More documentation is needed for the interventions of physiotherapy, psychoeducation, social and emotional support, nutrition, complementary- and complex-interventions.

Conclusions:
There is limited documentation for the efficacy of different rehabilitation interventions for breast cancer patients. The documentation from this review indicates that physical activity after primary cancer treatment may increase QoL and reduce fatigue. Patients might also have some benefits on QoL from CBT interventions. More documentation is needed for the effect of interventions of physiotherapy, psychoeducation, and social and emotional support. There is still a critical need for further research focusing on rehabilitation interventions throughout and after treatment among breast cancer patients.

Executive summary

Rehabilitation of Breast Cancer Patients

BACKGROUND

Breast cancer is the leading cause of cancer in women worldwide. In 2007 in Norway 2761 new instances of breast cancer were diagnosed. In all 33889 women living in Norway have once been diagnosed with breast cancer. The breast cancer survival rate has increased, due to improvements in early diagnostic procedures followed by more tailored and/or more aggressive therapies. More patients are long-term survivors and live with the long-term side effects of the disease and treatment. Rehabilitation medicine is based on a holistic approach to medical care, using the combined expertise of multiple caregivers. Different rehabilitation programmes have been developed to treat the side effects occurring after the treatment of breast cancer. Although rehabilitation of breast cancer patients has been a priority during the last years, there still a need for evidence on which types of interventions are the most effectual.

MANDATE

The Central Norway Regional Health Authority requested the Norwegian Knowledge Centre for the Health Service (NOKC) to perform a systematic review (SR) on the rehabilitation of breast cancer patients.
To investigate whether such programmes are effective we need to know the following:

i) the efficacy of single treatments for rehabilitation of breast cancer patients
ii) whether the combination of different treatments, e.g. a rehabilitation programme, is better than a single treatment
iii) what type of combinations are most effective

METHOD

A group of experts in areas related both to generic medical rehabilitation and to more specific breast cancer treatment was organized to evaluate the existing literature. Systematic searches in relevant databases were carried out. These databases were: Cochrane Library, The Centre for Reviews and Dissemination databases, Medline, Embase, Cinahl, PsycINFO, AMED and PEDro until September 2008. Selections of relevant studies were conducted by two separate reviewers. Data were retrieved from included studies by one person and checked by another person.

Inclusion criteria:
Study design: Randomised controlled trials (RCTs).
Population: Female breast cancer patient who have undergone surgery, and may or

may not have undergone irradiation, chemotherapy, or hormonal therapy.
Intervention: Physical exercise, physiotherapy, psychosocial interventions, nutritional therapy, complementary therapy or complex interventions.
Outcomes: somatic, psychological, and social outcomes.

RESULTS

We summarised results from 46 RCTs (54 publications). Seven studies addressed physiotherapy; 11 studies (15 publications) evaluated different types of exercise; 18 studies (22 publications) evaluated different psychosocial interventions. Two studies evaluate nutrition and five studies evaluate different complementary interventions. Three studies evaluate a complex rehabilitation programme. Ten of the included studies were of high quality (most on physical activity), while the remaining 36 studies were of moderate quality. Due to variations in intervention and outcome measurements it was not possible to perform meta-analyses. We divided the studies according to when the intervention was given, either during primary cancer treatment (chemotherapy or radio therapy) or after primary cancer treatment (could include hormonal therapy).

Physiotherapy

Breast cancer patients received physiotherapy for treating lymphedema and to improve shoulder motility. Three studies evaluated manual lymph drainage (MLD) as an additional treatment for lymphedema; the studies do not show significant benefit of MLD. One study showed a decrease in lymphedema with complex decongestive therapy (lymph drainage, compression bandage, evaluation, medical exercise and skin care) compared to standard physiotherapy. Three studies showed that effect of physiotherapy do not seem to be influenced by the timing of interventions. Six studies are done after Axillary lymph node dissection (ALND) and not by sentinel lymph node biopsy (SLNB), while one study was done in a mixed population with both ALND and SLNB surgery.

Physical activity

Quality of life (QoL) is an outcome in ten studies. Four studies showed that physical activity after primary cancer treatment may improve QoL (short term). Three studies showed that physical activity after primary treatment may reduce fatigue. A physical activity intervention during primary cancer treatment showed varied result, and more studies are needed in order to give any conclusion of effect. We did not find any significant effect on mood outcomes after physical activity interventions. Three studies showed that early physical activity was not associated with aggravated lymphedema (including weight training).

Psychosocial interventions

We included 18 randomised controlled trials under the heading psychosocial interventions. We divided the psychosocial interventions into three categories; psychoeducation[2], cognitive behavioural therapy[3], and social and emotional support

[2] Psychoeducation; is education about a certain situation or condition that causes psychological stress.

interventions. Six RCTs examined the effect of psychoeducational information. There were inconsistencies from the interventions examined. Seven RCTs examined the effect of Cognitive Behavioral Therapy (CBT); one of these studies was of high quality. Four studies found an improvement in QoL when the intervention was given after primary cancer treatment. There were inconsistencies from the interventions examined the effect of CBT during cancer treatment. Five studies have addressed social and emotional support interventions during breast cancer treatment, but the impact of these interventions on patients' quality of life, wellbeing, and functioning is still unclear.

Nutrition

We identified two randomized controlled trials on nutritional interventions for breast cancer survivors after primary cancer treatment. The effect of nutritional intervention after cancer treatment is unclear.

Complementary interventions

Five randomized controlled trials examined the effect of complementary interventions in the rehabilitation of breast cancer patients. Altogether these results suggest that a complementary intervention during cancer treatment may have some effect on moods. Outcomes were addressed only in a few studies, so it was difficult to conclude about the effect.

Complex intervention

Three randomised controlled trials investigated the effect of a complex rehabilitation programme for breast cancer patients. These three studies showed different results. The results therefore indicate that a complex intervention after cancer treatment still has unclear effect on QoL and moods. This was addressed in three studies with different results.

CONCLUSION

Although these studies report some positive outcomes, due to the small number of studies and the heterogeneity of interventions, it is not possible to draw generic inferences about the key elements of rehabilitation interventions of breast cancer patients. These interventions could still be useful for breast cancer patients, but we lack high quality research on the issue.

However, this review does underline some promising results.

- There is some evidence that physical activity after breast cancer treatment improved quality of life and reduced fatigue.
- There is some evidence that CBT intervention after breast cancer treatment increased overall QoL.

[3] Cognitive-behavioral therapy is a form of psychotherapy that emphasizes the important role of thinking in how we feel and what we do.

- There are some promising results that physical activity is not associated with aggravated lymphedema.

Further research is needed on the time, mode and intensity on these interventions. Single studies in this review are showing promising, but insufficiently documented effects on important questions in rehabilitation of breast cancer patients. There is insufficient evidence to show whether physiotherapy or MLD was more beneficial than standard care for lymphedema or shoulder function. There is insufficient evidence to define optimal psychoeducational or social and emotional support interventions from this review. There is also insufficient evidence from these studies to determine the most beneficial nutrition or complementary interventions.

FURTHER RESEARCH IS NEEDED

There is need for further research on the effect of rehabilitation interventions among breast cancer patients. Few of the studies in the present review include patients going through new long-term medical treatments regiments for breast cancer; new studies should address this. Additional research might profitably assess whether some interventions are more effective for certain subgroups of breast cancer patients.

CONTACT INFORMATION

The Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to provide information leading to good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy and no responsibility to implement policies.

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Abbreviations

ALND - Axillary lymph node dissection
SLNB – Sentinental lymph node biopsy
CBT – Cognitive behavioral therapy
MLD - Manual lymph drainage
QoL – Quality of life

Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk våren 2005 en forespørsel fra lederen i en arbeidsgruppe i Helse Midt-Norge om å bistå i utredningen av faggrunnlaget for rehabilitering av brystkreftpasienter. Bakgrunnen for forespørselen var at Helse Midt-Norge ønsket å bygge opp et rehabiliteringssenter som i størst mulig grad skal benytte metoder som er dokumentert virksomme.

Kunnskapssenteret overtok det overordnede administrative ansvaret for utredningsarbeidet og supplerte arbeidsgruppen med ytterligere tre representanter. Forsker Ida-Kristin Ø Elvsaas var prosjektleder ved oppstart av prosjektet, og Lene Kristine Juvet har vært prosjektleder ved ferdigstillelse av dette arbeidet. Forskningsbibliotekar Sari Ormstad har utført de systematiske søkene som ligger til grunn for rapporten. Geir Smedslund vært behjelpelig med de statistiske utregningene.

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Gruppen har bestått av spesialister i fysikalsk medisin og rehabilitering, onkologi, allmennmedisin, psykiatri, treningsfysiologi og fysioterapi. Kunnskapssenteret har i tillegg bidratt med kompetanse innen ernæring.

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Problem formulation

Different treatment- and rehabilitation programmes for breast cancer patients have been developed. It is therefore paramount that rehabilitation teams have an extensive understanding of the effectiveness and safety of interventions to in the best possible way initiate and complete the rehabilitation process.

To investigate the effects of rehabilitation programmes we need to know the following:

iv) the effect of single treatment modalities used in rehabilitation of breast cancer patients,
v) the effect of combining different treatments, e.g. a rehabilitation programme, compared to single treatments, and
vi) what type of combinations are most effective.

Therefore, the aim of this report is to systematically review the literature regarding the effects of rehabilitation of breast cancer patients with respect to the following interventions and outcomes**:**

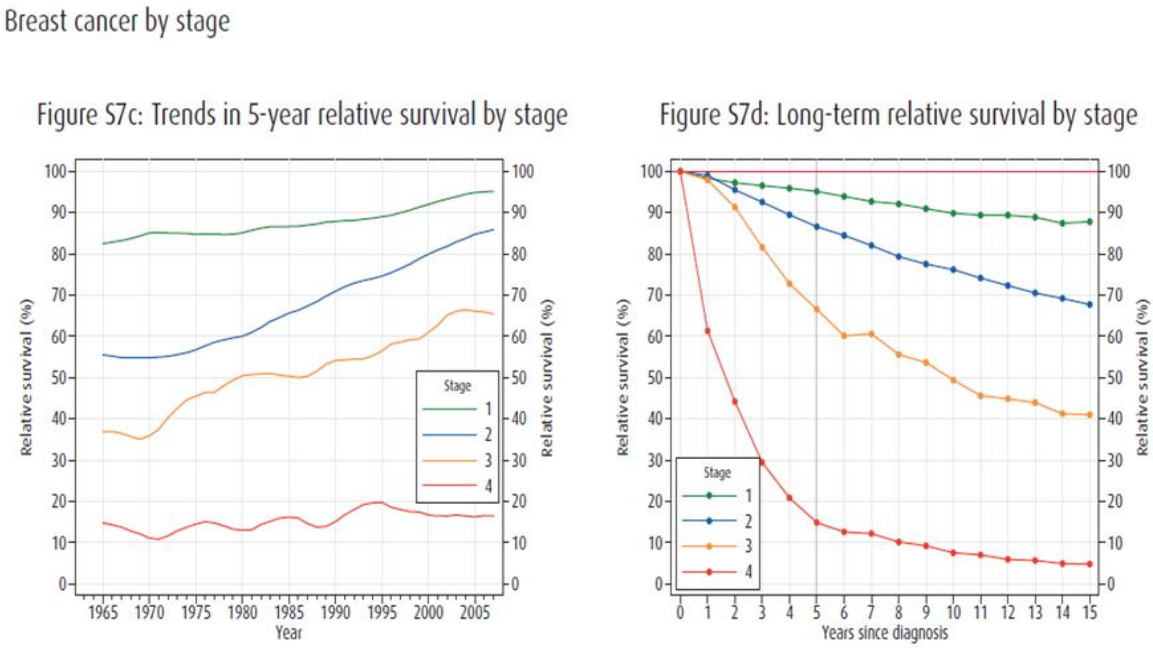
Interventions:
- Physical exercise
- Physiotherapy
- Psychosocial interventions
- Nutrition
- Complementary treatment
- Complex interventions

Outcomes:
- Somatic outcomes
- Psychological outcomes
- Social outcomes

Background

Breast cancer is the most common cancer in women worldwide; in 2002 an estimated 1.15 million new cases of invasive breast cancer were diagnosed (1). In Norway 2761 new cases were diagnosed in women in 2007 (2), and the probability of an arbitrary woman being diagnosed with breast cancer during her lifetime is about 10-13% . In Norway by the end of 2007, a total of 33 889 women were alive that had ever been diagnosed with breast cancer (2); among these women, 38% were diagnosed more than 10 years ago. The 5-year relative survival rate for breast cancer patients in Norway is 86% (1998-2002) (figure 1).

Figure 1. Trends in 5-year survival of breast cancer patients in Norway (2).



Because of its high incidence and relatively good prognosis, breast cancer is the most prevalent cancer among women in the world and in Norway today. However, breast cancer is still the leading cause of cancer-related death among women in many developed countries, and is the most common cause of death of women in Norway aged 40–60 years (2). Breast cancer mortality rates have declined, possibly due to earlier detection, improvements in surgical resection, radiation, and systemic therapies (3). Thus, as more patients survive breast cancer, the number of women living with long-term side effects also increases (3).

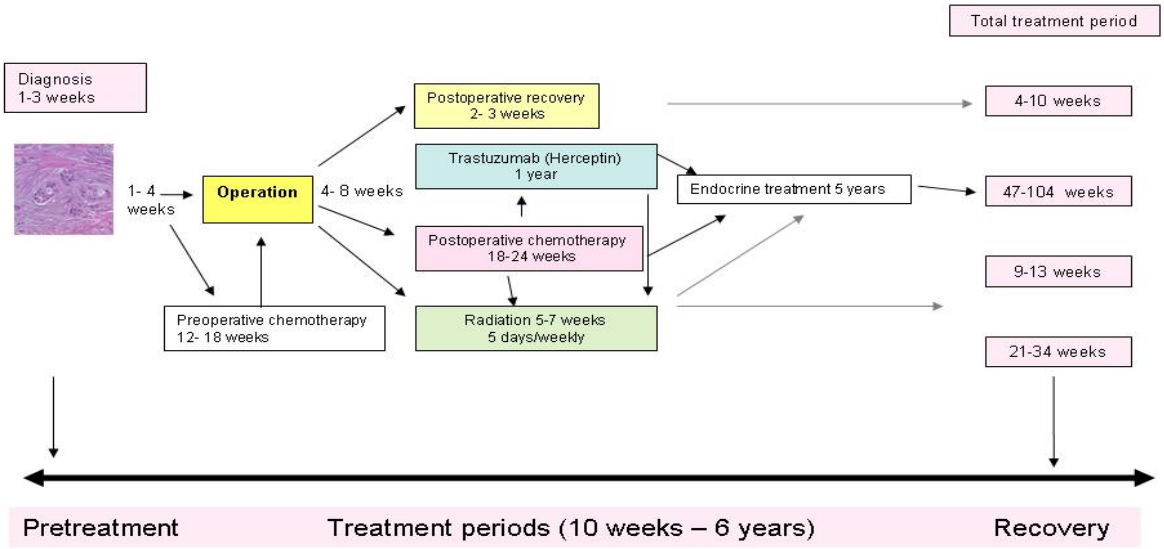
CLINICAL PRACTICE

Today, three screening tests are routinely in use for detection of breast cancer: mammography, physical breast exam, and breast self-exam. When a breast tumor is detected, a more detailed examination can be done (mammogram and/or ultrasound and/or MRI (Magnetic Resonance Imaging). The final diagnosis is performed by microscopic examination of fine-needle aspirations (cytology) or a biopsy (histology) (4). Even though the routines related to breast cancer diagnosis are efficient in Norway, patients may have to wait several weeks before treatment. This delay waiting period may impose additional psychological challenges for the woman.

Treatment options of breast cancer patients and morbidities.

Breast cancer treatment involves multiple medical disciplines. The treatment depends on the patients age, menopausal status as well as disease stage and pathological features; type, tumour grade, multifocal receptor status, and family predisposition (4). Disease stage is determined by tumour size, the number and location of lymph nodes involved, and the presence or absence of distant metastatic disease. The treatment consists of local treatments such as surgery and radiotherapy, systemic treatment such as chemo- and hormone therapy, and monoclonal antibodies (5;6) (figure 2).

Figure 2. Time period from time of verification of breast cancer and throughout treatment period.



Surgery

Surgical procedures have been modified during the last decades (7). With *radical mastectomy* (Halsteds method), major side effects occurred (extensive and frequent arm and shoulder morbidities). It was therefore replaced by m*odified radical mastectomy* in the 1970-80's. Postsurgical side effects were reduced without increase in local relapses or decreased survival rates. Breast conserving treatment was then developed. Randomized studies showed that only removing the tumour (lumpectomy) and a rim of normal surrounding breast tissue were as safe as modified radical treatment, if the patient was treated with postoperative radiotherapy to the whole breast (8;9).

Axillary lymph node dissection (ALND) is now done in less than 50 % of the patients due to sentinel lymph node biopsy (SLNB) (10;11). The status of the axilla is one of the most important prognostic factors in breast cancer. Subsequent decisions on supplementary treatment depend on how much lymph nodes are affected as well as other patient and tumour characteristics.

Mastectomy is still recommended for patients with large tumours and for patients when irradiation is contraindicated. Other factors may need to be taken into account as well when consider mastectomy (e.g. genetic factors and high risk of relapse) (4). For these patients, breast reconstruction can be performed concomitantly with mastectomy or at a later time.

Irradiation

The advantage of breast conserving surgery is offset by the need for several weeks of radiation therapy to prevent local recurrence (12). The extent of irradiation depends on the type of surgery and involvement of axillary lymph nodes (4). After mastectomy the thoracic wall, the lymph nodes in axilla and fossa supraclava are the target of radiation (12), and after lumpectomia the whole breast is the target (13). All patients will receive daily fractions for 5-7 weeks.

Systemic (neo) adjuvant treatment

Systemic therapy is indicated for patients with high and intermediate risk of cancer recurrence. In most cases systemic treatment is given shortly after surgery (adjuvant), e.g. endocrine- and/or chemotherapy; some patients also receive monoclonal antibody therapy, e.g. trastuzumab (Herceptin). In some cases, chemotherapy is given before surgery (neoadjuvant) to try to shrink the tumour (down-stage) to make surgical removal possible. The type of chemotherapy or monoclonal antibody treatment is selected based on the type, size, and grade of the tumour and the molecular characteristics and involvement of lymph nodes in the axilla. Adjuvant or neoadjuvant chemotherapy in Norway is given with a combination of an anthracycline-based regimen, F(5-fluorouracil)E (Epirubicin) C (Cyklophosphamid), 6 courses with 3 week intervals. Other combinations of chemotherapies can be given depending on tumour characteristics. Endocrine therapy is only given to patients after histologically proven estrogen (ER) and/or progesterone (PgR) receptors. Various hormone modulating drugs may be used for 5 years to prevent estrogen from further stimulating possible remaining tumor cells in patients. The endocrine treatment does not start until after the chemotherapy is finished due to a slight risk for thrombosis and other possible interactions (4) (see fig.1). Only patients with histological proven HER-2 positive tumours are candidates for the monoclonal antibody trastuzumab (Herceptin) for a period of one year (4;14) (fig. 2).

Side effects of regular treatment

Several health problems/side effects may develop following breast cancer diagnosis and treatment (presented in Table 1). Side effects can follow surgery, either ALND or SLNB, but are less common and often less severe following SLNB (10). Common side effects are temporary or permanent numbness of the skin on the inside of the upper arm, temporary or long-term limitation of arm and shoulder movements, and swelling of the breast and arm called lymphedema. Lymphedema is the most significant of these side effects and may develop into a permanent health problem. Significant lymphedema is reported in 10-50 % of women who have had axillary lymph node dissection and approximately 5-20 % of women who have had sentinel lymph node biopsy. Lymphedema may result in cosmetic deformity, loss of functionality, physical discomfort, recurrent episodes of erysipelas, and psychological distress. Pain is reported by 12 - 51% of patients 1 year after treatment (15), most frequently due to nerve injuries during surgery; the treatment is often pharmacological.

Early side effects due to radiation can include irritation, rubor in the skin during radiation treatment, and tiredness resulting in reduced physical activity. The majority of skin reactions disappear a few weeks after treatment is completed. Late side ef-

fects can include slightly darker skin in the treated area and continued sensitivity to sun exposure. Later development of teleangectasis, skin- and lung fibrosis may occur. If the axilla has been irradiated, there is an increased risk of reduced mobility of the shoulder, lymhedema, especially after ALND and when several lymph nodes have been affected (16). Pulmonary sequela as radiation pneumonitis (incidence 2-29%) is rarely of clinical consequence.

Side effects of chemotherapy shows individual variation and is also depending on the type of drug used (17). Common acute side effects are: alopecia (hair loss), nausea, fatigue, increased risk of weight gain, increased risk of infection, and temporary effects on bone marrow with lower blood counts, especially white blood cells (leucocytes).

The most common side effect of monoclonal antibodies (trastuzumab) is influenza-like symptoms, but more important are the reported cardiotoxic effects (4;14).

The most common side effect of endocrine therapy is weight gain, symptoms of menopause, hot flashes, and vaginal dryness. One drug (Tamoxifen) has two rare, but more serious side effects; a slightly increased risk of developing cancer of the uterus (endometrial cancer) and a slightly increased risk of developing blood clots (thrombosis) (18). Some drugs may cause an increased risk of osteoporosis and bone fractures (18).

Cardiac toxicity is a concern in breast cancer survivors (17). There is known for a long time that anthracyclines cause acute and chronic cardiotoxicity. However, the cardiotoxic effects of radiation therapy, hormonal therapy (including tamoxifen and the aromatase inhibitors), and chemotherapy with taxanes and trastuzumab treatment have emerged more recently (4;14;17). A single breast cancer patient may receive anthracyclines, trastuzumab and radiotherapy before commencing hormonal therapy (17).

One major consequence of breast cancer and associated treatments is weight gain. Physical inactivity has also been observed as a consequence of various breast cancer treatment modalities (3). There is some studies that show an association between weight gain and increased breast cancer recurrence and mortality (19;20).

Common long term side effects and consequences after breast cancer are listed in table 1.

Table 1. Long term side effects and consequences after breast cancer treatment

Problem type	Side effects related to the disease	Side effects related to treatments	Type of treatment
Fatigue Depression	X	x	Chemotherapy Endocrine therapy Irradiation
Lymphedema	X	x	Surgery Irradiation
Shoulder movement impairments	X	x	Surgery, Axillary dissection Irradiation
Weight gain		x	Chemotherapy Endocrine therapy Hormone therapy
Cardio-respiratory		x	Chemotherapy Irradiation Monoclonal antibodies
Skeletal Bone marrow Osteoporosis		x	Chemotherapy Endocrine therapy (Aromatase Inhibitors)
Pain	x	x	Surgery Chemotherapy
Slightly increased risk of thrombosis (blood clot)		x	Chemotherapy Endocrine therapy

REHABILITATION

Rehabilitation, in general, is the process of helping a person to reach the fullest physical, psychological, and social potential with regard to his or her physiological or anatomic impairments, environmental limitations, desires, and life span (21). Patients, their families, and their rehabilitation teams work together to set realistic goals and to develop and carry out plans to reach optimal functionality.

Rehabilitation medicine is based on a holistic and comprehensive approach to medical care, making use of the combined expertise of multiple caregivers. A health-care team is defined as a group of health-care professionals from different disciplines who share common values and objectives. Assessment, treatment planning, and therapy are optimally provided by rehabilitation professionals' involved in occupational therapy, physical therapy, psychology and neuropsychology, cognitive therapy, recreational therapy, fitness training, rehabilitation nursing, social work, dietary science, and case management. The team involved with a particular patient is largely determined by the needs of the patient, the nature of the disorder, and the structure of the setting in which rehabilitation is being conducted.

Treatment plans or rehabilitation plans are generated from goals that arise from the clinical evaluation of the patient. This plan is a tool that patients, families, and caregivers or other treating professionals examine for prognosis and expectations. The

specific strategies can be directed by the physician, other rehabilitation specialists, or, most ideally, mutually derived by the patient and the rehabilitation team through the interdisciplinary process.

Rehabilitation of breast cancer patients

Definition of cancer rehabilitation

Cancer rehabilitation is a process that helps the patient and the next of kin to maintain best possible physical, social, psychological, and occupational functionality with the limitations that the illness and treatment create (22-24). An understanding of various breast cancer treatment regimens and their possible side effects as well as the duration is important. In addition, it is paramount that the rehabilitation teams have profound knowledge about all therapies to apply and the specific interventions available to each treatment regimens that might accomplish the goals in a rehabilitation process.

Optimal recovery and prevention of treatment complications are the main goals of rehabilitation. Rehabilitation should lead to optimal physical and psychological recovery.

Rehabilitation interventions and endpoints

Rehabilitation is a process in which different caregivers use a combination of their specific treatment modalities. In the following paragraphs we will therefore describe the most common modalities.

Physiotherapy

Physiotherapy for breast cancer patients is based on the same principles as for other patient groups, although they have some special problems related to their cancer and its treatment. Physiotherapy uses both passive and active stimuli in prevention, treatment and rehabilitation. It involves careful examination of the musculoskeletal system and the application of knowledge, stimuli, and skills.

Breast cancer treatment can result in pulmonary and upper extremity morbidities with early or late manifestations. Impaired shoulder function and development of arm lymphedema, i.e. an arm volume difference between the arms of >150 ml or circumferential arm difference of >2 cm, are common side effect of treatment for early breast cancer. Therefore, complications following cancer treatment, such as lymphedema, scar adherence, pulmonary complications, range of motion, and muscle strength, are of major importance.

Water displacement, circumference measurement, and tissue tonometry are important methods used to evaluate the status of lymphedemous limbs. Goniometers and dynanometers are used to measure the range of motion and muscular force/endurance, respectively.

Relatively little is known about possible benefits of physiotherapy on shoulder-/arm-, muscular-, and cardiovascular function in the postoperative phase.

A systematic review of physical therapy interventions for lymphedema highlighted the need for studies with high methodological quality to establish evidence on the efficacy of methods such as manual lymph drainage (25).

Physical activity

Physical activity is defined as any activity resulting in energy expenditure above resting level (26). *Exercise and training* is defined as leisure-time physical activity that is performed repeatedly over an extended period of time with the intent to improve performance, physical and/or physiological fitness, and health (26).

Today, physical activity is usually an integrated part of the rehabilitation process for various chronic diseases. Studies on possible effects of physical activity on breast cancer patients and survivors are relatively new. The first studies were published in the 1970's and 1980's (27).

In physical activity studies there are major variations in the types and lengths of interventions and in assessment measures and outcome measures. The interventions may include a variety of supervised or home based exercise programmes. A variety of different endpoints such as well-being, quality of life, weight gain, recurrence, and mortality are used to assess the effects of physical activity interventions. The large number of women surviving many years post breast cancer diagnosis has put forward and interest in studying long-term effects of breast cancer and its treatment regiments on quality of life. Quality of life outcomes include a wide range of measures of physical, functional, and emotional well-being, as well as measures of physical performance.

Important factors in choosing an outcome measure are test-retest reliability, longitudinal validity, sensitivity to change, and interpretability of the outcome to measure the effect of a physical activity intervention. In assessment of physical fitness, it is important to identify whether the information relates to performance and/or health-related fitness. In general, effects of physical activity are documented using different endpoints principally divided into those endpoints that can be measured objectively (such as aerobic capacity, muscle strength, balance) and those subjectively measured in self-reported questionnaires (measuring different dimensions of health-related quality of life, i.e. physical and social functioning or symptoms like fatigue, pain, anxiety and depression). In breast cancer rehabilitation commonly used inventories of quality of life in physical activity is "functional assessment of cancer therapy – breast cancer" (FACT-B).

Psychosocial interventions

All breast cancer patients' deal with the existential, emotional, social, and psychological problems related to their situations. Approximately 50% of all breast cancer patients suffer from emotional distress (28), which includes symptoms that range

from sadness and worry to disabling depression and anxiety (29). This is the rationale for the use of psychosocial interventions in rehabilitation of breast cancer patients. The most frequent psychosocial interventions in breast cancer rehabilitation are: (a) social support (30-33), (b) psychoeducation of patients with distress and aversive symptoms (34), (c) emotional support (35) and (d) cognitive behavioral therapy (CBT) (36).

Cognitive behavioural therapy (CBT) is a form of psychotherapy where cognitive and behavioural methods are used by themselves or in combination. The therapy may be individual or in groups, face to face or by phone. Individual face to face is far most common.

A wide range of endpoints are normally used to evaluate signs and symptoms of distress and include emotional, cognitive, physiological and behavioral aspects. In breast cancer rehabilitation commonly used inventories of distress in psychosocial interventions are: i) "Profile of Mood States" (POMS), ii) "Beck Depression Inventory" (BDI), iii) Spielberger's State-Trait Anxiety Inventory (STAI), iv) Quality of life questionnaire EORTC QLQ-C30, and v) "Hospital Anxiety and Depression Scale (HADS) (36).

Nutrition and body composition

The way to achieve a healthy body weight is to balance energy intake (food and drink) with energy used (physical activity). The healthiest way to reduce calories is to reduce intake of added sugars, saturated and trans-fats, and alcohol, which provide a lot of calories, but few or no essential nutrients. Calorie intake can also be reduced by decreasing the size of food portions and limiting the intake of foods and drinks that are high in calories, fat, and/or refined sugars, and which provide few nutrients.

Weight gain and body composition changes are common after breast cancer diagnosis (37). Women who are overweight or obese at the time of diagnosis or who gain weight following diagnosis are at higher risk of adverse clinical outcomes. Unhealthy weight conditions, compounded with or caused by weight gain after diagnosis, are a considerable challenging for women with breast cancer during and after treatment. Overweight or obesity is an established negative prognostic factor in breast cancer (38). The prognosis after onset of breast cancer is poorer in obese women who have gained weight after the diagnosis and treatment of breast cancer, compared with women with normal weight. Co-morbidities associated with obesity, including cardiovascular disease (CVD) and diabetes, may negatively impact quality of life and survival in this population. Despite the prevalence of weight gain in women with breast cancer and its adverse effects, little research has been done on preventive and therapeutic interventions targeting reduction of weight and/or body fat (37). Proactive nutritional interventions should ideally form an integral part of cancer therapy with the aim of improving clinical outcomes and quality of life (3).

Food-based randomised controlled trials are defined as RCTs using interventions that offer advice on healthy foods or specific diets such as high fibre diets and/or weight-loss programmes. In general, the effects of diets are documented by using different outcomes which are principally divided into those outcomes that can be measured objectively and those measured subjectively.

Complementary interventions

A substantial number of breast cancer patients are using complementary and alternative medicine in parallel with their conventional treatments. Complementary refers to methods that are used to complement, or add to, conventional cancer medicine (39;40). Complementary methods are not given to cure disease; rather they may help control symptoms and improve well-being. Some of the methods, such as massage therapy, yoga and meditation that are categorised as complementary have actually been referred to as supportive in the past (39;40).

A wide range of endpoints are normally used to evaluate signs and symptoms of complementary treatments.

Method

This review has been developed through collaboration of a multidisciplinary group of health care professionals with experience in the fields of oncology, physical medicine, rehabilitation, physiotherapy, and psychiatry together with researchers from the Norwegian Knowledge Centre for the Health Services (NOKC). The work was carried out according to the NOKC handbook for systematic reviews (41).

IDENTIFICATION OF LITERATURE

Criteria for inclusion and exclusion were established through discussions in the multidisciplinary group guided by a research librarian and HTA methodologists. Articles were selected for inclusion according to the following criteria:

Inclusion criteria

Population:

- female breast cancer patients who
    - have undergone surgery
    - may be treated with one or more of the following:
        - radiation therapy
        - chemotherapy
        - hormonal therapy

Intervention:

- physical exercise (endurance, strength, mobility exercises, and coordination)
- physiotherapy (active or passive interventions)
- nutrition
- psychosocial interventions
    - social support, group therapy
    - management
        - of the illness
        - of the treatment
    - psychoeducation
    - cognitive and/or behavioral therapy

    - other psychotherapy
- complementary therapy
- complex interventions

Outcome:

- somatic outcome (lympedema, shoulder function, fatigue, body weight, BMI, hot flashes)
- psychological outcome (QoL, mood, anxiety, depression, cancer related stress)
- social outcome (coping)

Study design:

- randomized controlled trials (RCT)

Exclusion criteria

- studies with low quality
- studies with less than 20 participants in each group
- studies on patients with metastatic cancer
- studies that included other cancer types, where data were not presented separately for breast cancer patients
- studies that only report recurrence and survival as outcomes

Literature search

Systematic searches in relevant databases were carried out (up to September 2008). These were:

- Cochrane Library
- The Centre for Reviews and Dissemination data bases
- Medline
- Embase
- Cinahl
- PsycINFO
- AMED
- PEDro

Selection of articles

Selections of relevant studies were conducted by two reviewers working separately. First all abstracts identified in the search were read by two reviewers, and the irrelevant abstracts were excluded. Then the articles in their entirety were evaluated according to inclusion and exclusion criteria (attachment 3), and studies that did not meet the inclusion criteria were excluded. Disagreements were resolved by consensus or a third reviewer.

Data extraction and assessment of quality

Data were retrieved from included studies by one person and checked by another person in the working group. Details of participants and settings were collected and presented in the table of 'Characteristics of included studies' (appendix 5). Methodological quality was assessed by two reviewers using our checklist for randomized controlled trials (41). Studies were given a score as high, moderate or low quality (table 2).

Table 2. Methodological quality ranging

Ranging	Criteria
High	Applies if all or most criteria from the checklist are fulfilled; where criteria are not fulfilled, the unfulfilled criteria are considered unlikely to significantly alter the conclusions of the study or review.
Moderate	Applies if some of the criteria from the checklist are fulfilled; where criteria are not fulfilled or are not adequately described, the unfulfilled criteria are considered unlikely to significantly alter the conclusions of the study or review.
Low	Applies if few or no criteria from the checklist are fulfilled; where criteria are not fulfilled or are not adequately described, the conclusions of the study or review are considered likely or very likely to alter the conclusions of the study or review.

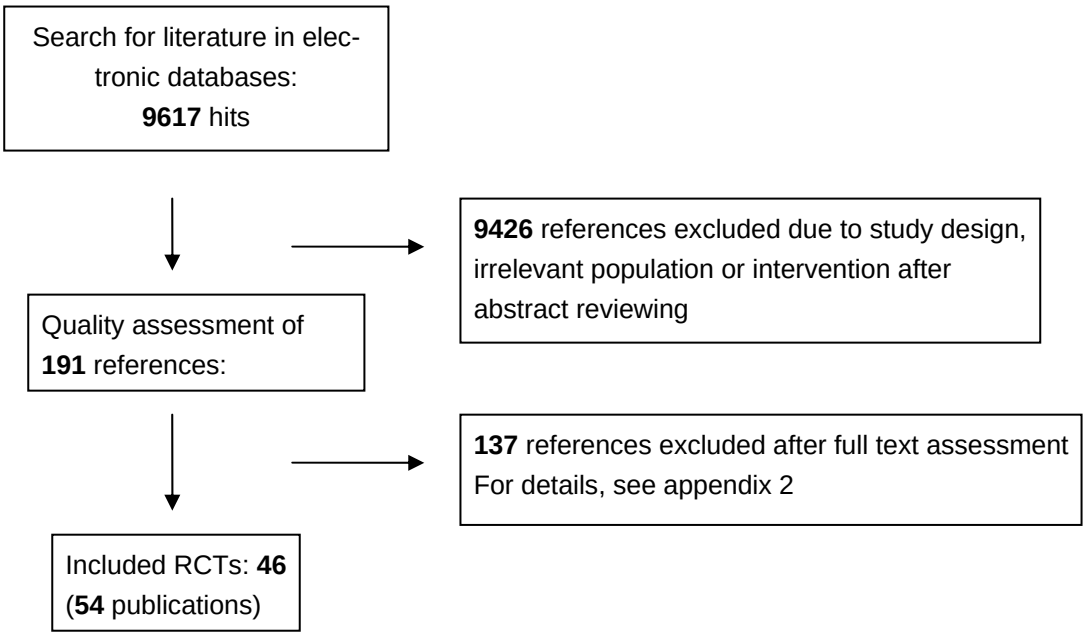
Analyses

Due to variations in study populations, intervention, and outcome it was not possible to perform meta-analysis. Thus, data from the included studies are presented in tables and qualitatively summarized.

Results

The titles and abstracts of a total of 9617 articles were screened for relevance (see inclusion criteria). The majority of these articles did not fulfil the inclusion criteria, and some were duplicates. 9427 references were excluded after abstract reviewing due to irrelevant study design, population or intervention. 190 articles were considered relevant and included for quality assessment. We further excluded 136 articles due to poor study quality or failure to fulfil the inclusion criteria. Only studies with high or moderate methodological quality were included in the final summary, i.e. 46 randomized controlled trials reported in 54 publications (figure 3).

Figure 3. Flow diagram over identified literature



INCLUDED STUDIES

We included 46 randomized controlled trials (54 publications) including 5645 patients in the knowledge base for this report. Seven studies addressed physiotherapy (42-48), 11 studies (15 publications) evaluated different types of exercise (49-63), 17 studies (21 publications) evaluated different psychosocial interventions (64-86) . Two studies addressed nutrition (87;88), and five studies addressed complementary interventions (89-93). Three studies evaluated complex rehabilitation programmes with more than one of these interventions (94-96). The time since diagnosis varied widely between studies and in some cases within studies. Stage of treatment also varied between the included studies. We divided the studies according to when the intervention was given, either during primary cancer treatment (chemotherapy or radio therapy) or after primary cancer treatment (could include hormonal therapy).

Methodological quality of included studies.

The methodological quality of included studies was assessed using the checklist for randomized controlled trials (attachment 4). The result of the quality evaluation is shown in table 3. Of the included studies, 10 were deemed to be of high quality, and 35 of moderate quality (table 3). In most quality rating scales blinding is evaluated on several levels, such as blinding of patients, care providers and outcome assessors. These scales are often used to test the quality of placebo-controlled medication studies. However, the nature of RCTs testing interventions that are covered in this review is different. In these trials it is nearly impossible to blind the patients to the intervention they were assigned to. There is also difficult to blind the care providers to the intervention they are giving to the patients. Thus, the studies would still get high methodological quality if there are limitations on the blinding of patient and care providers. The most common methodological shortcomings were failure or inadequate methods to blind the outcome assessment, and inadequate concealment of allocation in studies with moderate quality An intention to treat (ITT) analysis was done in 18 of 46 studies (table 3, criteria 8). The failure of these studies to follow all patients was generally modest, with an average loss to follow up of 14 % overall and ranging from 0% to 39% (Appendix 5).

Table 3: Methodological quality assessment: Randomized controlled trials (publications) on the effectiveness of rehabilitation intervention for breast cancer patients

Study			Criteria*											Total /11	Quality
			1	2	3	4	5	6	7	8	9	10	11		
Physiotherapy	During treatment	Cinar et al. 2008 (42)	+	?	+	+	-	+	-	?	+	+	+	7	Moderate
		Lee et al. 2007 (43)	+	+	-	+	-	-	+	+	+	+	+	8	Moderate
		Lauridsen et al. 2005 (47)	+	+	?	+	-	-	+	-	+	+	+	7	Moderate
		Jansen et al. 1990 (46)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
	After treatment	Didem et al. 2005 (45)	+	+	+	+	+	-	-	?	+	+	+	8	Moderate
		Mc Neely et al. 2004 (48)	+	+	+	+	-	-	+	?	+	+	+	8	Moderate
		Andersen et al. 2000 (44)	+	?	?	+	-	-	-	+	+	+	+	6	Moderate
Physical activity	During treatment	Mutrie et al. 2007 (56)	+	+	+	+	-	-	+	+	+	+	+	9	High
		Courneya et al. 2007a, 2007b(51;52)	+	+	+	+	-	-	-	+	+	+	+	8	High
		Mock et al. 2005 (55)	+	+	+	+	-	-	-	+	+	+	+	8	High
		Segal et al., 2001 (63)	+	+	+	+	-	-	+	+	+	+	+	9	High
	After treatment	Milne et al. 2008 (54)	+	+	+	+	-	-	-	+	+	+	+	8	High
		Vallance et al. 2008, 2007 (57;58)	+	+	+	+	-	-	-	+	+	+	+	8	High
		Daley et al. 2007 (53)	+	+	+	+	+	-	+	+	+	+	+	10	High
		Courneya et al. 2003 (50)	+	+	+	+	-	+	+	+	+	+	+	10	High
		Basen-Engquist et al 2006 (49)	+	?	+	+	-	-	-	+	+	+	+	7	Moderate
		Ahmed et al, 2006, Ohira et al 2006, Schmitz et al. 2005 (59;60;62)	+	?	+	+	-	-	+	-	+	+	+	7	Moderate
		Pinto et al. 2005 (61)	+	+	-	+	-	-	-	+	+	+	+	7	Moderate
Psycho education	During treatment	Sandgren et al. 2007, 2003 (72;81)	+	?	?	+	-	-	-	?	+	+	+	5	Moderate
		Coleman et al. 2005 (74)	+	+	-	+	-	+	-	-	+	+	+	7	Moderate
		Yates et al. 2005 (85)	+	+	+	+	-	-	-	-	+	+	+	7	Moderate
	After treatment	Meneses et al. 2007 (71)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
		Owen et al. 2005 (80)	+	+	-	+	-	-	-	?	+	+	+	6	Moderate
		Stanton et al. 2005 (84)	+	+	+	+	-	-	+	-	+	+	+	8	Moderate
CBT	During treatment	Kissane et al 2003 (78)	+	+	+	+	-	-	-	+	+	+	+	8	High
		Cohen et al. 2007 (69)	+	?	+	+	-	-	+	?	+	+	+	7	Moderate
		Antoni et al. 2006a, 2006b (65;66)	+	?	+	+	-	-	+	+	+	+	+	8	Moderate
	After treatment	Dirksen et al. 2007 (70)	+	+	+	+	-	-	-	-	+	+	+	7	Moderate
		Savard et al. 2005 (82)	+	?	-	+	-	-	-	+	+	+	+	6	Moderate

Study			Criteria*											To-tal /11	Quality
			1	2	3	4	5	6	7	8	9	10	11		
		Simpson et al. 2002, 2001 (83;86)	+	?	+	+	-	+	-	?	+	+	+	7	Moderate
		Edelman et al. 1999 (75)	+	+	+	+	-	-	-	?	+	+	+	7	Moderate
Social and emotional support	During treat-ment	Classen et al. 2007 (68)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
		Arving et al. 2007 (67)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
		Andersen et al. 2007, 2004 (64;73)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
		Manne et al. 2005 (79)	+	?	+	+	-	-	-	+	+	+	+	7	Moderate
	After treatment	Fukui et al. 2000 (76)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate
Nutr ition	After treatment	Saquib et al. 2008 (87)	+	?	+	+	-	-	-	-	+	+	+	6	Moderate
		Thomson et al. 2005 (88)	+	+	+	+	-	-	-	-	+	+	+	7	Moderate
Complementary interventions	During treat-ment	Deng et al. 2007 (90)	+	+	+	+	+	-	+	+	+	+	+	10	High
		Banerjee et al. 2007 (89)	+	+	+	+	-	-	-	?	+	+	+	7	Moderate
		Walker et a. 1999 (93)	+	?	?	+	-	-	-	+	+	+	+	6	Moderate
	After treatment	Fenlon et al. 2008 (91)	+	+	+	+	-	-	-	-	+	+	+	7	Moderate
		Öster et al. 2006 (92)	+	+	?	+	-	-	-	-	+	+	+	6	Moderate
Complex In-terventions	During treatment	Denmark-Wahnefried et al. 2008 (94)	+	?	+	+	-	-	-	-	+	+	+	6	Moderate
	After treatment	Hartmann et al. 2007 (95)	+	-	+	+	-	-	-	-	+	+	+	6	Moderate
		Cho et al. 2006 (96)	+	?	+	+	-	-	-	?	+	+	+	6	Moderate

Note: + = yes, – = no, ? = unclear

*The criteria on the checklist were questions addressing the following issues 1) adequate methods of randomization, 2) adequate allocation concealment, 3) adequate methods of blinding, 4) equal group placing , 5) blinded group placing, 6) blinded caregivers, 7) blinded outcome assessment, 8) Intention to treat analysis, 9) description of withdrawals or drop-outs, 10) reliable outcome measurements, 11) precise results (p value, CI)

PHYSIOTHERAPY

Seven RCTs involving 548 patients examined the effect of physiotherapy on breast cancer patients. All studies were of moderate methodological quality. Four of the studies examined the effect of physiotherapy during primary breast cancer treatment (table 4), while three studies examined the effect of physiotherapy after primary treatment (table 5). Two studies were from Denmark, two were from Turkey, one from Australia, one from Canada and one from Netherland. More detailed study information is available in appendix 5a and 5b.

The effect of physiotherapy during primary breast cancer treatment

Four RCTs involving 401 patients examined the effect of physiotherapy on shoulder function during primary breast cancer treatment (table 4). One study showed that physiotherapy improved shoulder mobility while there were no difference between the groups on lymphedema and postoperative complications (42). One study showed no effect of pectoral stretching on shoulder function, arm swelling and QoL (43). One study (46) compared immediate and delayed (8 days) shoulder exercise after surgery. No differences in shoulder motion between the groups were found after one month. One study (47) with 139 patients, compared early (6-8 weeks) and late (25-27 weeks) team instructed physiotherapy after surgery. A significant difference in shoulder function were found when the first group received physiotherapy compared to no physiotherapy in the delayed group. No difference in shoulder motion between the groups was found after the last follow up when both groups had received physiotherapy (47). The effect of physiotherapy seemed not to be influenced by the timing of interventions.

Table 4. Results of the randomized trials on the effect of physiotherapy during breast cancer treatment

Study	Population	Intervention	Outcome	Follow-up	Results
Cinar et al. 2008 (42) Tyrkey	N = 57 breast cancer patients with modified radical mastectomy	Int: postoperative exercise and individual physiotherapy, and then 8 weeks home exercise Control: only home exercise	Primary: shoulder mobility, functional capacity, lymphedema, and postoperative complications	Postoperative at fifth day, and first, third and six months	Flexion, abduction and adduction movement of the shoulder joint and the functional questionnaire scores were significantly better in the treatment group compared to the control group ($p<0.01$). There were no statistical differences in the development of lymphedema and postoperative complications between the groups.
Lee et al. 2007 (43) Australia	N = 61 Upper quadrant problems following breast cancer treatment	Pectoral stretching program or control	Primary: Shoulder function Secondary: strength of shoulder muscles, arm swelling and QOL	Post radiotherapy (after ca. 6 weeks) and 7 months after radiotherapy	There was no difference in any outcome between groups.
Lauridsen et al. 2005 (47) Denmark	N=139 Breast cancer stages: I and II	Team instructed physiotherapy (6 weeks) starting 6th vs 26th postoperative week	Shoulder function was assessed by the Constant Shoulder Score (CSS)	Follow-up at weeks 7, 13, 26 and 56.	Team instructed physiotherapy instituted significantly improved shoulder function regardless of the how long after surgery it was started. No significant difference in shoulder function was found between the two groups at week 56.
Jansen et al. 1990 (46) Netherlands	N=144 Breast cancer stages: I-II	Immediate (1 day postoperate) vs delayed (8 day postoperative) shoulder exercise	Shoulder function Wound drainage	Follow-up at 1 and 6 months	No significant difference in shoulder motion and drainage volume between the two groups at 1 and 6 month after intervention.

ROM = range of motion, CI= 95 % confidence interval

The effect of physiotherapy after primary breast cancer treatment

Three RCT involving 147 patients examined the effect of physiotherapy on lymphedema after primary breast cancer treatment (table 5). One study (44) compared standard treatment with or without manual lymphatic drainage (MLD). One study (45) compared standard physiotherapy to complete decongestive physiotherapy. One study (48) compared compression bandaging with or without manual lymph drainage (MLD). Two studies (44;48) found no difference in reduction of arm lymphedema by MLD. One study reported decreased lymphedema following complex decongestive therapy, including lymph drainage, compression bandaging, elevation, medical exercise, and skin care compared to standard physiotherapy (45).

These studies were not able to show any benefit from MLD compared with physiotherapy, exercise, or compression bandaging on development of lymphedema. All these studies have limitations (all have moderate quality), and further research is needed before drawing conclusions can be drawn.

Table 5. Results of the randomized trials on the effect of physiotherapy after breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Didem et al. 2005 (45) Turkey	N= 53 Breast cancer patients with mild-moderate degree lymphedema	Complex decongestive physiotherapy (CDP) vs standard physiotherapy (SP)	Lymphedema (circumference and volumetric measurements) Shoulder flexion	Post intervention (4 weeks)	Higher mean reduction in lymphedema in the CDP group compared to standard physiotherapy (55.7% vs 36%) (p<0.05). No significant difference in shoulder external rotation between groups.
Mc Neely et al. 2004 (48) Canada	N=50 Breast cancer patients with lympedema diagnosis	Compression bandaging (CB) without or with manual lymph drainage (MLD)	Lymphedema (circumference and volumetric measurements)	Post intervention (4 weeks)	No significant difference lymphedema with or without MLD. Compression bandaging alone were effective in reducing lymphedema (p<0.001)
Andersen et al. 2000 (44) Denmark	N=44 Early breast cancer patients with lymphedema	Manuel lymph drainage (MLD) 8 weeks vs standard physiotherapy	Lymphedema (volumetric measurements Lymphedema symptoms	Post intervention (3 month).	No difference in lymphedema with or without MLD after 3 month (48% vs 60 %)(p = 0.66). No difference in patient reported lymphedema symptoms.

PHYSICAL ACTIVITY

We identified 15 publications from 11 trials that evaluated the effect of physical activity on 1514 breast cancer patients. Mode, intensity and timing of exercise differed across studies. Eight of the studies were deemed to be of high methodological quality, while three were of moderate methodological quality. Four studies examined the

effect of physical activity during primary breast cancer treatment (table 6), and seven studies examined the effect of physical activity after primary treatment (table 7). Four studies were from Canada, four were from USA, two were from UK, and one from Australia. More detailed study information is available in appendix 5c and 5d.

We divided the outcome measures in the 11 studies into five categories: (i) quality of life, (ii) fatigue, (iii) lymphedema, (iv) mood, and (v) body mass index. These outcome measures were acquired from several questionnaires, both cancer-specific and generic questionnaires. The conseptualization of QoL takes into accout both functioning and patients satisfaction in a multidimentional construct. QoL measurement composite of the ability to perform everday activities that reflect physical, psychosocial and social well-being. QoL measument could therfore include measurements of physical functioning and fatigue. Ten studies measured QoL. In measuring QoL we found that five out of the ten studies used both FACT-B and FACT-G (50%), three used SF-36 (33%), one used used FACT- Anemia scale (10%), one study used CARES (10%). One study measured FACT-B, FACT-G and SF-36 (63). Fatigue were measured in eight of eleven studies. QoL assesment by FACT-G include fatigue as FACT-F subscales. In measuring fatigue, four out of eight studies used FACT –F (50%), while three out of eight studies used PFS (38%), one used SCFS (12%).

Physical activity during primary breast cancer treatment

Four studies examined the effect of physical activity during treatment, the sample sizes ranged from 119 to 242 in these studies (table 6). Three studies assessed the effect of supervised exercise and one study the effect of homebased/unsupervised exercise programme (55). Mode and intensity of physical activity differed across studies. The interventions lasted from 6 weeks to 26 weeks. More detailed information on these studies is available in appendix 5c.

Quality of life

QoL was an outcome in three studies. Two studies found no differences in QoL measurements (using SF-36 and FACT) between patients randomised to different form of supervised exercise intervention and controls (52;63). One study reported effect on FACT-B scales but not on FACT-G scales (56). And one study reported significant better self esteem that persisted after 6 month (51). Self-reported physical functioning was assessed in two studies. Segal et al (63) compared the effect of different walking regimes. A statistically difference in physical functioning was found between the control group and the home-based exercise group in favour of the exercise group, but not between the supervised intervention group and control group. No significant difference in physical function was reported in another study (55).

Fatigue

Three studies assessed the effect of physical activity on fatigue. No differences in fatigue were seen between the physical activity intervention group and the control

group receiving standard care on fatigue outcome (using Piper fatigue scale or FACT scale)(51;52;55;56).

Lymphedema

Lymphedema was reported in one study. The incidence and symptoms of lymphedema were similar for the intervention group and the control group (52).

Mood

Two studies measured mood outcomes (e.g. anxiety, "event related distress," and depression). None of these studies showed any effect on any mood scale after physical activity intervention (51;52;56).

Altogether, these results indicate that it is still unclear if physical activity during cancer treatment improves quality of life outcomes in breast cancer patients. In the studies that assessed fatigue and mood, there were not observed any effects on fatigue or mood after physical activity during cancer treatment.

Table 6. Results of the randomized trials on the effect of physical activity during primary breast cancer treatment

Study	Population	Intervention	Outcome	Follow-up	Results
Mutrie et al. 2007 (56) UK	N = 203 Breast cancer stage 0-III	Supervised 12 week group exercise programme in addition to usual care, compared with usual care	QOL (FACT-G, FACT-B) Fatigue (FACT-Fatigue) Depression (BDI) Mood	12 weeks and 6 months	There was an effect on QoL after exercise intervention on FACT-B scale (effect estimate 2.5 (CI 1.0-3.9), p=0.0007) while no significant effect on QoL on FACT-G scale which were the primary outcome. At six month these effect were maintained. No differences were found between groups for other outcomes.
Courneya et al. 2007a (52) Canada	N = 242 Breast cancer stage I-IIIA	Usual care (UC), supervised resistant exercise (RET), supervised aerobic exercise (AET)	Cancer-specific QoL (FACT-Anemia) Fatigue (FACT-An) Depression (CES-D) Anxiety (STAI) Psychososial functioning (RSES) Lymphedema	Median 17 weeks (95% CI 9-24 weeks)	Improved self-esteem subscale was superior in the AET (Mean cange 1.3 (CI 0.2-2.3), p=0.015) and RET (Mean cange 1.3 (CI 0.3-2.4), p=0.018) groups compared with UC. All other changes in patient-related outcomes favoured the exercise groups but did not reach statistical significance. Neither intervention caused lymphedema or significant adverse events.
Courneya et al. 2007b (51) Canada	Same as Courneya et al. 2007	Same as Courneya et al. 2007	Same as Courneya et al. 2007	6 months follow up of Courneya et al. 2007	RET group reported significantly higher self-esteem than the UC group (adjusted mean diff 1.6, 95% CI 0.1-3.2, p=0.032). AET group reported significantly lower anxiety than the UC group (adjusted mean diff -4.7, 95% CI -9.3-0.0, p=0.049). All other changes in patient-related outcomes favoured the exercise groups but did not reach statistical significance.

Study	Population	Intervention	Outcome	Follow-up	Results
Mock et al. 2005 (55) USA	N = 119 Breast cancer stage 0 – III	Homebased moderate intensity walking exercise programme (6 week), compared with usual care	Fatigue (PFS- total score) Physical functioning (MOS SF-36)	Pre and post intervention	The ITT analysis revealed no significant group differences on fatigue or physical functioning. When considering those patients who adhered to the exercise intervention, an effect on fatigue of exercise was demonstrated.
Segal et al., 2001 (63) Canada	N = 123 Breast cancer stage I – II	Control (CG) Self directed (SD)- Supervised (SU)–exercise (three arms)	Physical functioning (SF-36) QoL (SF-36, FACT-G and FACT-B)	Post intervention (26 weeks)	Physical functioning: Significant difference between SD and CG (9.8 points; p = 0.01) but no significant difference between SU and CG (6.3 points; p = 0.09) No significant difference between the three groups on the other functioning scales in SF-36.

CI= 95 % confidence interval, SF-36 = medical outcome survey short form - 36, FACT-G = functional assessment of cancer therapy - general, FACT-B = functional assessment of cancer therapy – breast cancer, BDI=Bech Depression Inventory, PFS=Piper Fatigue Scale, PAQ= physical Activity Questionnaire, CES-D = Center for Epidemiologic Studies-Depression Scale, RSES = *Self esteem* (Rosenberg Self-Esteem Scale
STAI= Spielberger's State-Trait Anxiety Inventory

Physical activity after primary breast cancer treatment

Seven studies (ten publications) examined the effect of physical activity after primary breast cancer treatment. The sample sizes ranged from 46 to 377 in these studies (table 7). The interventions lasted from 12 weeks to 6 month. More detailed information on the studies is available in appendix 5d.

Quality of life

QoL was an outcome in six studies. Physical activity was associated with a significant short-time increase in QoL (using FACT, SF-36 or CARES-SF) for patients randomised to physical activity versus control (49;50;53;54;58;60). Only one study assessed the longer term impact of physical activity, and the the effect was not maintained after 6 months (57).

Fatigue

Three studies assessed the effect of physical activity on fatigue (aerobic training and home-based physical activity). All three studies found statistically significant decrease in fatigue (using different fatigue scales) compared to the control group receiving standard care (50;54;61). Daley et al found a decrease in fatigue in both physical activity group and in the placebo physical activity group (53). Higher baseline fatigue measurements were observed in the intervention group compared to the control group in Courneya et al. (50).

Lymphedema

Lymphedema was the outcome measure in two studies. The incidence and symptoms of lymphedema were similar for weight training patients and patients on

a waiting list (59). Moderate daily physical activity did not aggrevate lymphedema compared to control group (49).

Mood

Four studies measured mood outcomes (e.g. anxiety, "event related distress," and depression). Three studies found no difference between groups in any mood scale (53;60;61). Notably Daley et al reported a significant decrease in depression both in the physical activity group and the placebo group compared to usual care group (53). One study showed an effect on social physique anxiety of physical activity (54).

Body mass index

Three studies used body mass index as outcome measures. No differences in BMI were seen between intervention group and control groups in these studies (53;61;62). A significant decrease in body fat and increase in lean body mass were found in the weight training group compared to patients on the waiting list (62).

Altogether, these results showed that physical activity after cancer treatment improved short term quality of life outcomes in breast cancer patients. Aerobic training and home-based physical activity resulted in clinically important improvement in fatigue. The incidence of lymphedema was not aggravated by physical activity. No effect of physical activity was observed on mood outcomes.

Table 7. Results of the randomized trials on the effect of physical activity after primary breast cancer treatment

Study	Population	Intervention	Outcome	Follow-up	Results
Milne et al. 2008 (54) Australia	N = 58 Breast cancer survivors within 2 years of completing adjuvant therapy	Combined aerobic and resistance exercise programme Immediate exercise (IEG) or delayed exercise (DEG) (cross over study)	Primary: overall QOL measured by the FACT-B and FACT-G scale. Fatigue (SCFS) Social physique anxiety (SPAS-7)	12 weeks No measurement after cross over.	QOL increased and fatigue and anxiety decreased in the IEG from baseline to 12 weeks; FACT-B: (IEG: 110.5 (±10.3) vs DEG 82.6 (±14.3), p<0.001), FACT-G: (IEG: 86.4 (±8.3) vs DEG 64.1 (±11.2), p<0.001), Fatigue (IEG: 11.9 (±3.2) vs DEG 17.4 (±4.7), p<0.001), Anxiety (IEG 15.3 (±6.2) vs DEG 21.0 (±5.7), p<0.001),
Vallance et al. 2008 (57) Canada	Same as Vallance et al. 2007, 266 of 377 completed 6 months follow-up	Same as Vallance et al. 2007	Same as Vallance et al. 2007	6 months	No differences were found between groups for QoL or fatigue at 6 months follow-up.
Vallance et al. 2007 (58) Canada	N = 377 Breast cancer stage I-IIIA	Standard recommendations to physical activity (PA), printed material on breast cancer-specific PA (PM), step pedometer (PED), and PM plus PED (COM).	QoL by FACT-B scale, Fatigue (FACT-Fatigue Scale)	12 weeks	The COM group reported significantly improved QOL (mean diff 5.8, (CI 2.0–9.6), p=0.003) compared with PA group. The COM group reported significantly reduced fatigue (mean diff 2.3, (0.0–4.7), p=0.052) compared with PA group.
Daley et al 2007 (53) UK	N = 108 Women treated for localized breast cancer 12 to 36 months previously.	Supervised aerobic exercise therapy or exercise-placebo (body condition) and usual care	QoL measured by FACT-G and FACT-B. Fatigue(PFS) Depression (BDI) physiological and physical health outcomes (BMI)	8 weeks	Exercise therapy had short term benefit on QoL (FACT-G mean difference 9.8 (CI 2.2-17.4), p=0.004; FACT-B mean difference 13.14 (CI 3.4-22.8), p=0.002), A significant (marginal) effect on QoL and fatigue was observed at 8 weeks between exercise-placebo and usual care group. Depression decreased in both exercise and placebo–exercise groups vs usual care (mean difference -6 (CI -10 to -2) P=0.001 at 8 weeks). No diference were observed in physical health outcomes.
Courneya et al. 2003 (50) Canada	N = 53 Early stage breast cancer with no evidence of recurrent or progressive disease	Aerobic training 3 times a week for 15 weeks compared to control group	Primary: changes in peak oxygen consumption and overall QOL (FACT-B and FACT-G) Fatigue (FACT)	15 weeks	Overall QoL increased compared control group (FACT-B mean diff 8.8 points (CI 3.6-14), p=0.001; FACT-G mean diff 5.2 (CI 1.0-9.3, p=0.016). Fatigue (subscale of FACT) decresed in the physical activity group (mean diff -7.3 (CI -12.2 to -2.3). No diference were observed in bodyweight and BMI

Study	Population	Intervention	Outcome	Follow-up	Results
Basen-Engquist et al. 2006 (49) USA	N = 60 Women diagnosed with breast cancer within 7 years.	6-month, 21-session intervention to incorporate short periods of moderate activity into daily routines (Lifestyle programme) Vs standard care (SC)	Physical performance, QoL (SF-36) Body composition (BMI) Lymphedema (arm circumferences)	Post intervention (6 month)	QoL: lifestyle group reported better QoL in general health; Lifestyle 77.2 (SD 13), SC 67.1 (SD 14), p=0.006). No diference was observed after the intervention on body composition between the two groups. No diference was observed after the intervention on lymphedema between the two groups.
Ohira et al. 2006 (60)	N =85 women (2 studies) Early stage (0-II) breast cancer patients.	Weight training twice a week over 6 month vs non-intervention control group	Quality of life; Physical and psychososcial global score (CARES-SF) (scale 0 – 100) Depression symptoms (CES- D)	Post intervention (6 month)	Physical global score improved by 2.1 points in the physical activity group vs a decrease by 1.2 points in the control group (p=0.006). Psychosocial score improved by 2.5 points in the physical activity group vs 0.3 points in the control group (p=0.02). No difference in depressive symptoms between the groups.
Ahmed et al, 2006 (59)	Same study as Ohira 2006 N =46 women	Same study as Ohira 2006	Lymphedema (arm circumferences)	Same study as Ohira 2006	No difference in arm circumferences, self-reported incidence (p=0.40) or symptom (p=0.22) of lymphedema between the weighttraining and waiting list group.
Schmitz et al. 2005 (62)	Same study as Ohira 2006	Same study as Ohira 2006	Body fat Body mass BMI	Same study as Ohira 2006	Increase in lean body mass 0.88 vs 0.02 kg (p=0.008) for immediate treatment Decrease in body fat -1.15 % vs 0.23 % (p=0.03) for immediate treatment
Pinto et al. 2005 (61) USA	N =86 Early stage (0-II) breast cancer patients	Home-based physical activity (PA), instructions delivered via telephone vs standard care	Moods (POMS) Fatigue (Linear Analoge Scale Fatigue) Body esteem (BES) BMI	Post intervention (12 weeks) and 6, 9 months post baseline	No difference in POMS total mood disturbance between the groups. PA group have higher vigor (POMS subscale) than controls (2.72 vs 0.48 p = 0.001). PA group have reduced fatigue compared to controls (-15.39 vs 0.62 p = 0.001). Changes in BES did not differ between the two groups, except for a small difference in the PA group with respect to BES physical condition (2.21 vs 6.76; p=0.02). No difference in BMI between the groups.

CI= 95 % confidence interval , BMI= Body Mass Index, SF-36 = medical outcome survey short form - 36, FACT-G = functional assessment of cancer therapy - general FACT-B = functional assessment of cancer therapy – breast, SCFS= Schwartz Cancer Fatigue Scale, PFS=Piper Fatigue Scale, SPAS-7= Social Physique Anxiety Scale-7items, POMS = Profile of Mood States, BES= Body esteem scale, QoL= quality of life, CARES-SF = cancer rehabilitation evaluation system short form, CES-D = Center for Epidemiologic Studies-Depression Scale, RSES = *Self esteem* (Rosenberg Self-Esteem Scale

PSYCHOSOCIAL INTERVENTIONS

We included 18 randomised controlled trials (22 publications) under the heading psychosocial interventions, with altogether 3272 patients (Tables 8, 9, 10, 11, 12 and 13). One study was deemed to be of high quality (78), and the remaining studies were of moderate methodological quality. All studies were published between 1999 and 2008. Ten studies were from USA, three studies were from Australia, two from Canada, one from Japan, one from Israel and one from Sweden.

We divided the psychosocial interventions into three categories: (a) psychoeducation, (b) cognitive behavioural therapy, and (c) social and emotional support interventions. We divided the outcome measures in the 18 studies into five categories: (i) quality of life, (ii) mood, (iii) fatigue, (iv) health behaviour (behavioural approaches to health), and (v) social functioning (coping). These outcome measures were acquired from several inventories, where some of the most common have been reviewed by Mandelblatt et el. (98). In measuring QoL we found that three out of the 18 studies used FACT-B (17%), three used EORTD-QLQ-C30 (17%), one study used SF-36 (5.5%), eventually another one used QLI (5.5%) and one other used EuroQoL-5D (5,5%). In measuring mood, eight out of 18 studies used POMS (44%), while six out of 18 studies used HADS (33%). Two of the studies also used both POMS and HADS (68;76). In measuring clinical symptoms, health behaviour and social functioning, a great variety of different measurements were used (see tables 8-13).

Results are presented in tables 8-13, mainly as mean scores between the intervention group and the control group [or *mean difference* (SD)] if available. Interaction effects between the intervention group and the control group were partly subjected to a two-way analysis of variance (ANOVA) and are thereby indicated by an F-score. In studies that reported the interaction effects with F-values as endpoints (64;69;70;73;76;79;81;82), we converted the F-score post hoc to standardized mean difference (SMD) with confidence interval, and present both standardized mean differences [SMD (CI)] and F-values (tables 8 and 10-13). Two studies reported mean scores and interaction effects with F-values, but not mean score differences as their endpoints (79;82). For these studies we also reported SMD (CI) calculated post-hoc, in addition to the interaction effects with F-values (see tables 11 and 12).
Since some interventions had more than one follow-up measurement, we are reporting the first measurement after the interventions and determining to what extent the differences are sustained in the following measurements. Post-scores and follow-up results are presented in tables 8-13.

Psychoeducational information

Six RCTs (seven publications) involving 1318 patients examined the effect of "psychoeducational information" as psychosocial rehabilitation. Three studies examined the effect of "psychoeducational information" during primary breast cancer treatment (table 8), while three studies examined the effect of "psychoeducational information" after primary cancer treatment (table 9). Five studies were from USA and

one from Australia. More detailed study information is available in appendix 5e and 5f.

Psychoeducational information during primary breast cancer treatment

Three RCTs (4 publications) involving 437 patients examined the effect of "psychoeducational information" during primary treatment of breast cancer patients (table 8). Psychosocial educational information was given by telephone by trained cancer educators (usually nurses). One of the studies applied only standard care to control group (81). The other two studies had control groups with some educational information; these studies showed no or very small benefits from the intervention examined (74;85).

Quality of life

Two out of three studies measured the effect of educational information on quality of life. None of these studies found significant effect on any of the quality of life scales used. One study used FACT-B (81) and one study used EORTC-QLQ-C-30 (85) for measuring QoL.

Mood

All three studies measured mood outcomes (e.g. anxiety, "event related distress," and depression). None of these studies showed any effect of psycoeducational interventions on any mood scale. Two studies used POMS (74;81); and one study used HADS for measuring depression and anxiety (85). Coleman et al (74) also used VAS-W scale for measuring cancer related anxiety.

Fatigue

One study assessed the effect of educational material on breast cancer patients (85). A modest short time benefit was seen with an educational intervention by phone (85) when focusing on fatigue management (FACT-F and RPFS).

Altogether, we found no effects on QoL or moods, while a short time benefit for fatigue where seen of a psychoeducational interventions during cancer treatment in this review.

Table 8. Results of randomized control trials on the effect of educational information during primary treatment of breast cancer.

Study	Population	Intervention	Outcome	Follow-up	Results
Sandgren et al 2003 (81), Sandgren et al 2007 USA	N=222 (218) Stages I-III breast cancer.	Group1: Standard care Group 2: Health education by telephone Group 3: Emotional expression by telephone	Perceived Stress Scale Self-efficacy (CBI Cancer Behavior Inventory) QoL (FACT-B) Mood (POMS)	Post intervention-scores (5 month). Follow up study at 13 month	No treatment effects were obtained for QoL (FACT-B) or mood (POMS) post intervention. Group 2 reported greater knowledge and perceived control than group 1; SMD 0.39 (CI 0.04-.074), F(1,218)=4.78, p=0.03. No differences between the three groups on self-efficacy or social constraints were observed after interventions. No treatment effects from the intervention were obtained for QoL (FACT-B) or moods (POMS) after 13 month follow up.

Study	Popu-lation	Intervention	Outcome	Follow-up	Results
Coleman et al. 2005 (74) USA	N=106 Nonme-tastatic breast cancer, stage 0, I, II or III.	Group1 and 2: Edu-cational materials via mailed resource kit. In addition in group 2: 13 months of telephone social support and educa-tion (weekly con-tact)	Mood (POMS) Cancer-related anxiety (VAS-W) Symptoms relevant to breast cancer (SES)	Scores were measured during the intervention 3, 5, 8 months after sur-gery.	No significant differences between the groups were observed after intervention. Mailed educational resource kit alone ap-peared to be as effective, and cost-effective, as the telephone social support provided by oncology nurses.
Yates et al. 2005 (85) Austra-lia	N=109 Stage I-II breast cancer	Group 1: The con-trol group received general cancer education Group 2: Received general cancer education and Psy-choeducational intervention given at the clinic and by phone over three 10-20 minutes ses-sions 1 week apart for the intervention group.	Cancer-related fatigue (RPFS (scale 0-10) and FACT-F (scale 0-4)). Cancer self-efficacy QoL (EORTC-QLQ-C30) Anxiety and De-pression (HADS)	Post inter-vention-scores (7 weeks) and follow-up at 10 and 13 weeks	The intervention group received significantly short time benefit (post intervention 7 weeks) in minimization of intensity and im-pact on fatigue on daily life compared to the control group; mean change 1.0 (SD 2.8) vs 2.6 (SD 2.8), p=0.01). Piper fatigue scale; mean change 0.5 (SD 2.8) vs 2.1 (SD 2.8), p=0.01). FACT-F; mean change 0.1 (SD 0.7) vs 0.3 (SD 0.7), p=0.04). However, no differences were observed between baseline and later assessments (week 10 and 13). There were no significant effects of the intervention for cancer self-efficacy, quality of life, anxiety or depression.

CI= 95 % confidence interval, SMD= standardized mean difference, QoL= quality of life, FACT-B = functional assessment of cancer therapy – breast, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, EORTC-QLQ-C30 = The European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire, RPFS = Revised Piper Fatigue Scale, CBI = Cancer Behavior Inventory, VAS-W= Visual Ana-logue Scale-Worry, SES= Symptom Experience Scale, PSS= Perceived Stress scale.

Psychoeducational information after breast cancer treatment

Three RCTs involving 881 patients examined the effect of "psychoeducational infor-mation" as psychosocial rehabilitation after primary treatment of breast cancer pa-tients (table 9). More detailed study information is available in appendix 5f. Psycho-social educational information was given by computer systems, internet, videotapes, or by trained cancer educators (usually nurses) or combinations of these.

Quality of life

Two studies measured the effect of psychoeducational information on quality of life. One study showed significant effect on the quality of life using QoL –Breast cancer survivors scale (71). The other study did not show any effect of the intervention, and used FACT-B (80). Owen at al. reported in addition an effect on total health, i.e. "self-reported health status" (80) for participants with a low self-reported health status.

Mood

Two studies measured mood outcomes (e.g. cancer related distress and depression). None of these studies showed any effect of psychoeducational interventions on any of the mood scales. One study used CES-D for measuring depressive symptoms (84). Both studies used IES for measuring distress (80;84).

Fatigue

One study assessed the effect of educational material on breast cancer patients (84). A modest short time benefit was seen with an educational intervention by videotape (84) when focusing on fatigue management (SF-36).

Altogether, we found no effect of psychoeducational information after primary breast cancer treatment on QoL or moods, while a short time benefit was observed for fatigue.

Table 9. Results of randomized control trials on the effect of educational information after primary breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Meneses et al. 2007 (71) USA	N= 261 Stage O-II	Group 1: Experimental group: Psycho educational support Group 2: Waiting list control	QoL –Breast cancer survivors scale. (Scale 0-10, with lower scores indicating better QoL)	At 3 and 6 months after baseline	The experimental group showed a better overall QoL score (-0.309 (SD 0.834)) vs waiting list control group (0.042 (SD 0.752), compared to baseline scores (equal for the groups), p<0.001. After 6 month still a higher overall QoL for the experimental group, but less pronounced, p<0.001.
Owen et al. 2005 (80) USA	N=62 patients Breast cancer Stage 0-III	"Self guided internet coping" in a 12 week intervention vs waiting list controls	QoL (FACT-B), QoL (EuroQol-5D "feeling thermometer" of overall health) Distress (IES). Physical well-being (MSAS).	Post intervention-scores at 12 weeks	No significant main effects after intervention were observed for QoL, IES, or MSAS assessments. A treatment effect was observed for self reported health status (Euro QoL 5D) for participants with a low self-reported health status: SMD 1,05 (CI 0.51-1.58), F(1,39) =16.4, P<0.001
Stanton et al. 2005 (84) USA	N= 558 Breast cancer stage I-II	Group1 (CTL): Only standard National Cancer Institute print material (NCIPM). Group2 (VID): NCIPM and peer-modeling videotape Group3 (EDU): NCIPM, videotape, two sessions with a trained cancer educator.	Fatigue/ vitality (SF-36) Cancer-specific distress (IES-R) Depressive symptoms during one week (CES-D)	Post intervention-scores (6 month) and follow-up at 12 months	No significant effects on cancer-specific distress or depressive symptoms were observed after intervention or at follow-up (12 month). Group2 (VID) produced improvement in fatigue at 6 months relative to group 1 (CTL) (p=0.0185). Fatigue/vitality CTL mean change 3.35 (SD 18.09), VID mean change 9.17 (SD 18.12) and EDU mean change 5.62 (SD 19.54). After 12 month the effect were no significant differences.

CI= 95 % confidence interval, SMD= standardized mean difference, QoL= quality of life, SF-36 = medical outcome survey short form - 36, FACT-B = functional assessment of cancer therapy – breast, CES-D = Center for Epidemiologic Studies-Depression Scale, IES-R=Revised Impact of Events Scale, PTGI= Posttraumatic Growth Inventory, EORTC-QLQ-C30 = The European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire, MSAS= memorial Symptom Assessment scale.

Cognitive Behavioral Therapy

Seven RCTs (9 publications) involving 903 patients examined the effect of Cognitive Behavioral Therapy (CBT). Three of the studies (4 publications) examined the effect of CBT during primary breast cancer treatment (table 10), while four studies (5 publications) examined the effect of CBT after primary breast cancer treatment (table 11). Two studies were from USA, two were from Australia, two were from Canada

and one from Israel. More detailed study information is available in appendix 5g and 5h.

CBT during primary breast cancer treatment

Three RCTs (4 articles) involving 616 patients examined the effect of CBT during primary cancer treatment in the rehabilitation of the breast cancer patients (table 10). More detailed information is available in appendix 5g.

Quality of life

One study adressed quality of life (QoL) measurements after CBT intervention. Antoni et al. (66) measured different QoL outcomes; both positive outcomes and stress management showed an effect of the intervention. No effect of the intervention were measured by FACT-G total score (66).

Mood outcomes

All three CBT intervention studies measured mood outcomes (e.g. anxiety, "event related distress" and depression). All of these studies found some changes in mood scales. Kissane et al. (78) found effect of the intervention on anxiety (HADS) scale but not other mood scales. Cohen et al. (69) found effect on overall psychological distress (GSI and PSI scales). Antoni et al (65) found effect on emotional distress (IES and ABS scales) but not on anxiety scale.

Fatigue

One study assessed the effect of CBT on patients with fatigue (69). A modest short time benefit was seen with CBT intervention during cancer treatment (69) when focusing on fatigue management (FSI).

Altogether, these results showed that cognitive behavioural therapy during cancer treatment improved some mood scales in breast cancer patients.

Table 10. Cognitive behavior therapy (CBT) in rehabilitation during primary breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Kissane et al 2003 (78) Australia	N=303 Early stage breast cancer stages I and II.	Cognitive-existential group psychotherapy (CEGT) 20 weekly sessions plus 3 relaxation classes. Control group received only 3 relaxation classes	Mood Mental attitude to cancer. (MILP, ABS, HADS, MAC, FAD; family functioning	Post intervention-scores (6 month). Follow-up at 12 month	A trend toward improvement in anxiety for CEGT group vs control; HADS mean score -0.8 (SD 3.3) vs -0.1 (SD 3.4), p=0.05. There were no significant differences between the two groups on any of the other psychological variables.
Cohen et al. 2007 (69) Israel	N=114 Early stage breast cancer stages I and II.	CB group: Cognitive-behaviour group. RGI group: relaxation and guided imagery. Control group: received standard care in the oncology unit	Brief symptoms Inventory (BSI) Global Severity Index (GSI) to measure overall psychological distress Perceived Stress Scale (PSS) Fatigue Symptom Inventory (FSI)	Pre-Post intervention –scores and follow up at 4 month	Psychological distress and fatigue was reduced in both interventions group compared to control. GSI; SMD=0.59 (CI 0.19-0.99) F(2,111)=8.48, P<0.001 PSS; SMD=0.63 (CI 0.23-1,03) F(2,111)=9.68, P<0.001 Fatigue (FSI); SMD=0.82 (CI 0.41-1.23) F(2,111)= 16.45, P<0.001. There were no significant differences between the two groups on BSI. Psychological distress was still reduced in both interventions group compared to control after 4 month follow up, Fatigue were only lower in the RGI group at 4 month follow up.
Antoni et al. 2006a (65) USA	N=199 Breast cancer stages I,II and III.	CBT group: CBT stress management techniques Control group: received condensed educational version of the	Though intrusion and avoidance (IES) Interviewer-rated anxiety (Hamilton anxiety symptom score) Emotional stress (ABS)	Follow-up at 3 and 9 moth after intervention ended	The CBT intervention reduced reports of thought intrusion, more than the control condition. IES; SMD=0.43, P<0.03 (6 mth). And SMD=0.29, P=0.005 (12 mth). Anxiety; no between group differences at any time. The CBT intervention reduced emotional stress more than the control condition only after 12 mth, ABS; SMD=0.43, P<0.01
Antoni et al. 2006b (66) USA	Same study as Antoni 2006a.	Same study as Antoni 2006a.	Different QoL outcomes; Positive outcomes; (PSOM) Stress managements; (MOCS) QoL (FACT-G)	Same study as Antoni 2006a.	The CBT intervention reduced emotional stress more than the control condition only after 12 mth, PSOM; SMD=0.39, P<0.04 The CBT intervention reduced emotional stress more than the control condition only after 12 mth, MOCS; SMD=0.33, P<0.004 No interventions effect on QoL by FACT-G total score, only on subscales.

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale, MILP= Monash Interview for Liaison Psychiatry, ABS= Affects Balance Scale , FAD=Family Assessment Device, IES= Impact pf Event scale, PSOM= Positive states of mind, MOCS=Measure of current status, PSS= Perceived Stress scale, BSI= Brief Symptom Inventory, GSI= Global Severity Index, FSI= Fatigue symptom Inventory, FACT-G = functional assessment of cancer therapy – general.

CBT after primary breast cancer treatment

Four RCTs (5 articles) involving 287 patients examined the effect of Cognitive Behavioral Therapy (CBT) after primary cancer treatment in the rehabilitation of the breast cancer patients (table 11). More detailed information is available in appendix 5h.

Quality of life

All four studies addressed quality of life (QoL) after CBT intervention. All of these studies reported significant improvements in QoL (using the "FLIC" (75), "QLI" (83), QoQ-C33 global QoL-scales (82) and FACT-B (70)). All studies show short terms effect on QoL outcomes, some differences between the three studies that measure long term effects were observed (75;82;86).

Mood outcomes

All four CBT intervention studies measured mood outcomes (e.g. anxiety, "event related distress" and depression). Two of four studies found improvements in mood (82;83), while two studies found no difference between CBT and control group. Three studies (70;75;83) used POMS, while the other study used HADS (82), STAI-S and CED-D (70), and one (83) study used SCL-90-R in addition to POMS.

Health behavior

One of the four CBT articles monitored changes in health behavior, i.e. "coping strategies" (83), but showed no effect.

Fatigue

Two studies assessed the effect of CBT on patients with fatigue (70;82). A benefit was seen with CBT intervention after cancer treatment in only one of these studies (70) when focusing on fatigue management (FSI).

Altogether, these results showed that cognitive behavioural therapy after cancer treatment improved short term quality of life outcomes in breast cancer patients. The effects on moods were only seen in half of the studies.

Table 11. Cognitive behavior therapy (CBT) as rehabilitation after primary treatment of breast cancer patients.

Study	Population	Intervention	Outcome	Follow-up	Results
Dirksen et al. 2008 (70) USA	N=81 Stage I-III breast cancer patients	CBT Insomnia intervention (CBT-I); received stimulus control instructions, sleep restriction therapy and sleep education. Component control group (CC); received sleep education and hygiene only (10 weeks).	Fatigue (POMS-subcale) Anxiety (STAI-S) Depresseion (CES-D) QoL (FACT-B)	Pre-Post intervention – scores	CBT-I intervention group had improvements in Fatigue and QoL (group-time interaction) compared to CC group. Fatigue by POMS:, SMD=0.61 (CI 0.14-1.09) F(1.70) =6.54, P=0.01 QoL by FACT-B:, SMD=0.56 (CI 0.09-1.03), F(1.70)=5.42, P=0.02 No statistically significant group differences were observed with respect to depression and anxiety compared to control group
Savard et al. 2005 (82) Canada	N=57 Stage I-III breast cancer patients	Group1: Waiting-list control Group2: Cognitive-behavioral therapy (CBT). Multimodal approach combining cognitive, behavioral and educational strategies, Eight weekly group sessions.	Sleep difficulties (IIS) Current and past psychiatric disorders (SCID), Objective sleep Insomnia severity (ISI), Depression and anxiety (HADS) Fatigue (MFI), QoL (QoQ-C33 global)	8 week waiting list design, later outcomes excluded. At 3, 6 and 12 months	Post treatment CBT group vs pretreatment wait list control group Anxiety; between group-time interaction SMD 0.62 (CI 0.08-1.15), $F_{1,45}$= 5.19, P<0.05 Depression; between group-time interaction SMD 0.55 (CI 0.02-1.08), $F_{1,48}$= 4.14, P<0.05 Quality of life; between group-time interaction SMD 0.63 (CI 0.11-1.18), $F_{1,48}$= 5.69, P<0.05 No statistically significant differences were observed with respect to fatigue compared to waiting list control group
Simpson et al 2002 (86) Canada	N=89 breast cancer stage 0, I, or II	Support group (based on CBT) six weekly 90 minute sessions delivered by trained psychiatrist (SCID). Both groups received standard psychosocial care.	Mood (SCL-90-R, POMS) Depression (BDI) Coping strategies (MAC, DWII) QoL (QLI)	Post intervention – scores (6 weeks). Follow-up at 1 and 2 years	Intervention group had less depression vs control measured by BDI (6.5 vs 10.4; p<0.01), less mood disturbance by POMS (4.0 vs 20.4, t=2.15; p<0.05), and better overall QoL global score (23.0 vs 20.6, p<0.01). One year after intervention there was no statistically significant difference between the two groups. Two years after the intervention, improved total functionality was measured by GAF compared to control (85.7 vs. 82.3), also less depression by BDI, less overall mood by POMS and better QoL compared to the control groups.
Simpson et al 2001 (83) Canada	Se Simpsons 2002	Se Simpsons 2002	ISSI (Interview schedule for social integration) with subgroup ADAT (among others)	1 year follow-up assessment	One year after the intervention there was no statistically significant difference between the two groups in the different ISSI subscales. Social support measured by ISSI, (subgroup: "adequacy of close relationships" i.e. ADAT) was better at two-year follow-up (p<0.10).

Study	Popu-lation	Intervention	Outcome	Follow-up	Results
Edelman et al 1999 (75) Austra-lia	N= 60 Breast cancer stage I or II.	Supportive therapy vs Cognitive behavioral therapy (CBT). Each group comprised 8-9 participants, who met weekly for 2 hours over 12 weeks.	Mood (POMS subscales: anxiety, de-pression, anger and vigor). QoL (FLIC) Social support (7-points Likert scale) Self esteem (RSES)	Post inter-vention-scores (12 weeks). Follow-up at 4 months	CBT group intervention showed improved self-esteem (-2.27, p=0.024) and QoL (-12.07 p=0.027) These differences between groups were no longer apparent at the 4 month follow-up. There were no significant differences be-tween the two groups on any of the other psychological variables

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, SCID= Structured clinical interview for DSM-III-R, SCL-90-R= Symptom checklist, MAC= Mental adjustment to cancer scale, DWII= dealing with illness inventory, QLI= Quality of life index, FLIC = Functional Living Index, RSES = *Self esteem* (Rosenberg Self-Esteem Scale), MFI= Multidi-mensional Fatigue Inventory , QLQ-C30+3= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, FACT-B = functional assessment of cancer therapy – breast, CES-D = Center for Epidemiologic Studies-Depression Scale, STAI= State-Trait Anxiety Inventory (STAI).

Sosial and emotional suppport

Five RCTs (six publications) involving 1051 patients examined the effect of sosial and emotional support as psychosocial rehabilitation. Four studies (5 publications) examined the effect of sosial and emotional support during primary breast cancer treatment (table 12), while one study examined the effect of social and emotional support after primary cancer treatment (table 13). Three studies were from USA, one from Sweden and one from Japan. More detailed study information is available in appendix 5i and 5j.

Social and emotional support during primary breast cancer treatment

Four RCTs (5 publications) with 1001 breast cancer patients assessed the effect of social and emotional support on health and well-being of breast cancer patients. These supportive interventions were delivered by trained therapists (psychologist and/or psychiatrist) in a group setting at the hospital (table 12). More detailed study information is available in appendix 5i.

Quality of life

One study assesses QoL outcomes after social and emotional support. Intervention group had better scores on global QoL after intervention (67).

Mood

All four studies reported mood as an outcomes (e.g. anxiety, “event related distress” and depression). Two of the studies (64;68;73) used POMS, while the other two used MHI-18 and BEC (79) or HADS (67). Cancer spesicfic distress (IES) and anxiety were measured by all studies. Three studies did not observe any difference in distress between the groups (64;68;73;79). One study showed less distress after individual therapy (67). One study showed reduced anxiety in the intervention group (64;73), while the other three studies did not measured any group difference on

anxiety (67;68;79). Depresssion was an outcome in all the studies but only one study did measure a significant group difference (79), while the other three studies did not (64;67;68;73).

Fatigue

One of the four studies assessed the effect of supportive interventions on fatigue (a subscale of POMS). No significant difference was observed between the intervention and the control group (64;73).

Health behavior

One out of the four support intervention studies addressed health behavior (64;73), but reported no statistically significant effect.

Social functioning

One out of the four support intervention studies addressed social functioning (64;73), but reported no statistically significant effect.

Altough a number of studies have addressed social and emotional support interventions during breast cancer treatment, the impact of these interventions on patients quality of life, wellbeeing, and functioning is still unclear.

Table 12. Results of randomized controlled trials on the effect of social and emotional support intervention during primary treatment of breast cancer.

Study	Population	Intervention	Outcome	Follow-up	Results
Classen et al. 2008 (68) USA	N=357 patients: Breast cancer stage I, II or IIIa	Group 1: Standard care (SC) with educational control condition. Group 2: Supportive-expressive group therapy supposed to reduce distress.	Total mood disturbance (POMS) Depression (HADS) Anxiety (HADS) Helpless/hopeless (MAC) Distress (IES) Distress (Yale informational support)	Follow-up at 3, 6, 12, 18 and 24 month after randomization	There were no significant differences between the two groups on the POMS scale. There were no significant differences between the two groups on the HADS, MAC, IES scales or Yale informational support for the secondary outcomes. However, small significant effects were observed on these scales when the analysis included an extreme outliner in the control group.
Arving et al. 2007 (67) Sweden	N=179 patients: Breast cancer stage I, II or III	Group 1 Individual psychosocial support by oncology nurse (INS). Group 2 Support by psychologist (IPS). Group 3 standard care (SC).	QoL (EORTC QLQ-C30) Depression and Anxiety (HADS) Distress (IES) Anxiety (STAI-S)	Follow-up at 6thmonth post intervention.	Intervention group had better scores on global QoL/health status (Group by time); INS 67 (SD 23), IPS 68 (SD 21) and SC 60 (SD 24); P<0.05 (after 6 month). In addition, more patients in the intervention groups improved clinically on distress IES intrusion); INS 8 (SD 6), IPS 9 (SD 8) and SC 13 (SD 10); P<0.05 (after 3 month) There were no significant group differences between the two groups on the other scales.

Study	Population	Intervention	Outcome	Follow-up	Results
Andersen et al. 2004, 2007 (64;73) USA	N=227 patients: Breast cancer stage II or III	Psychosocial intervention group with stress reduction vs control group (assessments only).	Stress (IES) Emotional distress. anxiety, depression, fatigue (subscales of POMS) Social adjustment (SNI) Perceived social support scale (PSS) Health behaviors with subscales	Post intervention-scores (4 months) And follow up 12 month, ((64)	Intervention group had improved measurements by the Mood scale (POMS as a three-way interaction depended upon initial levels of stress: SMD 0.27 (CI 0.01-0.53), F(1,193) = 4.13, p<0.05. Reduced anxiety (subscale of POMS); SMD 0.27 (CI 0.01-0.53),F(1,193) = 4.15, p<0.05. Some significant improvements in subscales of PSS ; SMD 0.31 (CI 0.05-0.57), F= 5.36, p< 0.05 No significant difference in depression and fatigue scale (subscales of POMS). Intervention group had still an effect on the POMS scale after 12 month follow up (three-way interaction - cancer stress); SMD 0.27 (CI 0.01-0.53), F(1,179) = 4.02, p<0.05. There were no significant differences between the two groups on IES scale after 4 or 12 month.
Manne et al. 2005 (79) USA	N= 238 patients as couples: Breast cancer stage I, II or IIIa	Psychosocial intervention Couple-focused Group (CG) intervention vs usual care (UC)	General distress (MHI-18; Anxiety, Depression, BEC) Cancer-specific distress (IES)	Post intervention-scores (7 week), follow-up at 6 month.	CG intervention had lower depressive symptoms at post-scores (MHI); SMD 0.28 (CI 0.02-0.54) F(1,226)= 4,37, p=0.0376, These differences were no longer significant 6 month after intervention. There were no significant differences between the two groups on the other general distress scales or IES. Women with unsupportive partners and/or with more physical impairment benefited most from the intervention. Subgroup-analyses: Less distress in intervention group with real attendees.

CI= 95 % confidence interval SMD = standardized mean difference, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale, IES = Impact of Event Scale, SNI = Social Network Index, PSS = Perceived social support scale, MHI-18 = Mental Health Inventory-18, BEC= Loss of behavioral and Emotional control, Yale=Yale Social Support Index, QLQ-C30+3= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, STAI-S= State-Trait Anxiety Inventory – State, CARES= Cancer Rehabilitation Evaluation System.

Social and emotional support after primary breast cancer treatment

One RCT with 50 breast cancer patients assessed the effect of social and emotional support after primary treatment on mood. The supportive intervention was delivered by trained therapists (both psychologist and psychiatrist) in a group setting at the hospital (table 13). More detailed study information is available in appendix 5j.

Mood

One study assessed mood outcomes using three different scales (POMS, MAC and HADS) (76). There were no significant effects of the inteventions on the HADS and MAC scales, but significant improvement in the POMS scale for the interventions group compared with control group.

Table 13. Results of randomized controlled trials on the effect of social and emotional support interventions after primary breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Fukui et al 2000 (76) Japan	N=50 Breast cancer Grade 2-3.	Psychosocial group intervention with a wait list design.	Psychological distress and coping (POMS) Mental adjustments to cancer (MAC) Clinical anxiety and depression (HADS)	Post intervention-scores (6 week), follow-up at 6 month.	There were no significant differences between the two groups on the HADS scale and MAC scale (except for "fighting spirit".) However, small significant effects were observed on the POMS-scale. Improvement in Total mood disturbance (TMD); 13.8 (SD 21.3) the intervention group vs 24.6 (SD 27.5) in the control group (p=0.003). Women who had undergone chemotherapy treatment benefited more from the intervention on TMD (POMS scale) SMD 0.90 (CI 0.32-1.49), F=9.73, p=0.003. These differences between groups were sustained at the 6 month follow-up.

CI= 95 % confidence interval SMD = standardized mean difference, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale.

NUTRITION

We identified two randomized controlled trials on nutritional interventions for breast cancer survivors after primary cancer treatment (table 14). Both studies were of moderate methodological quality. The interventions was the multicenter diet intervention Women Healty Eating and Living (WHEL) study intiated in 1993, with the aim to determine if diet can reduce breast cancer recurrence. More detailed study information is available in appendix 5k.

Body weight

Both studies assessed body weight as an outcome. The intervention group in the largest study had a small but significant weight loss 1 year after the intervention (87), but no between group differences were observed after 4 years. Thomson et al found no differences in body weight, BMI or body composition during the study period of 48 months (88).

Altogether these results suggest that the effect of nutritional intervention on body weight is still unclear.

Table 14. Results of the randomized trials on the effect of nutrition

Study	Population	Intervention	Outcome	Follow-up	Results
Saquib et al. 2008 (87) USA	N = 2718 Breast cancer survivors stage I-IIIA after completed conventinal therapy.	The dietary intervention aimed for eight servings of fruit and vegetables. The comparison group was advised to follow general dietary guidelines for cancer prevention.	Body weight	1 and 4 year	The intervention group had a small but significant weight loss at 1 year (intervention; -0.05 ±0.12 vs control; 0.71±0.11, P<0.0001), but no between-group weight differences was observed at 4 years.
Thompson et al. 2005 (88) USA	N = 72 Breast cancer survivors stage I-IIIA after completed conventinal therapy.	The dietary intervention aimed for eight servings of fruit and vegetables. The comparison group was advised to follow general dietary guidelines for cancer prevention.	Body weight, BMI, Body compositions.	Follow up at 6,12, 24 or 36 and 48 month	There were no significant difference in body weight and BMI during measurement, at 6, 12, 24 or 36 and 48 months.

BMI=body mass index

COMPLEMETARY INTERVENTIONS

Five RCTs involving 441 patients examined the effects of complementary interventions in the rehabilitation of breast cancer patients. One study was of high methodological quality (90), while four studies were of moderate methodological quality. Three studies examined the effect of complementary interventions during primary breast cancer treatment (table 15), while one study examined the effect of complementary interventions after primary cancer treatment (table 16). Two studies were from UK, one from USA, one from India and one from Sweden. More detailed study information is available in appendix 5l and 5m.

Complementary interventions during primary breast cancer treatment

Three RCTs involving 236 patients examined the effect of complementary intervention during primary treatment of the breast cancer patients (table 15). The interventions were acupuncture, yoga or rexalation training. More detailed information is available in appendix 5l.

Quality of life

One study adressed quality of life (QoL) after relaxation training, and reported improved QoL (93).

Mood outcomes

Two studies adressed moods after complementary interventions (e.g. mood, anxiety, "event related distress" and depression). One study on a yoga intervention reported improvement on a mood rating scale, but no difference in anxiety (HADS) or depression (HADS, SCID) (89). One study on relaxation training reported improve-

ments in anxiety (HADS), depression (HADS) and emotional suppression (CECS) compared with controls (93).

Hot flahes

One study with an acupuncture intervention measured incidence of hot flashes, no significant difference were showed between the groups (90).

Altogether these results suggest that a complementary intervention during cancer treatment may have some effect on moods. Effects on QoL and hot flashes were only addressed in one study and it was therefore difficult to conclude about the effect.

Table 15. Results of randomized controlled trials on the effect of complementary interventions during primary breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Deng et al. 2007, (90) USA	N=72 Breast cancer patients with hot flashes .	Group 1: Sham acupuncture vs. Group 2: true acupuncture. Cross over study at 6 weeks	Incidence of hot flashes	Post intervention at 6 weeks	Incidence of hot flashes was reduced in the acupuncture groups after 6 weeks but did not reach statistical significance.
Banerjee et al. 2007 (89), India	N=68 patients: Breast cancer stage II or III	Group 1: Control supportive counseling group vs. Group 2: Yoga intervention (6 weeks)	Depression and anxiety (HADS) Self report measurements of psychological stress (PSS)	Post intervention at 6 weeks.	Intervention yoga group had a decrease in anxiety (42,8 %) and depression (57.5 %) from baseline measurements vs control groups had an increase in anxiety (28 %) and in depression (24 %) from baseline measument, p<0.001. Intervention yoga group had a decrease in perceived stress (25.9 %) from baseline measuments vs control groups had no change in perceived stress from baseline measurements, p<0.001.
Walker et al. 1999 (93), UK	N=96 patients: Breast cancer stage I - III	Group 1: control condition standard care (C); vs. Group 2: Experimental group; Relaxation training (E);	Coping with stress (EPQ and CECS) QoL (GQOL) Mood (MRS) Psychiatric disorders (SCID and HADS)	Reporting post interventions results.	Intervention group reported improved psychological wellbeing: Intervention group had an decrease in mood rating scale (MSR E; 73.29 (SD 44.77) vs C; 70.19 (SD 41.30), P=0.01), and the had higher QoL (GQOL: E; 3.29 (SD 0.80) vs C; 2.90 (SD 0.66),P=0.03) The intervention also reduced emotional suppression (CECS total E; 47.58 (SD 10.64) vs C; 52.13 (SD 9.63), P=0.02) There were no significant differences between the two groups on the other scales.

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, HADS= Hospital Anxiety Depression Scale, PSS= Perceived Stress scale , EPQ= Eysenck Personality Questionnaire - revised, CECS= Courtauld Emotional Control Scale, GQOL=Global self-rated Quality of Life, MRS= Mood Rating Scale, SCID= Structured clinical interview for DSM-III-R.

Complementary interventions after primary breast cancer treatment

Two RCTs involving 205 patients examined the effects of complementary interventions after primary treatment of the breast cancer patients (table 16). The interventions were relaxation training or art therapy. More detailed information is available in appendix 5m.

Quality of life

One study adressed quality of life (QoL) outcome after complementary interventions. The study found no differences between the groups on QoL assessment after relaxation training (91).

Hot flahes

One study on relaxation training measured the incidence of hot flashes, with a significant short term reduction for intervention group compared with controls (91).

Mood outcomes

One study addressed anxiety after relaxation training. The study found no differences between the groups on anxiety (STAI) assessment (91).

Coping

One study addressed coping outcomes after complementary interventions. This study found no significant total score difference between the groups on coping (CRI) assessment after art therapy (92).

Effects on the outcomes; QoL, hot flashes, moods and coping were only addressed in one study and it therefore was difficult to conclude about the effect.

Table 16. Results of randomized controlled trials on the effect of complementary interventions after primary breast cancer treatment.

Study	Population	Intervention	Outcome	Follow-up	Results
Fenlon et al. 2008 (91), UK	N=150 Primary breast cancer	Group 1: control standard care vs. Group 2: Relaxation training (1 session), following by self relaxation by audiotapes at home.	Incidence of hot flashes (severity descriptions) Distress caused by hot flashes; Hunter menopausescale QoL (FACT-ES) Anxiety (STAI)	1 and 3 month follow up after intervention.	Intervention group had a small reduction in the incidence of hot flashes (median difference; 7 (CI 4-11), severity of hot flashes (median difference; 0.54 (CI 0.11-1.01) and distress caused by hot flashes (median difference 1 (CI 0-2), after 1 month follow up. All p<0.01. There were no significant differences between the two groups on these outcomes after 3 month. There were no significant differences between the two groups on QoL and anxiety.

Study	Population	Intervention	Outcome	Follow-up	Results
Öster et al. 2006 (92) Sweden	N=55 patients: Breast cancer patient with non-metastatic cancer	Group 1: Control group vs. Group 2: individual art therapy intervention for reflection over her situation.	Coping Resources Inventory (CRI)	Post assessment at 2 month. Follow-up at 6 month.	There were no significant differences between the two groups on total coping resources inventory scales. A significant higher scores were obtain by the study group on social domain subscale of CRI ($p<0.05$)

CI= 95 % confidence interval, QoL= quality of life, FACT-ES= Functional Assessment of cancer Therapy – endocrine subscal, STAI= State-Trait Anxiety Inventory, CRI= Coping Resources Inventory

COMPLEX INTERVENTIONS

Three randomised controlled trials including 352 women investigated the effects of a comprehensive rehabilitation programme for breast cancer patients. All studies were of moderate methodological quality. One study examined the effect of complex interventions during primary breast cancer treatment (table 17), while two studies examined the effect of complex interventions after primary cancer treatment (table 18). These studies were from USA, Germany and South Korea. More detailed study information is available in appendix 5n and 5o.

Complex interventions during primary breast cancer treatment

One RCT involving 90 patients examined the effects of complex interventions during primary treatment of the breast cancer patients (table 17). The interventions consisted of physical activity and diet restrictions. More detailed information is available in appendix 5n.

Quality of life and mood outcomes

Both quality of life (QoL) and mood outcome after physical activity and diet interventions were addressed in the included study (94). The study found no difference between the groups on QoL and mood assessment after complex rehabilitation programme during primary cancer treatment (94).

Body composition

One study address many aspects of body composition, a significant difference between the group were only found on body fat (lower in the intervention group with restricted diet and physical activity)(94). No difference were found on body weight and BMI (94).

Altogether these results indicate that a complex intervention (diet and exercise) during cancer treatment have small effect on QoL and moods. This was only addressed in one study and it is therefore difficult to conclude.

Table 17. Results of the randomized trials on the effect of complex interventions

Study	Population	Intervention	Outcome	Follow-up	Results
Denmark-Wahnefried et al. 2008 (94) USA	N = 90, newly diagnosed breast cancer patients stage I-IIIA on adjuvant chemotherapy	Calcium-rich diet (CA), CA + physical activity (EX), and CA + EX + high fruit and vegetable, low-fat diet (FVLF)	Primary: body composition (body fat, body weight, BMI), QoL (FACT-G), anxiety and depression (HADS)	6 months	QoL, anxiety and depression: no differences between groups observed Body composition: significant decrease in the CA+EX+FVLF-group on percentage of body fat compared to other groups (+0.7% ± 2.3% (CA), +1.2% ± 2.7% (CA+EX), and +0.1% ± 2% (CA+EX+FVLF, p=0.047). No signinficant different between the groups in body weigth or BMI

CI= 95 % confidence interval, QoL= quality of life, FACT-G= Functional Assessment of cancer Therapy – general, HADS= Hospital Anxiety Depression Scale, BMI= body mass index.

Complex interventions after primary breast cancer treatment

Two RCT involving 262 patients examined the effects of complex interventions after primary cancer treatment of the breast cancer patients (table 18). The complex interventions in both studies consisted of psychoeducational and physical activity interventions. Physiotherapy was also part of the complex intervetions in one study (96). More detailed information is available in appendix 50.

Quality of life and mood outcomes

Both studies addressed quality of life (QoL) outcome, while one of the studies address psychosocial adjustment outcome after complex interventions. Cho et al. showed a significant effect of the intervention on QoL assessment and psychosocial adjustment (96). The other study showed no difference between the groups on QoL assessment after complex rehabilitation programme after primary cancer treatment (95).

Motility

One study adressed motility of the arm after complex rehabilitation. Motility (ROM) was significantly improved in the intervention group relative to the control group (96).

Altogether these results indicate that a complex intervention (psychoeducational and physical activity) after cancer treatment have unclear effect on QoL and moods.

Table 18. Results of the randomized trials on the effect of complex interventions

Study	Population	Intervention	Outcome	Follow-up	Results
Hartmann et al. 2007 (95) Germany	N = 197, breast cancer diagnosis confirmed by histology not longer than 5 years ago	Group A: 3-week step by step rehabilitation programme (1-week sojourn 4 and 8 months later) Group B: 4-week rehabilitation programme	Primary: global quality of life (gQoL) using ECORT-QoL-C30 Secondary: other dimensions of QoL	End of 3-4 week stay and after 12 months	No significant differences between groups observed on gQoL, emotional function and cognitive function after 4-weeks of the two rehabilitation programmes. For a subgroup of patients with impaired cognitive function at baseline, this difference between groups became significant (p=0.0098).
Cho et al. 2006 (96), South Korea	N = 65 Breast cancer stage I – II after primary breast cancer treatment	Comprehensive rehabilitation for 10 weeks (psychology-based education, physical activity and peer support group activity) vs usual control (waiting list)	Range of motion (ROM) Psychosocial adjustment Quality of Life QoL (measured by a 10 cm visual analog scale)	No follow-up except for pre-post intervention	ROM were significantly increased in the intervention (11.5±7.8 %) compared to the control group (1.3±4.8 %) (p=0.000). Psychosocial adjustment was increased in the intervention group by 2.9±6.3 points while it decreased in the control group by 3.0±6.3 points (p=0.000). QoL was increased in the intervention by 0.9±1.3 points while it decreased in the control group by 0.1±1.0 points (p=0.002).

QoL= quality of life, ROM= Range of motion, EORTC-QLQ-C30 =The European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire.

Discussion

This review addressed the effect of different interventions in the rehabilitation of breast cancer patients. We identified 46 RCTs that assessed physiotherapy, physical activity, psychosocial interventions, nutrition, complementary interventions, and complex interventions in the rehabilitation of breast cancer patients. We did not identify any Norwegian RCTs that could be included in this systematic review with our criteria for inclusion.

We found limited documentation on the effect of physiotherapy, psychoeducation, social and emotional support, nutrition and complementary intervention. The included studies showed that patients may have some benefits from physical activity and CBT interventions especially after primary breast cancer treatment. No quantitative analysis could be performed due to the heterogeneity of interventions employed and the diversity of outcome measurements used.

Thus, at present the evidence base to guide how to best achieve clinical, physical, and mental rehabilitation of breast cancer patients is limited. However, the findings of this review do underline some areas of specific interest and the necessity to ask for more studies.

PHYSIOTHERAPY

Of the seven RCTs examining the effect of physiotherapy, four studied the effect of physiotherapy on arm lymphedema and three investigated the effect on shoulder function. Based on the included trials, it could not be shown that physiotherapy and manual lymph drainage (MLD) are better than normal care. Shoulder mobility improved after physiotherapy, but the results were influenced by the type of surgery performed, i.e. breast conserving therapy or modified radical mastectomy.

The internal validity, i.e. the methodological quality, of the individual studies, was moderate. Measurement errors (uncertainties), which are important in pre- and post examinations, were only stated in two of the studies. Most studies specified the duration of the intervention, but lacked information about training intensities. As-

sessment of the applicability of the results demands that patient characteristics and interventions are described precisely enough for clear inferences to be made concerning which, where, and how patients should be treated. Pertinent outcome measurements are also important for clinical relevance.

Methodological shortcomings were lack of therapist and observer blinding, imbalance between groups in baseline characteristics, different surgical procedures, different durations and magnitudes of arm lymphedema, heterogeneity in shoulder function, and co-interventions. Blinding of patients and therapists in RCTs on rehabilitation is seldom possible, but a feasible alternative is to evaluate expectations for the treatment response in both the intervention and control groups in advance, for both patients and therapists as done in some of the studies (43;44;47). Intention-to-treat analysis is an essential feature of an RCT but was done in only two of these studies (43;44).

All studies on physiotherapy, except Lee et al. (43) (both ALND and SLNB patients) were on patients who received the ALND procedure that involves extensive removal of lymph nodes in the axilla. More than half of the patients operated today undergo SLNB instead of ALND. ALND is associated with more severe postoperative arm morbidity in early breast cancer patients (10;99), and long term evaluation of ALND versus SLNB showed lesser upper extremity morbidity in patients where SLNB was used (100). Positive lymph node(s) in the axilla is an important negative prognostic factor (101;102) for shoulder problems. Thus, interventions addressing clinical problems from the ALND surgical approach may not be relevant to patients undergoing the SLND technique.

Patient selection is a concern in these studies. The trial assessed by Lauridsen et al. (47) was criticise for exclusion of too many with prior shoulder problems by Cave et al. (103). Cave et al. also discussed using Constant Shoulder Score as method where pain is a part of the score. Only reducing pain by methods other than physiotherapy may have effect of the score.

Two recent systematic reviews evaluate the effectiveness of lymphedema therapy; a Finnish report (FINOHTA) (104) and a Cochrane review (105). Both systematic reviews concluded that compression sleeves are beneficial, but they stated that further studies are needed (104;105). The Cochrane review had different inclusion criteria from our report (at least 6 months follow up), and thus included only two studies that also were included in our review (44;45). The FINOHTA report had another study in common (48) with our systematic review.

There is a lack of high quality studies to guide conclusion on the effect of physiotherapy interventions to improve arm lymphedema or shoulder function after breast cancer surgery.

PHYSICAL ACTIVITY

We included 15 publications from 11 trials on the effects of physical activity for breast cancer patients. Based on the included trials, the level of scientific evidence regarding the effect of physical activity is moderate. There were some promising results with respect to the effect on improving QoL and reducing fatigue in patient receiving physical activity after primary cancer treatment. Another important finding from the included trials was that incidence and symptoms of lymphedema was not aggravated by aerobic training or weight training.

The methodological quality of included studies was high in 9 out of 11 studies, and moderate in two studies. Intention-to-treat analysis was used in all studies except one (59;60;62). The RCTs were homogenous with respect to populations included, but heterogeneous in terms of outcome measures such as questionnaires used to assess quality of life. The physical activity programmes were of different durations and types. So far, the characteristics of the different physical activity programmes have received little attention. Thus, any influence of physical activity frequency and intensity remain unclear. It is difficult to choose relevant endpoints to measure the effects of an intervention with physical activity. Measuring aerobic capacity will e.g. give useful information about the physiological effects of the programme, but yield no direct information about the patients' symptoms, well-being, and subjective physical functioning.

Based on the included trials, one important finding was that physical activity may increase QoL, when the interventions are given after primary cancer treatment. A systematic review of cancer patients in general who weighted the evidence on the impact of physical activity interventions on improving QoL during treatment and found it to be weak, whereas the evidence for interventions that where timed after treatment were judged as strong (97). Our study could not conclude about the effect of physical activity on any outcome variables from studies that give the intervention during primary cancer treatment due to inconsistency between the studies.

Eight studies assessed fatigue as an outcome; only the four studies that gave the intervention after treatment documented a significant reduction in breast cancer related fatigue. This agrees with a recent Cochrane report which states that exercise reduces cancer related fatigue (106). Subgroup analysis of breast cancer patients also significantly reduced fatigue, although they were not able to compare the studies given the intervention following cancer therapy in a meta-analysis because of high level of statistical heterogeneity was present (106). For all cancer types they found a decrease in fatigue both during cancer therapy and following cancer therapy (106). Another new systematic review stated that physical activity tended to have moderately stronger effect in decreasing fatigue when administrated during cancer therapy (107;108). In our review there is inconsistency in the studies that give the intervention during cancer treatment. The clinical setting is very different in receiving the physical activity intervention during cancer treatment. The time, mode and intensity differs also a lot in the included studies that are given the intervention during cancer treatment and could explain the inconsistency in this review.

Another important finding in our review was that incidence and symptoms of lymphedema was not aggravated by different types of physical activity (49;52;59). This is an important result, as all types of performed physical activity have been feared and earlier clinical guidelines has warned breast cancer survivors against vigorous, repetitive upper body exercise. A systematic review from 2005 did not find any significant effect regarding delayed exercise follow surgery; instead it supports the use of delayed programmes to reduce seroma formation (109).

Some of the included studies were also assessed in a Cochrane review from 2006 (110); both summarized the effect of exercise on women receiving adjuvant therapy for breast cancer. The Cochrane report (110) concluded that there is a lack of evidence on the relevant benefits and adverse effects of exercise. There are several ongoing or planned trials on this issue that will be of interest to follow. The report from World Cancer Research Fund (3) concluded that existing trials provide some evidence for the benefit of physical activity on post treatment quality of life for breast cancer survivors.

Based on the included trials, another interesting finding was that supervised physical activity may increase aerobic capacity and reduce body weight compared with standard care. Weight gain and reduced physical activity is frequently observed in breast cancer patients (37). Marked weight gain has been observed among women receiving systemic adjuvant chemotherapy (111-113) while physical activity is reduced in all groups of patients (111). Reduced physical activity may influence functional and psychological wellbeing, but may also have an impact on health outcomes. Recent studies suggest that physical activity may impact breast cancer recurrence and survival (114;115).

PSYCHOSOCIAL INTERVENTIONS

Conclusions about the effectiveness of psychosocial interventions are clouded by small sample sizes, different outcome measures, different assessment methods, and short follow-ups. The results for CBT interventions after primary cancer treatment, however, appear promising with respect to their short-term effects on improving QoL.

Of the 18 RCTs examined psychosocial interventions, six addressed the effect of psychoeducational information; seven addressed the effect of cognitive behavioral therapy (CBT), while five addressed the effect of social and emotional support. The interventions in these studies differed broadly. Some studies made use of individual or group therapies supervised by health professionals, either at home or in health clinics. Others were supportive self-care programmes carried out by either professionals or laymen such as spouses. In addition the interventions differed in composition for each of these three main categories, and many were multimodal. Different aspects were in focus in the different psychoeducational interventions. For instance three out of seven studies on CBT-interventions also had additional procedures e.g. sup-

port groups (83); existential group psychotherapy (78) or educational strategies (82). For the social and emotional support interventions, e.g. Andersen et al. (73) addressed stress reduction, coping skills, problem solving, and disease information. While Manne et al. (79) focused mainly on coping skills, Fukui et al. (76) included both health education, coping skills training, stress management, and psychological support. All interventions were intended to be applicable in clinical settings.

Few studies specified their primary endpoints, and many lacked calculations of statistical power. Results were reported as pre-post within-group effects (73;80;82;85), or as post-hoc analysis of subgroups e.g. two-way or three-way interaction effects such as time x group x "low stress" (73); one study (79) reported growth-curve values without any obvious comparisons to a control growth-curve slope, while the availability of absolute scores was poor.

We noted several methodological shortcomings in these studies. In four studies the intervention and control arms were imbalanced with respect to the disease stage (65;68;74;78). Few of the studies had ITT-analysis (65;66;78;79;82). Several studies included few patients. Few of the patients initially considered eligible were included in many studies. Thus there is concern about the representativeness of the study population.

The internal validity was moderate in many studies due to the application of few standardized interventions with multimodal treatments and inadequate procedure reporting. Due to the spectrum variety of outcome measurements and their respective instruments, it is difficult to calculate both internal consistencies/uncertainties and treatment effects.

The assessment instruments were predominantly well-known and validated in breast cancer populations with some generic (e.g. SF-36, POMS) and other cancer-specific inventories (e.g. FACT-B, EORTC-QLQ-C30). Some of the assessment instruments are less well-known, e.g. UCLA-3 (74). Nevertheless, most of the studies made use of inventories that are believed to have good internal consistencies with adequate Cronbachs alphas, and reliability with test-retest and inter-rater validations. The variations in internal validity are also described in earlier systematic reviews in this field (116).

There is limited evidence regarding psychosocial interventions. However, the results from CBT interventions appear promising with respect to their short-term effects on QoL. The results from other systematic reviews and metaanalyses have reached different conclusions about effects of psychosocial interventions on QoL outcome for cancer patients, although all state that more well-designed studies are needed (36;117-119). Two new systematic review are recently been published and stated that there is still limited evidence on the efficacy of psychosocial intervention for reducing fatigue (107;108;120). Kangas et al stated that the best result occurred if the psychosocial intervention are given after cancer treatment (107;108). Goedendrop et al. indicate that the best effect were seen when the interventions were specifically for fatigue.

There is no clear evidence to guide decisions about how psychosocial interventions may be designed to best assist rehabilitation of breast cancer patients. For some patients, psychosocial interventions may be helpful, but it is still unclear which patients benefit from different type of psychosocial interventions. Although subgroup analysis indicated that patients with high initial cancer-related stress might benefit more from social and emotional interventions, this needs to be investigated in new studies (73).

NUTRITION

Both the included studies were from USA and the multi-center diet intervention Women Healthy Eating and Living (WHEL). This study was initiated in 1993 and was conducted to determine if diet can reduce breast cancer recurrence. Conclusions about the effectiveness of nutrition interventions are still insufficient. Despite the prevalence of weight gain in women with breast cancer and its adverse effects, little research has been done on preventive and therapeutic interventions targeting reduction of weight and/or body fat (37). The WHEL study did not show any difference in additional breast cancer event or mortality after 7.3 years follow-up (121). The Women's Intervention Nutrition Study (WINS) indicate that a lifestyle intervention reducing dietary fat intake may improve relapse-free survival of breast cancer patient, although it did not reach statistical significant difference between the groups (122). Proactive nutritional interventions should ideally form an integral part of cancer therapy with the aim of improving clinical outcomes and quality of life (3). The benefits of achieve a healthy lifestyle go far beyond lowering cancer risk. They include lower risk of heart disease, high blood pressure, diabetes, and osteoporosis.

COMPLEMENTARY INTERVENTION

Five studies addressed the effect of complementary interventions. The interventions consist of acupuncture, yoga, art therapy, or relaxation training. Altogether these results suggest that complementary intervention after cancer treatment had small effect on the QoL and mood outcomes measured in these studies. Incidence on hot flashes were addressed in two studies, relaxation training intervention reduced the incidence, while acupuncture intervention also reduced the incidence but did not reach statistical significance. Conclusions about the effectiveness of complementary interventions could be clouded by small sample sizes, different outcome measures, different assessment methods, and short follow-ups. The popularity of complementary and alternative medicine (CAM) is illustrated by the fact that large numbers of patients subscribe to it (40). A number of CAM interventions aimed to improve symptoms or quality of life, and are backed of reasonable good evidence, e.g. acupuncture for nausea (123), aromatherapy for anxiety (40;124), music therapy for QoL (125), and relaxation therapy for stress (40).

COMPLEX INTERVENTIONS

Three studies addressed the effect of complex interventions. The results indicate that a complex intervention after cancer treatment with psychoeducational and physical activity that was investigated in two studies had unclear effect on QoL and moods (95;96). Conclusions about the effectiveness of complex interventions are clouded by small sample sizes, different outcome measures, different assessment methods, and short follow-ups.

LIMITATIONS OF THE INCLUDED STUDIES

A wide range of unidimensional and multidimensional outcome measures were used in the included studies which has prevented direct comparisons between studies. This makes it difficult to estimate effect sizes, and makes it impossible to combine the results from individual studies in a metaanalysis or even compare the different studies for outcome measures. Many trials had small sample size; thus a type II error is conceivable. The lack of no treatment control groups may be a reason for low effects of the interventions; however, it would seem unethical not to offer any intervention to women in need of rehabilitation.

This review does not imply that patients with breast cancer does not benefit from rehabilitation interventions, however we lack high quality research on this issue. Subgroups of breast cancer patient could still benefit from these interventions, but these goups could not be identified in our review. Understanding the variability of effects of different interventions is important to optimize the rehabilitation process.

IMPLICATIONS FOR FURTHER RESEARCH

As cancer patients survive longer after treatment, addressing the impact of breast cancer and its treatment on long-term outcomes becomes increasingly important. In particular, better management of cancer-related symptoms is critical for reducing suffering in cancer survivors. New high quality randomised controlled trials are warranted to assess the effectiveness of rehabilitation interventions in breast cancer patients. Few of the studies in this review have used patients who are going through new long-term medical treatments for breast cancer (adjuvant treatment with years of hormonal therapy); new studies should address this. There is a need for high quality randomised controlled trials assessing the effectiveness of physiotherapy in the treatment of arm lymphedema and disturbances in shoulder function in patients treated by SNLB for breast cancer. Additional research which addressing the importance of lifestyle interventions for breast cancer patients are also important for future recommendations. Additional research might fruitfully address whether psychosocial interventions are more effective for high-distress and high-risk patients. All RCTs in which participants and/or professionals cannot be masked to treatment arms should attempt to estimate participants' preferences.

The use of valid and reliable measures (e.g. on QoL) is essential. Ideally, any generic measures should be supplemented with a specific breast-cancer measure, which should provide detailed assessments which are sensitive to disease or treatment-related influences. Such measures should have undergone psychometric validation in a breast cancer population (126). If possible, objective performance-based measures should be used because these are less likely than self-reported measures to be influenced by emotional, social, economic, and cognitive factors, and they may enhance the potential to identify small declines in function as well as the mechanisms for those declines.

Thus, this more complex multidisciplinary treatment of breast cancer patients requires a more professional and better total management of breast cancer patients by using multidisciplinary breast cancer care in order to improve optimal recovery including improvement in quality of life of breast cancer patients (6;106;127).

Conclusion

There is limited evidence from the existing knowledge from RCTs to guide choices of interventions of any of the breast cancer rehabilitation interventions at this time. This does not imply that patients with breast cancer may not benefit from rehabilitation interventions, only that we lack high quality research on this issue.

However, this review does underline some promising results.

- There is some evidence that physical activity after breast cancer treatment improves quality of life and reduces fatigue.
- There is some evidence that CBT intervention after breast cancer treatment increase overall quality of life.
- There are some promising results that physical activity is not associated with aggravated lymphedema.

Further researches are needed on the time, mode and intensity on these interventions. No conclusions can be given for interventions thoughout treatment period Single studies in this review are showing promising, but insufficient documented effect on important question in rehabilitation of breast cancer patient. There is insufficient evidence to show whether physiotherapy or MLD was more beneficial than standard care for lymphedema or shoulder function. There is insufficient evidence to define optimal psychoeducational interventions beyond an information package that all cancer patients usually receive. Limitations in these studies include the lack of a no-intervention control group due to ethical dilemmas. There is also insufficient evidence to determine the most beneficial social and emotional support interventions from these studies. But there is some evidence that subgroups with high initial cancer-related stress will benefit more from social and emotional interventions. There is also insufficient evidence to determine the most beneficial nutrition or complementary interventions from these studies.

Clearly, more investigations are necessary, and future research is needed to improve the understanding of structured interventions; one should examine support groups and tailor psychological and physical activity interventions to meet the individual needs of distressed cancer patients.

References

REFERENCES

1. Parkin DM, Fernandez LM. Use of statistics to assess the global burden of breast cancer. Breast J 2006;12 Suppl 1:S70-S80.

2. Cancer Registry of Norway. Cancer in Norway 2007 - Cancer incidence, mortality, survival and prevalence in Norway. Oslo: Cancer Registry of Norway; 2008.

3. World Cancer Research Fund AIfCR. Food, nutrition, physical activity, and the prevention of cancer. A global perspective. Washington (DC): American Institute for Cancer Research (AICR) 2007.

4. Sosial og Helsedirektoratet. Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av pasienter med brystkreft. Nasjonale faglige retningslinger. 2007.

5. Norsk bryst cancer gruppe (NBCG).

6. Moulder S, Hortobagyi GN. Advances in the treatment of breast cancer. Clin Pharmacol Ther 2008;83(1):26-36.

7. Harris JR, Lippman ME, Veronesi U, Willett W. Breast cancer (1). N Engl J Med 1992;327(5):319-28.

8. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347(16):1233-41.

9. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347(16):1227-32.

10. Kim T, Giuliano AE, Lyman GH. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma: a metaanalysis. Cancer 2006;106(1):4-16.

11. Schlichting E, Harr ME, Sauer T, Babovic A, Karesen R. [Sentinel lymph node biopsy in breast cancer]. Tidsskr Nor Laegeforen 2006;126(16):2098-100.

12. Recht A, Edge SB, Solin LJ, Robinson DS, Estabrook A, Fine RE, et al. Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001;19(5):1539-69.

13. Recht A. Integration of systemic therapy and radiation therapy for patients with early-stage breast cancer treated with conservative surgery. Clin Breast Cancer 2003;4(2):104-13.

14. Johansen K, Lønning P, Naume B, Norderhaug I, Norum J, Jan Abel J, et al. Ny medikamentell behandling av brystkreft. Adjuvant behandling med trastuzumab ved tidlig stadium av brystkreft. Rapport fra Kunnskapssenteret 2006;Rapport nr 02 2006

15. Rietman JS, Dijkstra PU, Hoekstra HJ, Eisma WH, Szabo BG, Groothoff JW, et al. Late morbidity after treatment of breast cancer in relation to daily activities and quality of life: a systematic review. Eur J Surg Oncol 2003;29(3):229-38.

16. Lee TS, Kilbreath SL, Refshauge KM, Herbert RD, Beith JM. Prognosis of the upper limb following surgery and radiation for breast cancer. Breast Cancer Res Treat 2008;110(1):19-37.

17. Bird BR, Swain SM. Cardiac toxicity in breast cancer survivors: review of potential cardiac problems. Clin Cancer Res 2008;14(1):14-24.

18. Howell A. The 'Arimidex', Tamoxifen, Alone or in Combination (ATAC) Trial: a step forward in the treatment of early breast cancer. Rev Recent Clin Trials 2006;1(3):207-15.

19. Goodwin PJ, Esplen MJ, Winocur J, et al. Development of a weight management program in women with newly diagnosed locoregional breast cancer. I: Bitzer J, Stauber M, editors. Psychosomatic Obstretics and Gynecology.Bologna, Italy: Monduzzi Editore International Proceedings Divisions; 1995. p. 491-6.

20. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. BMJ 2007;335(7630):1134.

21. Regjeringen. Nasjonal strategi for habilitering og rehabilitering 2008-2011. St.prp. nr. 1, kapittel 9, 2007-08. 2008.

22. Dietz JH, Jr. Adaptive rehabilitation of the cancer patient. Curr Probl Cancer 1980;5(5):1-56.

23. Loge JH, Kaasa S, Hytten K. Disclosing the cancer diagnosis: the patients' experiences. Eur J Cancer 1997;33(6):878-82.

24. Lonning PE. Breast cancer prognostication and prediction: are we making progress? Ann Oncol 2007;18 Suppl 8:viii3-viii7.

25. Karki A, Simonen R, Malkia E, Selfe J. Efficacy of physical therapy methods and exercise after a breast cancer operation: a systematic review. Critical Reviews in Physical and Rehabilitation Medicine 2001;13:159-90.

26. Bouchard C, Tremblay A, Despres JP, Theriault G, Nadeau A, Lupien PJ, et al. The response to exercise with constant energy intake in identical twins. Obes Res 1994;2(5):400-10.

27. Winningham ML, MacVicar MG, Bondoc M, Anderson JI, Minton JP. Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. Oncol Nurs Forum 1989;16(5):683-9.

28. Kornblith AB, Ligibel J. Psychosocial and sexual functioning of survivors of breast cancer. Semin Oncol 2003;30(6):799-813.

29. National Comprehensive Cancer Network Distress Management Panel. *Clinical practice guidelines in oncology: Distress management, v. 1.2005*

30. Danhauer SC, Rutherford CA, Hurt G, Gentry S, Lovato J, McQuellon RP. Providing psychosocial group support for young women with breast cancer: findings from a wellness-based community collaboration. J Psychosoc Oncol 2007;25(1):103-20.

31. Arving C, Sjoden PO, Bergh J, Lindstrom AT, Wasteson E, Glimelius B, et al. Satisfaction, utilisation and perceived benefit of individual psychosocial support for breast cancer patients--a randomised study of nurse versus psychologist interventions. Patient Educ Couns 2006;62(2):235-43.

32. Samarel N. Therapeutic touch, dialogue, and women's experiences in breast cancer surgery. Holist Nurs Pract 1997;12(1):62-70.

33. Richardson A. Is breast cancer caused by late exposure to a common virus? Med Hypotheses 1997;48(6):491-7.

34. Golant M, Altman T, Martin C. Managing cancer side effects to improve quality of life: a cancer psychoeducation program. Cancer Nurs 2003;26(1):37-44.

35. Banning M. Advanced breast cancer: aetiology, treatment and psychosocial features. Br J Nurs 2007;16(2):86-90.

36. Tatrow K, Montgomery GH. Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: a meta-analysis. Journal of Behavioral Medicine 2006;29:17-27.

37. Rooney M, Wald A. Interventions for the management of weight and body composition changes in women with breast cancer. Clin J Oncol Nurs 2007;11(1):41-52.

38. Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. J Clin Oncol 2002;20(15):3302-16.

39. Ernst E, Schmidt K, Baum M. Complementary/Alternative therapies for the treatment of breast cancer. A systematic review of randomized clinical trials and a critique of current terminology. Breast J 2006;12(6):526-30.

40. Baum M, Cassileth BR, Daniel R, Ernst E, Filshie J, Nagel GA, et al. The role of complementary and alternative medicine in the management of early breast cancer: recommendations of the European Society of Mastology (EUSOMA). Eur J Cancer 2006;42(12):1711-4.

41. Bjørndal A. Slik oppsummerer vi forskning. Håndbok for Nasjonalt kunnskapssenter for helsetjenesten. 2006.

42. Cinar N, Seckin U, Keskin D, Bodur H, Bozkurt B, Cengiz O. The effectiveness of early rehabilitation in patients with modified radical mastectomy. Cancer Nurs 2008;31(2):160-5.

43. Lee TS, Kilbreath SL, Refshauge KM, Pendlebury SC, Beith JM, Lee MJ. Pectoral stretching program for women undergoing radiotherapy for breast cancer. Breast Cancer Res Treat 2007;102(3):313-21.

44. Andersen L, Højris I, Erlandsen M, Andersen J. Treatment of breast-cancer-related lymphedema with or without manual lymphatic drainage--a randomized study. Acta oncologica (Stockholm, Sweden) 2000;39(3):399-405.

45. Didem K, Ufuk YS, Serdar S, Zumre A. The comparison of two different physiotherapy methods in treatment of lymphedema after breast surgery. Breast Cancer Research & Treatment 2005;93(1):49-54.

46. Jansen RF, van G, de G, Rottier AB, Olthuis GA, van P. Immediate versus delayed shoulder exercises after axillary lymph node dissection. American Journal of Surgery 1990;160(5):481-4.

47. Lauridsen MC, Christiansen P, Hessov I. The effect of physiotherapy on shoulder function in patients surgically treated for breast cancer: A randomized study. Acta Oncologica 2005;44(5):449-57.

48. McNeely ML, Magee DJ, Lees AW, Bagnall KM, Haykowsky M, Hanson J. The addition of manual lymph drainage to compression therapy for breast cancer related lymphedema: a randomized controlled trial. Breast Cancer Research & Treatment 2004;86(2):95-106.

49. Basen-Engquist K, Taylor CLC, Rosenblum C, Smith MA, Shinn EH, Greisinger A, et al. Randomized pilot test of a lifestyle physical activity intervention for breast cancer survivors. Patient Educ Couns 2006;64(1-3):225-3.

50. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. Journal of Clinical Oncology 2003;21(9):1660-8.

51. Courneya KS, Segal RJ, Gelmon K, Reid RD, Mackey JR, Friedenreich CM, et al. Six-month follow-up of patient-rated outcomes in a randomized controlled trial of exercise training during breast cancer chemotherapy. Cancer Epidemiol Biomarkers Prev 2007;16(12):2572-8.

52. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. Journal of Clinical Oncology 2007;25(28):4396-404.

53. Daley AJ, Crank H, Saxton JM, Mutrie N, Coleman R, Roalfe A. Randomized trial of exercise therapy in women treated for breast cancer. Journal of Clinical Oncology 2007;25(13):1713-21.

54. Milne HM, Wallman KE, Gordon S, Courneya KS. Effects of a combined aerobic and resistance exercise program in breast cancer survivors: a randomized controlled trial. Breast Cancer Res Treat 2008;108(2):279-88.

55. Mock V, Frangakis C, Davidson NE, Ropka ME, Pickett M, Poniatowski B, et al. Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. Psychooncology 2005;14(6):464-77.

56. Mutrie N, Campbell AM, Whyte F, McConnachie A, Emslie C, Lee L, et al. Benefits of supervised group exercise programme for women being treated for early stage breast cancer: pragmatic randomised controlled trial. BMJ 2007;334(7592):517.

57. Vallance JK, Courneya KS, Plotnikoff RC, Dinu I, Mackey JR. Maintenance of physical activity in breast cancer survivors after a randomized trial. Med Sci Sports Exerc 2008;40(1):173-80.

58. Vallance JKH, Courneya KS, Plotnikoff RC, Yasui Y, Mackey JR. Randomized controlled trial of the effects of print materials and step pedometers on physical activity and quality of life in breast cancer survivors. Journal of Clinical Oncology 2007;25(17):2352-9.

59. Ahmed RL, Thomas W, Yee D, Schmitz KH. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. Journal of Clinical Oncology 2006;24(18):2765-72.

60. Ohira T, Schmitz KH, Ahmed RL, Yee D. Effects of weight training on quality of life in recent breast cancer survivors: The weight training for breast cancer survivors (WTBS) study. Cancer 2006;106(9):2076-83.

61. Pinto BM, Frierson GM, Rabin C, Truzno JJ, Marcus BH. Home-based physical activity intervention for breast cancer patients. Journal of Clinical Oncology 2005;#20;23(15):3577-87.

62. Schmitz KH, Ahmed RL, Hannan PJ, Yee D. Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin, and insulin-like growth factor axis proteins. Cancer Epidemiol Biomarkers Prev 2005;14(7):1672-80.

63. Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J, et al. Structured exercise improves physical functioning in women with stages I and II breast cancer: results of a randomized controlled trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2001;19(3):657-65.

64. Andersen BL, Farrar WB, Golden-Kreutz D, Emery CF, Glaser R, Crespin T, et al. Distress reduction from a psychological intervention contributes to improved health for cancer patients. Brain Behav Immun 2007;21(7):953-61.

65. Antoni MH, Wimberly SR, Lechner SC, Kazi A, Sifre T, Urcuyo KR, et al. Reduction of cancer-specific thought intrusions and anxiety symptoms with a stress management intervention among women undergoing treatment for breast cancer. Am J Psychiatry 2006;163(10):1791-7.

66. Antoni MH, Lechner SC, Kazi A, Wimberly SR, Sifre T, Urcuyo KR, et al. How stress management improves quality of life after treatment for breast cancer. J Consult Clin Psychol 2006;74(6):1143-52.

67. Arving C, Sjoden PO, Bergh J, Hellbom M, Johansson B, Glimelius B, et al. Individual psychosocial support for breast cancer patients: a randomized study of nurse versus psychologist interventions and standard care. Cancer Nurs 2007;30(3):E10-E19.

68. Classen CC, Kraemer HC, Blasey C, Giese-Davis J, Koopman C, Gronskaya Palesh O, et al. Supportive-expressive group therapy for primary breast cancer patients: A randomized prospective multicenter trial. Psychooncology 2008;17(5):438-Oncology.

69. Cohen M, Fried G. Comparing relaxation training and cognitive-behavioral group therapy for women with breast cancer. Research on Social Work Practice 2007;17(3):313-23.

70. Dirksen SR, Epstein DR. Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. J Adv Nurs 2008;61(6):664-75.

71. Meneses KD, McNees P, Loerzel VW, Su X, Zhang Y, Hassey LA. Transition from treatment to survivorship: effects of a psychoeducational intervention on quality of life in breast cancer survivors. Oncology Nursing Forum Online 2007;34(5):1007-16.

72. Sandgren AK, McCaul KD. Long-term telephone therapy outcomes for breast cancer patients. Psychooncology 2007;16(1):38-47.

73. Andersen BL, Farrar WB, Golden-Kreutz DM, Glaser R, Emery CF, Crespin TR, et al. Psychological, behavioral, and immune changes after a psychological intervention: A clinical trial. Journal of Clinical Oncology 2004;22(17):3570-80.

74. Coleman EA, Tulman L, Samarel N, Wilmoth MC, Rickel L, Rickel M, et al. The effect of telephone social support and education on adaptation to breast cancer during the year following diagnosis. Oncology Nursing Forum Online 2005;32(4):822-9.

75. Edelman S, Bell DR, Kidman AD. Group CBT versus supportive therapy with patients who have primary breast cancer. Journal of Cognitive Psychotherapy 1999;13(3):189-202.

76. Fukui S, Kugaya A, Okamura H, Kamiya M, Koike M, Nakanishi T, et al. A psychosocial group intervention for Japanese women with primary breast carcinoma. Cancer 2000;89(5):1026-36.

77. Gustafson DH, Hawkins R, Pingree S, McTavish F, Arora NK, Mendenhall J, et al. Effect of computer support on younger women with breast cancer. Journal of General Internal Medicine 2001;16(7):435-45.

78. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, Ikin J, et al. Cognitive-existential group psychotherapy for women with primary breast cancer: a randomised controlled trial. Psycho-Oncology 2003;12(6):532-46.

79. Manne SL, Winkel G, Grana G, Ross S, Ostroff JS, Fox K, et al. Couple-focused group intervention for women with early stage breast cancer. Journal of Consulting & Clinical Psychology 2005;73(4):634-46.

80. Owen JE, Klapow JC, Roth DL, Shuster Jr JL, Bellis J, Meredith R, et al. Randomized pilot of a self-guided Internet coping group for women with early-stage breast cancer. Annals of Behavioral Medicine 2005;30(1):54-64.

81. Sandgren AK, McCaul KD. Short-term effects of telephone therapy for breast cancer patients. Health Psychology 2003;22(3):310-5.

82. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. Journal of Clinical Oncology 2005;23(25):6083-96.

83. Simpson JS, Carlson LE, Trew ME. Effect of group therapy for breast cancer on healthcare utilization. Cancer Practice 2001;9(1):19-26.

84. Stanton AL, Ganz PA, Kwan L, Meyerowitz BE, Bower JE, Krupnick JL, et al. Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients. Journal of Clinical Oncology 2005;23(25):6009-18.

85. Yates P, Aranda S, Hargraves M, Mirolo B, Clavarino A, McLachlan S, et al. Randomized controlled trial of an educational intervention for managing fatigue in women receiving adjuvant chemotherapy for early-stage breast cancer. Journal of Clinical Oncology 2005;23(25):6027-36.

86. Simpson JS, Carlson LE, Beck CA, Patten S. Effects of a brief intervention on social support and psychiatric morbidity in breast cancer patients. Psycho-Oncology 2002;11(4):282-94.

87. Saquib N, Natarajan L, Rock CL, Flatt SW, Madlensky L, Kealey S, et al. The impact of a long-term reduction in dietary energy density on body weight within a randomized diet trial. Nutr Cancer 2008;60(1):31-8.

88. Thomson CA, Rock CL, Giuliano AR, Newton TR, Cui H, Reid PM, et al. Longitudinal changes in body weight and body composition among women previously treated for breast cancer consuming a high-vegetable, fruit and fiber, low-fat diet. Eur J Nutr 2005;44(1):18-25.

89. Banerjee B, Vadiraj HS, Ram A, Rao R, Jayapal M, Gopinath KS, et al. Effects of an integrated yoga program in modulating psychological stress and radiation-induced genotoxic stress in breast cancer patients undergoing radiotherapy. Integrative Cancer Therapies 2007;6(3):242-50.

90. Deng G, Vickers A, Yeung S, D'Andrea GM, Xiao H, Heerdt AS, et al. Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. Journal of Clinical Oncology 2007;25(35):5584-90.

91. Fenlon DR, Corner JL, Haviland JS. A randomized controlled trial of relaxation training to reduce hot flashes in women with primary breast cancer. J Pain Symptom Manage 2008;35(4):397-405.

92. Oster I, Svensk AC, Magnusson E, Thyme KE, Sjodin M, Astrom S, et al. Art therapy improves coping resources: a randomized, controlled study among women with breast cancer. Palliative and Supportive Care 2006;4(1):57-64.

93. Walker LG, Walker MB, Ogston K, Heys SD, Ah-See AK, Miller ID, et al. Psychological, clinical and pathological effects of relaxation training and guided imagery during primary chemotherapy. Br J Cancer 1999;80(1-2):262-8.

94. Demark-Wahnefried W, Case LD, Blackwell K, Marcom PK, Kraus W, Aziz N, et al. Results of a diet/exercise feasibility trial to prevent adverse

body composition change in breast cancer patients on adjuvant chemotherapy. Clinical Breast Cancer 2008;8(1):70-9.

95. Hartmann U, Muche R, Reuss-Borst M. Effects of a step-by-step inpatient rehabilitation programme on quality of life in breast cancer patients. Onkologie 2007;30(4):177-82.

96. Cho O-H, Yoo Y-S, Kim N-C. Efficacy of comprehensive group rehabilitation for women with early breast cancer in South Korea. Nursing & Health Sciences 2006;8(3):140-6.

97. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev 2005;14(7):1588-95.

98. Mandelblatt J, Armetta C, Yabroff KR, Liang W, Lawrence W. Descriptive review of the literature on breast cancer outcomes: 1990 through 2000. J Natl Cancer Inst Monogr 2004;(33):8-44.

99. Haid A, Koberle-Wuhrer R, Knauer M, Burtscher J, Fritzsche H, Peschina W, et al. Morbidity of breast cancer patients following complete axillary dissection or sentinel node biopsy only: a comparative evaluation. Breast Cancer Res Treat 2002;73(1):31-6.

100. Rietman JS, Geertzen JH, Hoekstra HJ, Baas P, Dolsma WV, de Vries J, et al. Long term treatment related upper limb morbidity and quality of life after sentinel lymph node biopsy for stage I or II breast cancer. Eur J Surg Oncol 2006;32(2):148-52.

101. Canavese G, Catturich A, Vecchio C, Tomei D, Gipponi M, Bruzzi P, et al. Prognostic role of lymph-node level involvement in patients undergoing axillary dissection for breast cancer. Eur J Surg Oncol 1998;24(2):104-9.

102. Jatoi I. Management of the axilla in primary breast cancer. Surg Clin North Am 1999;79(5):1061-73.

103. Cave J, Jones A. Physiotherapy improves shoulder function after treatment in women with early breast cancer. Cancer Treat Rev 2006;32(5):398-401.

104. Heidi Anttila, Anne Kärki, Ulla-Maija Rautakorpi, and the expert group. Lymphoedema therapy in breast cancer patients. Effectiveness, current practices and costs. Finohta's report 2007;30

105. Preston N, Seers K, Mortimer P. Physical therapies for reducing and controlling lymphoedema of the limbs. Cochrane Database of Systematic Reviews: Reviews 2008 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10 1002/14651858 CD003141 pub2 2008;

106. Cramp F, Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev 2008;(2):CD006145.

107. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull 2008;134(5):700-41.

108. Kangas M, Bovbjerg DH, Montgomery GH. "Cancer-related fatigue: A systematic and meta-analytic review of non-pharmacological therapies for cancer patients": Correction to Kangas, Bovbjerg, and Montgomery (2008). Psychol Bull 2009;135(1):172.

109. Shamley DR, Barker K, Simonite V, Beardshaw A. Delayed versus immediate exercises following surgery for breast cancer: a systematic review. Breast Cancer Research and Treatment 2005;90:263-71.

110. Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 2006;(4):CD005001.

111. Irwin ML, McTiernan A, Baumgartner RN, Baumgartner KB, Bernstein L, Gilliland FD, et al. Changes in body fat and weight after a breast cancer diagnosis: influence of demographic, prognostic, and lifestyle factors. J Clin Oncol 2005;23(4):774-82.

112. Goodwin PJ, Ennis M, Pritchard KI, McCready D, Koo J, Sidlofsky S, et al. Adjuvant treatment and onset of menopause predict weight gain after breast cancer diagnosis. J Clin Oncol 1999;17(1):120-9.

113. McTiernan A, Wu L, Chen C, Chlebowski R, Mossavar-Rahmani Y, Modugno F, et al. Relation of BMI and physical activity to sex hormones in postmenopausal women. Obesity (Silver Spring) 2006;14(9):1662-77.

114. Abrahamson PE, Gammon MD, Lund MJ, Britton JA, Marshall SW, Flagg EW, et al. Recreational physical activity and survival among young women with breast cancer. Cancer 2006;107(8):1777-85.

115. Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. JAMA 2005;293(20):2479-86.

116. Newell SA, Sanson-Fisher RW, Savolainen NJ. Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. J Natl Cancer Inst 2002;94(8):558-84.

117. Devine EC, Westlake SK. The effects of psychoeducational care provided to adults with cancer: meta-analysis of 116 studies. Oncol Nurs Forum 1995;22(9):1369-81.

118. Rehse B, Pukrop R. Effects of psychosocial interventions on quality of life in adult cancer patients: meta analysis of 37 published controlled outcome studies. Patient Educ Couns 2003;50(2):179-86.

119. Williams S, Dale J. The effectiveness of treatment for depression/depressive symptoms in adults with cancer: a systematic review. Br J Cancer 2006;94(3):372-90.

120. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Psychosocial interventions for reducing fatigue during cancer treatment in adults. Cochrane Database Syst Rev 2009;(1):CD006953.

121. Pierce JP, Natarajan L, Caan BJ, Parker BA, Greenberg ER, Flatt SW, et al. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the Women's Healthy Eating and Living (WHEL) randomized trial. JAMA 2007;298(3):289-98.

122. Chlebowski RT, Blackburn GL, Thomson CA, Nixon DW, Shapiro A, Hoy MK, et al. Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. J Natl Cancer Inst 2006;98(24):1767-76.

123. Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, Issell BF, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database Syst Rev 2006;(2):CD002285.

124. Fellowes D, Barnes K, Wilkinson SS. Aromatherapy and massage for symptom relief in patients with cancer (WITHDRAWN). Cochrane Database Syst Rev 2008;(4):CD002287.

125. Hanser SB, Bauer-Wu S, Kubicek L, Healey M, Manola J, Hernandez M, et al. Effects of a music therapy intervention on quality of life and distress in women with metastatic breast cancer. Journal of the Society for Integrative Oncology 2006;4(3):116-24.

126. Bottomley A, Therasse P. Quality of life in patients undergoing systemic therapy for advanced breast cancer. Lancet Oncology 2002;3:620-8.

127. Gomide LB, Matheus JP, Candido dos Reis FJ. Morbidity after breast cancer treatment and physiotherapeutic performance. Int J Clin Pract 2007;61(6):972-82.

EXCLUDED STUDIES (REASONS FOR EXCLUSION ARE LISTED IN APPENDIX 2)

Aghili M, Farhan F, Rade M. A pilot study of the effects of programmed aerobic exercise on the severity of fatigue in cancer patients during external radiotherapy. European Journal of Oncology Nursing 2007;11(2):179-82.

Akechi T, Taniguchi K, Suzuki S, Okamura M, Minami H, Okuyama T, et al. Multifaceted psychosocial intervention program for breast cancer patients after first recurrence: Feasibility study. [References]. Psychooncology 2007;16(6):517-Oncology.

Allard N. Day surgery and recovery in women with a suspicious breast lesion: evaluation of a psychoeducational nursing intervention. Can Oncol Nurs J 2006;16(3):137-53.

Allen SM, Shah AC, Nezu AM, Nezu CM, Ciambrone D, Hogan J, et al. A problem-solving approach to stress reduction among younger women with breast carcinoma: a randomized controlled trial. Cancer 2002;94(12):3089-100.

Aranda S, Schofield P, Weih L, Milne D, Yates P, Faulkner R. Meeting the support and information needs of women with advanced breast cancer: a randomised controlled trial. Br J Cancer 2006;95(6):667-73.

Arving C, Sjoden P-O, Bergh J, Lindstrom AT, Wasteson E, Glimelius B, et al. Satisfaction, utilisation and perceived benefit of individual psychosocial support for breast cancer patients-A randomised study of nurse versus psychologist interventions. Patient Education & Counseling 2006;62(2):235-43.

Badger T, Segrin C, Dorros SM, Meek P, Lopez AM. Depression and anxiety in women with breast cancer and their partners. Nurs Res 2007;56(1):44-53.

Badger TA, Braden CJ, Mishel MH. Depression burden, self-help interventions, and side effect experience in women receiving treatment for breast cancer. Oncology Nursing Forum 2001 Apr;28(3):567-74.

Badger TA, Braden CJ, Longman AJ, Mishel MM. Depression burden, self-help interventions, and social support in women receiving treatment for breast cancer. Journal of Psychosocial Oncology 1999;17(2):17-35.

Badgio PC, Worden BL. Cognitive functioning and aging in women. J Women Aging 2007;19(1-2):13-30.

Bar-Sela G, Atid L, Danos S, Gabay N, Epelbaum R. Art therapy improved depression and influenced fatigue levels in cancer patients on chemotherapy. Psychooncology 2007;16(11):980-4.

Bellver A. Efficacy of a group therapy on quality of life and emotional state in women with breast cancer. Psicooncologia 2007;4(1):133-42.

Bendz I, Fagevik OM. Evaluation of immediate versus delayed shoulder exercises after breast cancer surgery including lymph node dissection - A randomised controlled trial. Breast 2002;11(3):241-8.

Beurskens CHG, van Uden CJT, Strobbe LJA, Oostendorp RAB, Wobbes T. The efficacy of physiotherapy upon shoulder function following axillary dissection in breast cancer, a randomized controlled study. BMC Cancer 2007;7:166.

Bicego D, Brown K, Ruddick M, Storey D, Wong C, Harris SR. Exercise for women with or at risk for breast cancer-related lymphedema. Phys Ther 2006;86(10):1398-405.

Billhult A, Lindholm C, Gunnarsson R, Stener-Victorin E. The effect of massage on cellular immunity, endocrine and psychological factors in women with breast cancer - A randomized controlled clinical trial. Autonomic Neuroscience: Basic and Clinical 2008;140(1-2):88-95.

Blackburn GL, Wang KA. Dietary fat reduction and breast cancer outcome: results from the Women's Intervention Nutrition Study (WINS). Am J Clin Nutr 2007;86(3):s878-s881.

Bloom JR, Stewart SL, Johnston M, Banks P, Fobair P. Sources of support and the physical and mental well-being of young women with breast cancer. Social Science & Medicine 2001 Dec;53(11):1513-24.

Box RC, Reul-Hirche HM, Bullock-Saxton JE, Furnival CM. Physiotherapy after breast cancer surgery: Results of a randomised controlled study to minimise lymphoedema. Breast Cancer Research & Treatment 2002;75(1):51-64.

Box RC, Reul-Hirche HM, Bullock-Saxton JE, Furnival CM. Shoulder movement after breast cancer surgery: Results of a randomised controlled study of postoperative physiotherapy. Breast Cancer Research & Treatment 2002;75(1):35-50.

Braden CJ, Mishel MH, Longman AJ. Self-Help Intervention Project: women receiving breast cancer treatment. Cancer Practice: A Multidisciplinary Journal of Cancer Care 1998 Mar;6(2):87-98.

Budin WC, Hoskins CN, Haber J, Sherman DW, Maislin G, Cater JR, et al. Breast cancer: education, counseling, and adjustment among patients and partners: a randomized clinical trial. Nurs Res 2008;57(3):199-213.

Bultz BD, Speca M, Brasher PM, Geggie PHS, Page S. A randomized controlled trial of a brief psychoeducational support group for partners of early stage breast cancer patients. Psycho-Oncology 2000 Jul;9(4):303-13.

Cadmus LA. Exercise and quality of life during and after treatment for breast cancer. Dissertation Abstracts International: Section B: The Sciences and Engineering 2008;68(12-B):2008, pp-B.

Cameron LD, Booth RJ, Schlatter M, Ziginskas D, Harman JE. Changes in emotion regulation and psychological adjustment following use of a group psychosocial support program for women recently diagnosed with breast cancer. Psychooncology 2007;16(3):171-Oncology.

Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain Behav Immun 2007;21(8):1038-49.

Carlsson M, Arman M, Backman M, Hamrin E. Coping in Women with Breast Cancer in Complementary and Conventional Care Over 5 Years Measured by the Mental Adjustment to Cancer Scale. Journal of Alternative and Complementary Medicine 2005 Jun;11(3):441-7.

Chan CLW, Ho RTH, Lee PWH, Cheng JYY, Leung PPY, Foo W, et al. A randomized controlled trial of psychosocial interventions using the psychophysiological framework for Chinese breast cancer patients. Journal of Psychosocial Oncology 2006;24(1):3-26.

Coucke P, Barthelemy N, Jansen N, Triviere N, Jerusalem G. Ductal Carcinoma In Situ (DCIS): Can radiotherapy be avoided? Rev Med Liege 2008;63(2):75-81.

Courneya KS, Segal RJ, Gelmon K, Reid RD, Mackey JR, Friedenreich, et al. Predictors of supervised exercise adherence during breast cancer chemotherapy. Med Sci Sports Exerc 2008;40(6):1180-7.

Courneya KS, Jones LW, Mackey JR, Fairey AS. Exercise beliefs of breast cancer survivors before and after participation in a randomized controlled trial. International Journal of Behavioral Medicine 2006;13(3):259-64.

Courneya KS, McKenzie DC, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Moderators of the effects of exercise training in breast cancer patients receiving chemotherapy: a randomized controlled trial. Cancer 2008;112(8):1845-53.

Courneya KS, McKenzie DC, Reid RD, Mackey JR, Gelmon K, Friedenreich CM, et al. Barriers to supervised exercise training in a randomized controlled trial of breast cancer patients receiving chemotherapy. Ann Behav Med 2008;35(1):116-22.

Daley AJ, Crank H, Mutrie N, Saxton JM, Coleman R. Determinants of adherence to exercise in women treated for breast cancer. European Journal of Oncology Nursing 2007;11(5):392-9.

Daley AJ, Crank H, Mutrie N, Saxton JM, Coleman R. Patient recruitment into a randomised controlled trial of supervised exercise therapy in sedentary women treated for breast cancer. Contemporary Clinical Trials 2007;28(5):603-13.

De Rezende LF, Franco RL, De Rezende MF, Beletti PO, Morais SS, Costa Gurgel MS. Two exercise schemes in postoperative breast cancer: Comparison of effects on shoulder movement and lymphatic disturbance. Tumori 2006;92(1):55-61.

Del Bianco P, Zavagno G, Burelli P, Scalco G, Barutta L, Carraro P, et al. Morbidity comparison of sentinel lymph node biopsy versus conventional axillary lymph node dissection for breast cancer patients: Results of the sentinella-GIVOM Italian randomised clinical trial. Eur J Surg Oncol 2008;34(5):508-13.

Demark-Wahnefried W, Clipp EC, Lipkus IM, Lobach D, Snyder DC, Sloane R, et al. Main outcomes of the FRESH START trial: a sequentially tailored, diet and exercise

mailed print intervention among breast and prostate cancer survivors. J Clin Oncol 2007;25(19):2709-18.

Dong H-Y, Wang Z-F, Cai L. Correlation between quality of life and rehabilitative guidance education in the postoperative patients with breast cancer. Chinese Journal of Clinical Rehabilitation 2006;10(42):28-30.

Edgar L, Rosberger Z, Collet J-P. Lessons learned: Outcomes and methodology of a coping skills intervention trial comparing individual and group formats for patients with cancer. International Journal of Psychiatry in Medicine 2001;31(3):289-304.

Edgar LJ, Remmer J, Rosberger Z, Rapkin B. Evaluating a volunteer cancer support service. Journal of Psychosocial Oncology 2003;21(1):53-72.

Edgar,L., Rosberger,Z. & Nowlis,D. Coping with cancer during the first year after diagnosis. Assessment and intervention. Cancer 1992: 69, 817-828.

Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. Oncology Nursing Forum Online 2007;34(5):E51-E59.

Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. Effects of exercise training on fasting insulin, insulin resistance, insulin-like growth factors, and insulin-like growth factor binding proteins in postmenopausal breast cancer survivors: a randomized controlled trial. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 2003;12(8):721-7.

Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. Randomized controlled trial of exercise and blood immune function in postmenopausal breast cancer survivors. Journal of Applied Physiology 2005 Apr;98(4):1534-40.

Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Martin BS, et al. Effect of exercise training on C-reactive protein in postmenopausal breast cancer survivors: a randomized controlled trial. Brain, Behavior, & Immunity 2005 Sep;(5).

Fernandez E, Gallus S, La Vecchia C. Nutrition and cancer risk: an overview. Journal of the British Menopause Society 2006;12(4):139-42.

Filshie J. An RCT comparing preoperative brief hypnosis with an attention control on peroperative medication, pain and side-effects postoperatively. Focus on Alternative and Complementary Therapies 2008;13(1):47-8.

Fleissig A, Fallowfield LJ, Langridge CI, Johnson L, Newcombe RG, Dixon JM, et al. Post-operative arm morbidity and quality of life. Breast Cancer Res Treat 2006;95(3):279-93.

Forchuk C, Baruth P, Prendergast M, Holliday R, Bareham R, Brimner S, et al. Post-operative arm massage: a support for women with lymph node dissection. Cancer Nursing 2004 Jan;27(1):25-33.

Forchuk C, Baruth P, Prendergast M, Holliday R, Bareham R, Brimner S, et al. Post-operative Arm Massage: A Support for Women With Lymph Node Dissection. Holist Nurs Pract 2004 Sep;18(5):264-72.

Gold EB, Flatt SW, Pierce JP, Bardwell WA, Hajek RA, Newman VA, et al. Dietary factors and vasomotor symptoms in breast cancer survivors: The WHEL Study. Menopause 2006;13(3):423-33.

Gordon LG, Battistutta D, Scuffham P, Tweeddale M, Newman B. The impact of re-habilitation support services on health-related quality of life for women with breast cancer. Breast Cancer Research & Treatment 2005 Oct;93(3):217-26.

Gustafson DH, Hawkins R, McTavish F, Pingree S, Chen WC, Volrathongchai K, et al. Internet-based interactive support for cancer patients: Are integrated systems better?. J Commun 2008;58(2):238-57.

Gustafson DH, Hawkins R, Pingree S, McTavish F, Arora NK, Mendenhall J, Cella DF, Serlin RC, Apantaku FM, Stewart J, Salner A. 2001. Effect of computer support on younger women with breast cancer. Journal of General Internal Medicine., 16(7): 435-445.

Harris SR, Hugi MR, Olivotto IA, Levine M. Clinical practice guidelines for the care and treatment of breast cancer: 11. Lymphedema. CMAJ: Canadian Medical Associa-tion Journal 2001;164(2):191-9.

Harris SR, Hugi MR, Olivotto IA, Niesen-Vertommen SL, Dingee CK, Eddy F, et al. Upper extremity rehabilitation in women with breast cancer after axillary dissection: Clinical practice guidelines. Critical Reviews in Physical and Rehabilitation Medicine 2001;13(2-3):91-103.

Headley JA, Ownby KK, John LD. The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. Oncology Nursing Forum 2004 Sep;31(5):977-83.

Heim ME, Malsburg MLE, Niklas A. Randomized controlled trial of a structured training program in breast cancer patients with tumor-related chronic fatigue. On-kologie 2007;30(8-9):429-34.

Husted MA, Haugaard K, Soerensen J, Bokmand S, Friis E, Holtveg H, et al. Arm morbidity following sentinel lymph node biopsy or axillary lymph node dissection: A study from the Danish Breast Cancer Cooperative Group. Breast 2008;17(2):138-47.

Hutnick NA, Williams NI, Kraemer WJ, Orsega-Smith E, Dixon RH, Bleznak AD, et al. Exercise and lymphocyte activation following chemotherapy for breast cancer. Medicine & Science in Sports & Exercise 2005 Nov;37(11):1827-35.

Hwang JH, Chang HJ, Shim YH, Park WH, Park W, Huh SJ, et al. Effects of super-vised exercise therapy in patients receiving radiotherapy for breast cancer. Yonsei Med J 2008;49(3):443-50.

Irwin ML, Cadmus L, Alvarez-Reeves M, O'Neil M, Mierzejewski E, Latka R, et al. Recruiting and retaining breast cancer survivors into a randomized controlled exer-

cise trial: the Yale Exercise and Survivorship Study. Cancer 2008;112(11 Suppl):2593-606.

Jen KL, Djuric Z, DiLaura NM, Buison A, Redd JN, Maranci V, et al. Improvement of metabolism among obese breast cancer survivors in differing weight loss regimens. Obesity Research 2004 Feb;12(2):306-12.

Johnsson A, Fornander T, Olsson M, Nystedt M, Johansson H, Rutqvist LE. Factors associated with return to work after breast cancer treatment. Acta Oncol 2007;46(1):90-6.

Jones RB, Pearson J, Cawsey AJ, Bental D, Barrett A, White J, et al. Effect of different forms of information produced for cancer patients on their use of the information, social support, and anxiety: Randomised trial. BMJ: British Medical Journal 2006;332(7547):

Jones LW, Courneya KS, Fairey AS, Mackey JR. Does the theory of planned behavior mediate the effects of an oncologist's recommendation to exercise in newly diagnosed breast cancer survivors? Results from a randomized controlled trial. Health Psychology 2005 Mar;24(2):189-97.

Jones LW, Courneya KS, Fairey AS, Mackey JR. Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: a single-blind, randomized controlled trial. Annals of Behavioral Medicine 2004 Oct;28(2):105-13.

Karki A, Simonen R, Malkia E, Selfe J. Efficacy of physical therapy methods and exercise after a breast cancer operation: a systematic review. Critical Reviews in Physical and Rehabilitation Medicine 2001;13:159-90.

Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Simpson JM, Hansen RD. Progressive resistance training and stretching following surgery for breast cancer: study protocol for a randomised controlled trial. BMC Cancer 2006;6:273.

Kimman ML, Voogd AC, Dirksen CD, Falger P, Hupperets P, Keymeulen K, et al. Improving the quality and efficiency of follow-up after curative treatment for breast cancer--rationale and study design of the MaCare trial. BMC Cancer 2007;7:1.

Kissane DW, Love A, Hatton A, Bloch S, Smith G, Clarke DM, et al. Effect of cognitive-existential group therapy on survival in early-stage breast cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2004;22(21):4255-60.

Kligman L, Wong RKS, Johnston M, Laetsch NS. The treatment of lymphedema related to breast cancer: A systematic review and evidence summary. Supportive Care in Cancer 2004;12(6):421-31.

Larsson G, Starrin B. Relaxation training as an integral part of caring activities for cancer patients: Effects on wellbeing. Scandinavian Journal of Caring Sciences 1992;6(3):179-85.

Lauridsen MC, Torsleff KR, Husted H, Erichsen C. Physiotherapy treatment of late symptoms following surgical treatment of breast cancer. Breast 2000;9(1):45-51.

Lee V, Robin Cohen S, Edgar L, Laizner AM, Gagnon AJ. Meaning-making intervention during breast or colorectal cancer treatment improves self-esteem, optimism, and self-efficacy. Soc Sci Med 2006;62(12):3133-45.

Leon-Pizarro C, Gich I, Barthe E, Rovirosa A, Farrus B, Casas F, et al. A randomized trial of the effect of training in relaxation and guided imagery techniques in improving psychological and quality-of-life indices for gynecologic and breast brachytherapy patients. Psychooncology 2007;16(11):971-9.

Levine EG, Eckhardt J, Targ E. Change in post-traumatic stress symptoms following psychosocial treatment for breast cancer. Psycho-Oncology 2005 Aug;14(8):618-35.

Lindemalm C, Mozaffari F, Choudhury A, Granstam-Bjorneklett H, Lekander M, Nilsson B, et al. Immune response, depression and fatigue in relation to support intervention in mammary cancer patients. Support Care Cancer 2008;16(1):57-65.

Marchioro G, Azzarello G, Checchin F, Perale M, Segati R, Sampognaro E, et al. The impact of a psychological intervention on quality of life in non-metastatic breast cancer. European Journal of Cancer 1996 Aug;32A(9):1612-5.

McArdle JMC, George WD, McArdle CS, Smith DC, Moodie AR, Hughson AVM, et al. Psychological support for patients undergoing breast cancer surgery: a randomised study. BMJ 1996 Mar 30;312(7034):813-6.

Megens A, Harris SR. Physical therapist management of lymphedema following treatment for breast cancer: a critical review of its effectiveness. Physical Therapy 1998 Dec;78(12):1302-11.

Mishel MH, Germino BB, Gil KM, Belyea M, Laney IC, Stewart J, et al. Benefits from an uncertainty management intervention for African-American and Caucasian older long-term breast cancer survivors. Psycho-Oncology 2005;14(11):962-Oncology.

Miyashita M. A randomized intervention study for breast cancer survivors in Japan: effects of short-term support group focused on possible breast cancer recurrence. Cancer Nursing 2005 Jan;28(1):70-8.

Moadel AB, Shah C, Wylie-Rosett J, Harris MS, Patel SR, Hall CB, et al. Randomized controlled trial of yoga among a multiethnic sample of breast cancer patients: Effects on quality of life. J Clin Oncol 2007;25(28):4387-95.

Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncology Nursing Forum 1997 Jul;24(6):991-1000.

Mock V, Pickett M, Ropka ME, Lin EM, Stewart KJ, Rhodes VA, et al. Fatigue and quality of life outcomes of exercise during cancer treatment. Cancer Practice: A Multidisciplinary Journal of Cancer Care 2001 May;9(3):119-27.

Mock V, Frangakis C, Davidson NE, Ropka ME, Pickett M, Poniatowski B, et al. Exercise manages fatigue during breast cancer treatment: A randomized controlled trial. Psycho-Oncology 2005;14(6):464-Oncology.

Mustian KM, Katula JA, Zhao H. A pilot study to assess the influence of tai chi chuan on functional capacity among breast cancer survivors. The Journal of Supportive Oncology 2006;4(3):139-45.

Mustian KM, Palesh OG, Flecksteiner SA. Tai Chi Chuan for breast cancer survivors. Medicine and Sport Science 2008;52:209-17.

Najm WI. Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. Medical Acupuncture 2008;20(2):133.

Narvaez A, Rubinos C, Cortes-Funes F, Gomez R, Garcia A. Evaluation of effectiveness of a group cognitive-behavioral therapy on body image, self-esteem, sexuality and distress in breast cancer patients. Psicooncologia 2008;5(1):93-102.

Nikander R, Sievanen H, Ojala K, Oivanen T, Kellokumpu-Lehtinen PL, Saarto T. Effect of a vigorous aerobic regimen on physical performance in breast cancer patients - a randomized controlled pilot trial. Acta Oncol 2007;46(2):181-6.

Northouse L, Kershaw T, Mood D, Schafenacker A. Effects of a family intervention on the quality of life of women with recurrent breast cancer and their family caregivers. Psycho-Oncology 2005;14(6):478-Oncology.

Northouse LL, Walker J, Schafenacker A, Mood D, Mellon S, Galvin E, et al. A family-based program of care for women with recurrent breast cancer and their family members. Oncology Nursing Forum Online 2002 Nov;29(10):1411-9.

Oldervoll LM, Kaasa S, Hjermstad MJ, Lund JA, Loge JH. Physical exercise results in the improved subjective well-being of a few or is effective rehabilitation for all cancer patients? European Journal of Cancer 2004;40(7):951-62.

Patterson M, Maurer S, Adler SR, Avins AL. A novel clinical-trial design for the study of massage therapy. Complement Ther Med 2008;16(3):169-76.

Payne JK Held J, Thorpe J, Shaw H. Effect of exercise on biomarkers, fatigue, sleep disturbances, and depressive symptoms in older women with breast cancer receiving hormonal therapy. Oncol Nurs Forum 2008;2008 Jul;35(4):635-42.

Petersson LM, Nordin K, Glimelius B, Brekkan E, Sjoden PO, Berglund G. Differential effects of cancer rehabilitation depending on diagnosis and patients' cognitive coping style. Psychosomatic Medicine 2002 Nov;64(6):971-80.

Pickett M, Mock V, Ropka ME, Cameron L, Coleman M, Podewils L. Adherence to moderate-intensity exercise during breast cancer therapy. Cancer Practice: A Multidisciplinary Journal of Cancer Care 2002 Nov;10(6):284-92.

Price S, Lewith G, Thomas K. Acupuncture care for breast cancer patients during chemotherapy: a feasibility study. Integrative Cancer Therapies 2006;5(4):308-14.

Rabin C, Pinto BM, Frierson GM. Mediators of a Randomized Controlled Physical Activity Intervention for Breast Cancer Survivors. Journal of Sport & Exercise Psychology 2006;28(3):269-84.

Rabin CS, Pinto BM, Trunzo JJ, Frierson GM, Bucknam LM. Physical activity among breast cancer survivors: Regular exercisers vs participants in a physical activity intervention. Psycho-Oncology 2006;15(4):344-Oncology.

Rausch SM. Evaluating the psychosocial effects of two interventions, tai chi and spiritual growth groups, in women with breast cancer. Dissertation Abstracts International: Section B: The Sciences and Engineering 2008;68(8-B):2008, pp-B.

Rezende LFd, Beletti PO, Franco RL, Moraes SS, Gurgel MSC. [Random clinical comparative trial between free and directed exercise in post-operative complications of breast cancer]. Rev Assoc Med Bras 2006;52(1):37-42.

Richardson MA, Post-White J, Grimm EA, Moye LA, Singletary SE, Justice B. Coping, life attitudes, and immune responses to imagery and group support after breast cancer treatment. Alternative Therapies in Health & Medicine 1997 Sep;3(5):62-70.

Ritz LJ, Nissen MJ, Swenson KK, Farrell JB, Sperduto PW, Sladek ML, et al. Effects of advanced nursing care on quality of life and cost outcomes of women diagnosed with breast cancer. Oncology Nursing Forum 2000 Jul;27(6):923-32.

Rustoen T, Wiklund I, Hanestad BR, Moum T. Nursing intervention to increase hope and quality of life in newly diagnosed cancer patients. Cancer Nursing 1998 Aug;21(4):235-45.

Samarel N, Fawcett J, Tulman L. Effect of support groups with coaching on adaptation to early stage breast cancer. Research in Nursing & Health 1997 Feb;20(1):15-26.

Sandgren AK, McCaul KD, King B, O'Donnell S, Foreman G. Telephone therapy for patients with breast cancer. Oncology Nursing Forum 2000 May;27(4):683-8.

Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part II: Immunologic effects. Journal of Clinical Oncology 2001 Sep 5;23(25):6097-106.

Schover LR, Jenkins R, Sui D, Adams JH, Marion MS, Jackson KE. Randomized trial of peer counseling on reproductive health in African American breast cancer survivors. Journal of Clinical Oncology 2001 Apr 6;24(10):1620-6.

Schwartz AL, Winters-Stone K, Gallucci B. Exercise effects on bone mineral density in women with breast cancer receiving adjuvant chemotherapy. Oncology Nursing Forum Online 2007;34(3):627-33.

Scott JL, Halford WK, Ward BG. United we stand? The effects of a couple-coping intervention on adjustment to early stage breast or gynecological cancer. Journal of Consulting & Clinical Psychology 2004 Dec;72(6):1122-35.

Sebastian J, Manos D, Buenq MJ, Mateos N. Body image and self-esteem in women with breast cancer participating in a psychosocial intervention program. Clinica y Salud 2007;18(2):137-61.

Segar ML, Katch VL, Roth RS, Garcia AW, Portner TI, Glickman SG, et al. The effect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. Oncology Nursing Forum 1998 Jan;25(1):107-13.

Shamley DR, Barker K, Simonite V, Beardshaw A. Delayed versus immediate exercises following surgery for breast cancer: A systematic review. Breast Cancer Research & Treatment 2005;90(3):263-71.

Shapiro SL, Bootzin RR, Figueredo AJ, Lopez AM, Schwartz GE. The efficacy of mindfulness-based stress reduction in the treatment of sleep disturbance in women with breast cancer. An exploratory study. Journal of Psychosomatic Research 2003;54(1):85-91.

Shaw C, Mortimer P, Judd PA. A randomized controlled trial of weight reduction as a treatment for breast cancer-related lymphedema. Cancer 2007;110(8):1868-74.

Shaw C, Mortimer P, Judd PA. Randomized controlled trial comparing a low-fat diet with a weight-reduction diet in breast cancer-related lymphedema. Cancer 2007;109(10):1949-56.

Strauss-Blasche G, Gnad E, Ekmekcioglu C, Hladschik B, Marktl W. Combined inpatient rehabilitation and spa therapy for breast cancer patients: effects on quality of life and CA 15-3. 2005 Sep;28(5):390-8.

Stricker CT, Drake D, Hoyer K, Mock V. Evidence-based practice for fatigue management in adults with cancer: exercise as an intervention. Oncology Nursing Forum 2004 Sep;31(5):963-76.

Targ EF, Levine EG. The efficacy of a mind-body-spirit group for women with breast cancer: a randomized controlled trial. General Hospital Psychiatry 2002 Jul;24(4):238-48.

Thorsen L, Skovlund E, Strømme SB, Hornslien K, Dahl AA, Fosså, SD. Effectiveness of physical activity on cariorespiratory fitness and health-related quality of life in young and middle-aged cancer patients. Journal of Clinical Oncology 2005; 23(10):2378-88.

Vallance JKH, Courneya KS, Plotnikoff RC, Mackey JR. Analyzing theoretical mechanisms of physical activity behavior change in breast cancer survivors: results from the activity promotion (ACTION) trial. Ann Behav Med 2008;35(2):150-8.

Van der Pompe G, Antoni MH, Duivenvoorden HJ, De Graeff A, Simonis RFA, Van der Vegt SGL, et al. An exploratory study into the effect of group psychotherapy on cardiovascular and immunoreactivity to acute stress in breast cancer patients. Psychotherapy & Psychosomatics 2001;70(6):307-18.

Vos PJ, Garssen B, Visser AP, Duivenvoorden HJ, de H. Psychosocial intervention for women with primary, non-metastatic breast cancer: a comparison between participants and non-participants. Psychotherapy & Psychosomatics 2004 Sep;73(5):276-85.

Vos PJ, Visser AP, Garssen B, Duivenvoorden HJ, de Haes HCJM. Effects of delayed psychosocial interventions versus early psychosocial interventions for women with early stage breast cance. Patient Education and Counseling 2006 Feb;60(2):212-9.

Vos PJ, Visser AP, Garssen B, Duivenvoorden HJ, de Haes HCJM. Effectiveness of group psychotherapy compared to social support groups in patients with primary, non-metastatic breast cancer. Journal of Psychosocial Oncology 2007;25(4):37-60.

Watson T, Mock V. Exercise as an intervention for cancer-related fatigue. Physical Therapy 2004;84(8):736-43.

Watson,M., Denton,S., Baum,M. & Greer,S. Counselling breast cancer patients: A specialist nurse service. Counselling Psychology Quarterly 1998: 1, 25-34.

Wengstrom Y, Haggmark C, Forsberg C. Coping with radiation therapy: effects of a nursing intervention on coping ability for women with breast cancer. International Journal of Nursing Practice 2001 Feb;7(1):8-15.

Wingate L, Croghan I, Natarajan N, Michalek AM, Jordan C. Rehabilitation of the mastectomy patient: a randomized, blind, prospective study. Archives of Physical Medicine & Rehabilitation 1989 Jan;70(1):21-4.

Winzelberg AJ, Classen C, Alpers GW, Roberts H, Koopman C, Adams RE, et al. Evaluation of an internet support group for women with primary breast cancer. Cancer 2003;97(5):1164-73.

Wyatt GK, Donze LF, Beckrow KC. Efficacy of an in-home nursing intervention following short-stay breast cancer surgery. Research in Nursing & Health 2004 Oct;27(5):322-31.

Appendix

APPENDIX 1: SEARCH STRATEGY

The search strategy described was used for MEDLINE. This strategy slightly adapted for use with EMBASE, The cochrane Library, Cinahl, CRD, AMED, PEDro and PsycINFO. Searches were updated september 2008.
The other search strategies can be provided by request to
Nasjonalt kunnskapssenter for helsetjenesten /
Norwegian Knowledge Centre for the Health Services
www.kunnskapssenteret.no

Rehabilitering av brystkreft: søkestrategi i Ovid MEDLINE

Kontaktperson: Ida-Kristin Ørjasæter Elvsaas
Søk: Sari Ormstad
Database: MEDLINE 1966 to October Week 4 2006
Dato: 06.11.2006
Antall treff:
Brystkreft + Intervensjoner + Filter for systematiske oversikter: 41
Brystkreft + Intervensjoner + Filter for RCTer: 188
Totalt antall treff: 221 (overlapping mellom filtre: 8)
Kommentarer: Vi har valgt å bruke metodefilter utviklet av SIGN (med noen tilleggstermer) for å fange opp systematiske oversikter og Cochrane Highly Sensitive Search Strategy utviklet av CRD for å fange opp RCTer. Søket er avgrenset til følgende tidsrom (Entry Date): 15.09.2005-03.11.2006.

1. exp Breast Neoplasms/dh, rh [Diet Therapy, Rehabilitation]
2. exp Breast Neoplasms/
3. (breast adj3 (cancer$ or neoplasm$ or tumo?r$ or carcinoma$)).tw.
4. ((mamma or mammary) adj carcinoma$).tw.
5. mammary neoplasm$.tw.
6. ((infiltrating or invasive or mammary) adj duct$ adj carcinoma$).tw.
7. ((phyllo?d or phyllo?des) adj tumo?r$).tw.
8. (cystosarcoma$ or cysto sarcoma$ or cytosarcoma$).tw.

9. giant fibroadenoma$.tw.
10. breast mass$.tw.
11. (mammary adj2 tumo?r$).tw.
12. mamma tumo?r$.tw.
13. (mammary adj2 cancer$).tw.
14. mamma cancer$.tw.
15. ((breast or mammary) adj adenocarcinoma$).tw.
16. (breast adj (carcinogenesis or cancerogenesis)).tw.
17. mammary gland carcinogenesis.tw.
18. (breast adj2 metastas#s).tw.
19. mammary gland metastas#s.tw.
20. ((breast or mammary) adj2 sarcoma$).tw.
21. ((intraductal or ductal) adj carcinoma$).tw.
22. (paget$ adj2 disease$).tw.
23. or/2-22
24. exp Rehabilitation/ or Postoperative Care/ or Rehabilitation Nursing/ or "Recovery of Function"/ or Convalescence/
25. rehabilitat$.tw.
26. habilitat$.tw.
27. (neoplasm$ adj rh).tw.
28. (activit$ adj2 daily living).tw.
29. daily living activit$.tw.
30. adl$1.tw.
31. (chronic limitation$ adj2 activit$).tw.
32. independent living.tw.
33. (art adj (therap$ or treatment$)).tw.
34. bibliotherap$.tw.
35. dance therap$.tw.
36. early mobili?ation$.tw.
37. home rehab.tw.
38. music therap$.tw.
39. (occupation$ adj therap$).tw.
40. ergotherap$.tw.
41. (home adj (ot or pt)).tw.
42. (self adj (care or management)).tw.
43. (postoperative adj (care or procedure$ or therap$ or treatment$)).tw.
44. postsurgical care.tw.
45. surgical wound care.tw.
46. (recovery or recoveries).tw.
47. (convalescence$ or convalescent$).tw.
48. (range adj2 motion$).tw.
49. (readaptation$ or readjustment$).tw.
50. ((muscle or masculature) adj training).tw.
51. functional assessment$.tw.
52. sociotherap$.tw.
53. or/24-52
54. nutrition therapy/ or exp diet therapy/
55. nutrition therap$.tw.

56. ((diet or dietary) adj (therap$ or treatment$)).tw.
57. (calori$1 adj2 restriction$).tw.
58. ((fat or lipid) adj (restricted diet$ or restriction$)).tw.
59. (fat adj free diet$).tw.
60. (low adj (fat or lipid) adj diet$).tw.
61. (fat adj reduc$ adj diet$).tw.
62. (protein adj (restricted diet$ or restriction$)).tw.
63. (protein adj free diet$).tw.
64. (low adj protein diet$).tw.
65. borst diet$.tw.
66. giovanni diet$.tw.
67. protein poor diet$.tw.
68. hypoprotein diet$.tw.
69. (reducing diet$ or diet reducing).tw.
70. (sodium adj (restricted diet$ or restriction$)).tw.
71. (low adj (sodium or salt) adj diet$).tw.
72. (salt adj free diet$).tw.
73. ((salt or natrium) adj restriction$).tw.
74. saltless diet$.tw.
75. ((antineoplastic or anticancer or antineoplasm) adj diet$).tw.
76. macrobiotic$.tw.
77. mediterranean diet$.tw.
78. (restricted diet$ or (diet$ adj restriction$)).tw.
79. food restriction$.tw.
80. pritikin diet$.tw.
81. vegetarian$.tw.
82. weight control.tw.
83. (iron adj (therap$ or supplement$ or treatment$)).tw.
84. nutritional support.tw.
85. (protein adj (diet$ or meal$)).tw.
86. ((diet$ or food) adj supplement$).tw.
87. diet additive$.tw.
88. supplementary diet$.tw.
89. fortified food.tw.
90. (low calor$2 adj diet$).tw.
91. hypocaloric diet$.tw.
92. vitamin supplementation$.tw.
93. iron restriction$.tw.
94. (low iron adj (diet$ or intake)).tw.
95. potassium restriction$.tw.
96. (low potassium adj (diet$ or intake)).tw.
97. or/54-96
98. exp Exercise Movement Techniques/ or Physical Fitness/ or exp "Physical Education and Training"/
99. (exercise$ or exercising).tw.
100. ((breathing or respiration) adj therap$).tw.
101. ch?i kung.tw.
102. (gi gong or gigong).tw.

103. relaxation$.tw.
104. ((tai adj ji) or ((tai or thai) adj chi) or taiji or taijiquan or taichi).tw.
105. walking.tw.
106. yoga.tw.
107. (physical adj (fitness or condition$ or education or training or mobility or activit$ or exertion or effort)).tw.
108. gymnastics.tw.
109. calisthenics.tw.
110. aerobic danc$.tw.
111. (jump or jumping or hopping).tw.
112. (running or jogging).tw.
113. ambulation$.tw.
114. muscle strengthening.tw.
115. (muscular adj (strength or resistance) adj training).tw.
116. ((weight$1 adj2 lifting) or weightlifting or power lifting or weight training).tw.
117. pilates.tw.
118. stretching.tw.
119. plyometric$.tw.
120. cardiopulmonary conditioning.tw.
121. motion therap$.tw.
122. neuromuscular facilitation$.tw.
123. movement therap$.tw.
124. ((recreation or activity) adj therap$).tw.
125. gymnastic therap$.tw.
126. isometric training.tw.
127. climbing.tw.
128. cycling.tw.
129. lifting effort$.tw.
130. swimming.tw.
131. writing.tw.
132. technical training.tw.
133. (training adj (course$ or program$)).tw.
134. kinesi?therap$.tw.
135. or/98-134
136. exp Physical Therapy Techniques/
137. (physical adj (therap$ or treatment$ or medicine)).tw.
138. (physiotherap$ or physio therap$).tw.
139. (physiatrics or physiatrist$ or physiatry).tw.
140. kinetotherap$.tw.
141. ((acoustic or auditory) adj stimulation$).tw.
142. (balneology or balneotherap$ or balneo therap$).tw.
143. ammotherap$.tw.
144. bath$1.tw.
145. (spa adj (therap$ or treatment$)).tw.
146. thermal spring treatment$.tw.
147. (mud adj (therap$ or treatment$ or application$ or pack$1)).tw.
148. (fangotherap$ or fango therap$).tw.
149. (((peat or peloid) adj therap$) or pelotherap$).tw.

150. (sauna$ or sweat lodge$).tw.
151. (cryotherap$ or cryogenic therap$ or cryotreatment$ or cryothermy).tw.
152. (cold adj (therap$ or application$)).tw.
153. ((cold or ice) adj pack$1).tw.
154. ((electric$ adj stimulation$) or electrostimulation$).tw.
155. (electrotherap$ or electro therap$).tw.
156. electroacupuncture.tw.
157. tens.tw.
158. electroanalgesia.tw.
159. electronic muscle stimulation$.tw.
160. nmes.tw.
161. bioresonance therap$.tw.
162. interferential therap$.tw.
163. hydrotherap$.tw.
164. (kneipp adj (therap$ or treatment$)).tw.
165. ((water immersion or pool or whirlpool or aquatic) adj therap$).tw.
166. (hyperthermia or (hyperthermic adj (therap$ or treatment$))).tw.
167. ((infra red or infrared) adj therap$).tw.
168. pyretotherap$.tw.
169. fever therap$.tw.
170. (thermotherap$ or heat therap$).tw.
171. microwave therap$.tw.
172. (diathermy or diatherap$ or diathermia).tw.
173. electrodiathermy.tw.
174. endodiathermy.tw.
175. (high frequency adj therap$).tw.
176. inductothermy.tw.
177. (short adj wave adj (therap$ or treatment$)).tw.
178. ultrasonic therap$.tw.
179. extracorporeal shock therap$.tw.
180. phototherap$.tw.
181. light therap$.tw.
182. illumination therap$.tw.
183. photoradiation.tw.
184. colo?r therap$.tw.
185. (chromotherap$ or chromatotherap$ or chromopathy).tw.
186. heliotherap$.tw.
187. sunbathing.tw.
188. photon therap$.tw.
189. sunlight therap$.tw.
190. (low adj2 laser adj (therap$ or treatment$)).tw.
191. (low adj (level or power) adj laser irradiation$).tw.
192. lllt.tw.
193. laser biostimulation$.tw.
194. rewarming.tw.
195. (thalassotherap$ or thalasso therap$).tw.
196. seawater therap$.tw.

197. (continuous passive motion or cpm therap$ or continuous passive movement therap$).tw.
198. orthop?edic manipulation$.tw.
199. massage$.tw.
200. reflexology.tw.
201. zone therap$.tw.
202. rolfing.tw.
203. acupressure.tw.
204. (schiatsu or shiatzu or shiatsu).tw.
205. (tui na or tuina).tw.
206. functional training.tw.
207. ((joint or peripheral or spinal) adj mobili?ation$).tw.
208. manual therap$.tw.
209. bodywork$.tw.
210. ((manipulative or manipulation) adj therap$).tw.
211. ((hand-on or hands-on) adj therap$).tw.
212. myofascial release$.tw.
213. traction$1.tw.
214. vibration$1.tw.
215. ultrasound therap$.tw.
216. therapeutic ultrasound radiation.tw.
217. (climatotherap$ or (climatic adj (therap$ or treatment$))).tw.
218. ((nerve adj (stimulation$ or stimulus)) or neurostimulation$).tw.
219. magnetic stimulation$.tw.
220. (nerve cell adj (stimulation$ or excitation$)).tw.
221. or/136-220
222. exp Psychotherapy/ or Patient Care Team/ or exp Mental Health Services/ or exp Counseling/ or social support/ or Self-Help Groups/ or Hotlines/ or Caregivers/ or community health nursing/ or holistic nursing/ or oncologic nursing/ or psychiatric nursing/
223. psychotherap$.tw.
224. (aromatherap$ or aroma therap$).tw.
225. (autogen$ adj training).tw.
226. (behavio?r$1 adj (therap$ or modification$ or treatment$ or contract$)).tw.
227. conditioning therap$.tw.
228. (assertive$ adj training).tw.
229. patient contracting.tw.
230. ((aversive or aversion) adj therap$).tw.
231. covert sensitization.tw.
232. systematic desensitization therap$.tw.
233. biofeedback.tw.
234. (psychophysiologic$ adj feedback).tw.
235. (cognitive adj (therap$ or (behavio?r$ adj therap$) or restructuring)).tw.
236. cognition therap$.tw.
237. (rational emotive adj2 therap$).tw.
238. solution focused therap$.tw.
239. existential therap$.tw.
240. feminist therap$.tw.
241. (psychologic$ adj desensitization).tw.

242. meditation$.tw.
243. distraction$.tw.
244. cris#s intervention$.tw.
245. gestalt therap$.tw.
246. (hypnos#s or hypnotis$2 or hypnogenesis or mesmerism or hypnotherap$ or hypnoanalys#s).tw.
247. (suggestion or autosuggestion).tw.
248. individual therap$.tw.
249. insight therap$.tw.
250. logotherap$.tw.
251. persuation therap$.tw.
252. (psychoanalys#s or psycho analys#s).tw.
253. (dream adj (analys#s or interpretation$)).tw.
254. ((pet or animal assisted) adj therap$).tw.
255. imagery.tw.
256. directed reverie therap$.tw.
257. guided fantasy.tw.
258. mirroring.tw.
259. morita therap$.tw.
260. nondirective therap$.tw.
261. (client adj centered therap$).tw.
262. rogerian therap$.tw.
263. play therap$.tw.
264. (psychoanalytic$ adj (therap$ or treatment$ or interpretation$)).tw.
265. psychologic analys#s.tw.
266. free association$.tw.
267. transactional analys#s.tw.
268. ((psychotherapeutic or psychiatric therapeutic) adj process$).tw.
269. (acting adj out$1).tw.
270. catharsis.tw.
271. reality therap$.tw.
272. relationship therap$.tw.
273. cotherap$.tw.
274. cooperative therap$.tw.
275. multiple therap$.tw.
276. educational therap$.tw.
277. ((socioenvironmental or milieu) adj therap$).tw.
278. situational therap$.tw.
279. therapeutic communit$.tw.
280. patient pass$.tw.
281. ((group or community) adj (therap$ or treatment$)).tw.
282. ((couple$1 or triadic or conjoint or marital or marriage or sex) adj therap$).tw.
283. (family adj (therap$ or treatment$ or psychiatry or intervention$ or care or casework)).tw.
284. psychodrama.tw.
285. drama therap$.tw.
286. (online therap$ or cybercounsel?ing or e-therap$ or teletherap$).tw.
287. ((paradoxical or paradigmatic) adj technique$).tw.

288. reframing.tw.
289. symptom prescription$.tw.
290. spontaneous remission$.tw.
291. ((patient care or health care or healthcare or interdisciplinary health or transdisciplinary) adj team$).tw.
292. (multidisciplinary adj2 team$).tw.
293. ((interdisciplinary or multidisciplinary) adj treatment approach$).tw.
294. (mental health adj (service$ or community service$ or consultant$ or worker$)).tw.
295. mental hygiene service$.tw.
296. (community psychiatr$ adj service$).tw.
297. (counsel?ing or counsel?or$).tw.
298. (psychiatric adj2 emergency service$).tw.
299. (psychiatric adj (service$ or social service$)).tw.
300. (psychiatric$ adj social work).tw.
301. ((mental health or psychiatric) adj care).tw.
302. (pastoral adj (care or psychology)).tw.
303. ((social or psychosocial or psychological) adj support).tw.
304. (psychosocial adj (care or therap$)).tw.
305. (social adj (therap$ or network$)).tw.
306. ((psychosocial or psychological) adj networking).tw.
307. (self adj help adj (group$ or technique$ or device$)).tw.
308. therapeutic social club$.tw.
309. support group$.tw.
310. (community adj2 network$).tw.
311. (hotline$ or (hot adj line$)).tw.
312. ((phone or telephone) adj information service$).tw.
313. (caregiver$ or (care adj giver$)).tw.
314. health visitor$.tw.
315. visiting nurse$.tw.
316. ((community health or district or neighborhood or community based or community psychiatry or holistic or wholistic or oncologic$ or oncology or cancer or psychiatric$ or mental health) adj nursing).tw.
317. (nursing adj (care or support)).tw.
318. occupational health nurs$.tw.
319. creative arts therap$.tw.
320. poetry therap$.tw.
321. or/222-320
322. exp Complementary Therapies/
323. ((complementary or alternative) adj (therap$ or medicine)).tw.
324. alternative medical system$.tw.
325. acupuncture.tw.
326. (auriculoacupuncture or auriculotherap$).tw.
327. otoacupuncture.tw.
328. meridian$.tw.
329. (ching lo or jing luo or jingluo).tw.
330. acupoint$.tw.
331. neiguan.tw.
332. mox#bustion.tw.

333. needling.tw.
334. (anthroposophy or anthroposophical medicine).tw.
335. ((holistic or wholistic) adj (health or medicine or therap$)).tw.
336. (hom?eopath$ or hom?eotherap$).tw.
337. ((traditional or folk or indigenous or primitive or arabic or unani or arab or traditional latin american or mexican or indian or ayurvedic or hindu or siddha or tibet) adj medicine).tw.
338. ethnomedicine.tw.
339. ((folk or home) adj remed$).tw.
340. ((african or native american or oriental or chinese or tibetan) adj2 medicine).tw.
341. ayurveda.tw.
342. (kampo or kanpo).tw.
343. (chung adj hsueh).tw.
344. zhong yi xue.tw.
345. (mind adj body adj (technique$ or technic$ or medicine or relation$)).tw.
346. laughter therap$.tw.
347. mental healing.tw.
348. (psychophysiology or (physiologic$ adj psychology)).tw.
349. therapeutic touch.tw.
350. (laying adj3 hand$1).tw.
351. (reiki or leiki).tw.
352. ((musculoskeletal or spinal or cervical or lumbar) adj manipulation$).tw.
353. ((manipulative or manipulation) adj therap$).tw.
354. manipulative medicine.tw.
355. applied kinesiology.tw.
356. (ch?iropract$ or ch?irotherap$ or ch?iropraxi$).tw.
357. osteopath$.tw.
358. myofunctional therap$.tw.
359. myotherap$.tw.
360. naturopath$.tw.
361. natural remed$.tw.
362. (natural adj2 therap$).tw.
363. organotherap$.tw.
364. phytotherap$.tw.
365. (((herb or herbal) adj therap$) or herbal medicine or herbalism).tw.
366. (medicinal adj (herb$1 or plant$)).tw.
367. reflexotherap$.tw.
368. (spiritual adj (therap$ or healing)).tw.
369. ((faith or prayer or divine) adj healing).tw.
370. praying.tw.
371. radiesthesia.tw.
372. (qigong or qi or chi gong).tw.
373. (yin adj2 yang).tw.
374. wilderness experience$.tw.
375. outward bound.tw.
376. ((integrative or integrated) adj medicine).tw.
377. (orthomolecular adj (medicine or therap$)).tw.
378. megavitamin therap$.tw.

379. bioelectromagnetic application$.tw.
380. (magnet$ adj2 therap$).tw.
381. biomagnetic therap$.tw.
382. magnetotherap$.tw.
383. bioenergy.tw.
384. energetic method$.tw.
385. polarity therap$.tw.
386. chelation$1.tw.
387. gerson therap$.tw.
388. ((lifestyle or life style) adj (change$ or modification$)).tw.
389. (structural adj functional adj movement integration).tw.
390. postural therap$.tw.
391. alexander technique$.tw.
392. (feldenkrais adj (method$ or technique$)).tw.
393. hellerwork.tw.
394. trager method$.tw.
395. (oxygen adj2 therap$).tw.
396. hyperbaric oxygenation.tw.
397. ozone therap$.tw.
398. antihomotoxic medicine.tw.
399. cupping.tw.
400. hippotherap$.tw.
401. (neuraltherap$ or neural therap$).tw.
402. psychosomatic therap$.tw.
403. sound therap$.tw.
404. or/322-403
405. or/53,97,135,221,321,404
406. 23 and 405
407. 1 or 406
408. Meta-analysis/
409. meta analy$.tw.
410. metaanaly$.tw.
411. meta analysis.pt.
412. ((systematic or comprehensive or literature or quantitative or critical or integrative or evidence$) adj2 (review$1 or overview$1)).tw.
413. literature study.tw.
414. (critical adj (appraisal or analysis)).tw.
415. exp Review Literature/
416. cochrane.ab.
417. medline.ab.
418. embase.ab.
419. (psychlit or psyclit).ab.
420. (psychinfo or psycinfo).ab.
421. (cinahl or cinhal).ab.
422. science citation index.ab.
423. bids.ab.
424. cancerlit.ab.
425. reference list$.ab.

426. bibliograph$.ab.
427. hand-search$.ab.
428. relevant journals.ab.
429. manual search$.ab.
430. selection criteria.ab.
431. data extraction.ab.
432. 430 or 431
433. review.pt.
434. 432 and 433
435. or/408-429,434
436. comment.pt.
437. letter.pt.
438. editorial.pt.
439. animal/
440. human/
441. 439 not (439 and 440)
442. or/436-438,441
443. 435 not 442
444. 407 and 443
445. limit 444 to ed=20050915-20061103
446. clinical trial.pt.
447. randomized controlled trial.pt.
448. controlled clinical trial.pt.
449. randomized.ab.
450. placebo.ab.
451. Clinical Trials/
452. randomly.ab.
453. trial.ti.
454. or/446-453
455. Animals/
456. Humans/
457. 455 not (455 and 456)
458. 454 not 457
459. 407 and 458
460. limit 459 to ed=20050915-20061103
461. 445 or 460

APPENDIX 2: EXCLUDED STUDIES

Reference	Exclusion cause
Aghili et al. 2007	Not an RCT
Akechi et al. 2007	Not relevant population. Includes patients with recurrence
Allard et al. 2007	Not relevant population. Patient had intervention before surgery
Allen et al. 2002	Low methodological quality. Endpoints not defined.
Aranda et al. 2007	Not relevant population. Includes patients with metastatic cancer
Arving et al. 2006	No control group
Badger et al. 2007	Low methodological quality
Badger et al. 2001	Repeated measure experimental design
Badger et al. 1999	Low methodological quality
Badgio et al. 2007	Not an RCT
Bar-Sela et al. 2007	Not an RCT
Bellver et al. 2007	Spanish
Bendz et al. 2002	No control group, no sample size calculation
Beurskens et al. 2007	Group size n<20
Bicego et al. 2007	Not an RCT
Billhult et al. 2008	Group size n<20
Blackburn et al. 2007	Not relevant outcome measurements, metabolic endpoints
Bloom et al. 2001	Not a randomized controlled study (RCT)
Box et al. 2002a	Low methodological quality
Box et al. 2002b	Low methodological quality
Braden et al. 1998	Low methodological quality
Budin et al. 2008	Low methodological quality
Bultz et al. 2000	Low methodological quality
Cadmus et al. 2008	Not an RCT
Cameron et al. 2007	Low methodological quality
Carlson 2008	Not relevant population. Not possible to extract data for breast cancer alone.
Carlsson 2005	Nonrandomized controlled trial
Chan et al 2006	Group size 27, 16, 16 and 17
Coucke et al 2008	No relevant intervention
Courneya et al 2008	No relevant outcome measurements
Courneya et al 2006	No relevant outcome measurements
Courneya et al 2008	No relevant outcome measurements
Courneya et al 2008	No relevant outcome measurements
Daley el al. 2007	Not relevant outcome measurements
Daley el al. 2007	Not relevant outcome measurements

De Rezende 2006	Low methodological quality
Del Bianco el al. 2008	Not relevant intervention
Demark-Wahnefried el al. 2007	Not relevant population. Not possible to extract data for breast cancer alone.
Dong et al. 2008	Chinese paper
Edgar et al. 1992	Not relevant population. Includes patients with metastatic cancer
Edgar et al. 2001	Not relevant population. Not possible to extract data for breast cancer alone.
Edgar et al. 2003	Mixed colon and breast cancer. Not possible to extract data for breast cancer alone.
Epstein et al. 2007	Not relevant outcome measurements
Fairey et al. 2003	No relevant outcomes. Biomarkers' as outcomes variable
Fairey et al. 2005 a	No relevant outcomes. Biomarkers' as outcomes variable
Fairey et al. 2005 b	No relevant outcomes. Biomarkers' as outcomes variable
Fernandez et al. 2006	Review article
Filshie et al. 2008	Not relevant population, presurgery patients
Fleissig et al. 2006	Not relevant intervention
Forchuk et al. 2004 a	Low methodological quality
Forchuk et al. 2004 b	Low methodological quality
Gold et al 2006	Follow-up of findings in RCT
Gordon 2005	Three independent cohorts studied
Gustafson et al. 2008	Not relevant population. Includes patients with metastatic cancer
Gustafson et al. 2001	Not relevant population. Includes patients with metastatic cancer
Harris et al. 2001 a	Guideline
Harris S et al. 2001 b	Review article. No tables, study population not clearly described
Headley et al. 2004	Low participation in each group (n=16)
Heim et al. 2007	Not described stage of breast cancer
Ho et al. 2007	Chinese paper
Husted et al. 2008	Cohort study, not RCT
Hutnick et al. 2005	Not rehabilitation end point, reports on biomarkers
Hwang et al. 2008	Low participation in each group (intervention group n=17)
Irwing et al. 2008	Not relevant outcome measurements
Jen et al. 2004	Low participation in each group (n=13, n=11, n=13, n=11)
Johnsson et al. 2007	Not relevant outcome measurements
Jones et al. 2006	Not relevant interventions
Jones et al. 2004	Not health intervention, but intervention to increase physical activity
Jones et al 2005	Explorative follow-up study of Jones et al 2004
Kärki et al. 2001	Systematic review
Kilbreath et al. 2006	Study protocol
Kissane et al. 2004	No relevant outcomes.
Kimman et al. al	Study protocol
Kligman et al. 2004	Systematic review

Larsson et al. 1992	Low methodological quality
Lauridsen et al. 2000	Low methodological quality
Lee et al. 2006	Mixed colon and breast cancer. Not possible to extract data for breast cancer alone.
Leon-Pizarro et al. 2007	Mixed gynecology and breast cancer. Not possible to extract data for breast cancer alone.
Levine et al. 2005	Includes patients with metastatic cancer. Not possible to extract data for nonmetastatic cancer alone.
Lindemalm et al. 2008	Low participation in each group (n=10)
Marchioro et al. 1996	Low participation in each group (n=18)
McArdle et al. 1996	Low methodological quality
Megens et al. 1998	Critical review
Mishel 2005	Intervention 5-9 years after breast cancer surgery
Miyashita et al. 2005	Low methodological quality
Moadel et al. 2007	Population includes patient with recurrent cancer
Mock et al. 1997	Does not analyze outcomes based on findings in the randomized groups
Mock et al. 2001	Does not analyze outcomes based on findings in the randomized groups
Mock et al. 2005	Primary treatment, not rehabilitation
Mustian et al. 2006	Low participation in each group (n<20)
Mustian et al. 2008	Low participation in each group (n<20)
Najm et al. 2008	Comment on paper
Narvaez et al. 2008	Spanish
Nikander et al. 2007	Low participation in each group (n<20)
Northouse et al. 2005	Recurrent breast cancer
Northouse et al. 2002	Evaluation of program in an earlier study
Oldervoll et al. 2004	Review article
Patterson et al. 2008	Not relevant population. Not possible to extract data for breast cancer alone.
Payne et al. 2008	Low participation in each group (n<20)
Petersson et al. 2002	Does not analyze outcomes based on findings in the randomized groups
Pickett et al. 2002	Low methodological quality
Price et al. 2006	Study protocol
Rabin et al. 2006	No relevant outcomes
Rabin et al. 2006	Follow-up study with a longitudinal design, not RCT
Rausch et al. 2008	Low participation in each group (n<20)
Rezende et al. 2006	Population includes metastatic cancer
Rickardson et al. 1997	Low participation in each group (n=15 or n=16)
Ritz et al. 2000	Low methodological quality
Rustøen et al. 1998	No relevant outcomes
Samarel et al. 1997	Low methodological quality
Sandgren et al. 2000	Low participation in each group (n=17)
Savard, part II 2005	Cancer rehabilitation is not an end point
Schover et al. 2006	Not RCT
Schover et al. 2006	Not RCT

Schwartz et al. 2007	No relevant outcomes
Scott J et al. 2004	Low methodological quality. Size of intervention and control group not defined
Sebastian et al. 2007	Spanish
Segar et al. 1998	Low participation in each group (n=16)
Shamley et al. 2005	Systematic review
Shapiro et al. 2003	Low methodological quality
Shaw et al. 2007	Low participation in each group (n<20)
Shaw et al. 2007	Low participation in each group (n<20)
Strauss-Blasche 2005	No control group
Stricker et al. 2004	Review article
Targ et al. 2002	Includes patients with metastatic cancer
Vallance et al. 2008	No relevant outcomes
Thorsen et al. 2005	Not relevant population. Not possible to extract data for breast cancer alone.
Van der Pompe et al. 2001	Low methodological quality
Vos et al. 2004	Small sample size, N=15, n=19, and n=35
Vos et al. 2006	Small sample size, n=19, n=14, n=16, and n=18.
Vos et al. 2006	Low methodological quality
Watson et.al. 1988	Low methodological quality
Watson et.al. 2004	Review article
Wengstrom et al. 2001	Primary treatment, not rehabilitation
Wingate et al. 1989	Low methodological quality
Winzelberg et al. 2003	Low methodological quality
Wyatt et al. 2004	Low methodological quality

APPENDIX 3: QUESTIONAIRE FOR ASSESSING THE RELEVANCE OF A STUDY

Questionnaire for phase 2 – selection of papers

Following study is appraised (first author/year published /title):
……..
……..
Date for assessment:……. Done by following expert:…….

The relevance of the study:

Relevant population	**Sign in**
Women with breast cancer who 1. had surgery, but may still receive chemo or radiation therapy. 2. have completed their primary treatment	

Relevant intervention	**Sign in**
• Exercise (condition, strength, and coordination/motion exercise)	
• Physiotherapy: active and passive interventions	
• Nutrition	
• Psychosocial interventions • Cognitive behaviour therapy	
• Complementary interventions	

Relevant outcome	**Sign in**
▪ Somatic outcome	
▪ Psychological outcome	
▪ Social outcome	
▪ Economic outcome	

Relevant study design	**Sign in**
▪ Randomized controlled trial (RCT)	
▪ Controlled trial	

Conclusions:

Conclusions: *The study **excludes** for quality assessment:*	**Sign in**
Not relevant *population*	
Not relevant *intervention*	
Not relevant *outcome*	
Not relevant *study design*	

*The study **includes** for quality assessment:*	**Sign in**
Study retrieved for more detailed evaluation	

APPENDIX 4: CHECK LIST FOR STUDY QUALITY

Check list for critical appraisal of randomized controlled trials (RCT) developed by NOKC (41).

		YES	UNCLEAR	NO
1	Are the participants' disturbed equal (randomized) to the intervention and the control group?			
2	Was the randomization concealed?			
3	Were the treatment groups comparable at baseline (look for a table with characteristics for the groups)?			
4	Are the groups treated comparable except for the intervention treatment?			
5	Are the participants unaware of which group (blinded) they are assign in?			
6	Are the participants and caregivers aware of group allocation?			
7	Are the outcome assessors aware of group allocation?			
8	Are all the subjects analysed in the groups to which they were randomized? ("intention to treat")?			
9	Are there descriptions of withdrawals or dropouts in the study?			
10	Are the outcome measurements standardized, valid and reliable?			
11	How precise are these results? (Are confidence interval or p-value were reported?)			

APPENDIX 5: CHARACTERISTICS OF INCLUDED STUDIES

Appendix 5a. Physiotherapy during primary treatment of breast cancer

Study	Sample	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Cinar et al. 2008 (42) Tyrkia	N = 57 randomized to treatment group (TG, n=27) and home exercise programme (n=30) Patient drop out: 0 (0%)	Breast cancer patients with modified radical mastectomy Intervention during treatment	TG: postoperatively exercise and stretching. When drains removed, 15 sessions of individual physiotherapy programme. Then exercise at home for 8 weeks. Control: a form to perform the exercises by themselves after removal of the drains. Each exercise was thought by a physiotherapist until the exercise was performed properly.	Primary: shoulder mobility, functional capacity, lymphedema, and postoperative complications	Postoperatively at fifth day, and first, third and six months	Flexion, abduction and adduction movement of the shoulder joint and the functional questionnaire scores were significantly better in the treatment group compared to the control group. There were no statistical differences in the development of lymphedema and postoperative complications between the groups.		Moderate
Lee et al. 2007 (43) Australia	N=61, randomized to stretch group (n=31) or control (n=30). Mean age 55 ± 13 years (intervention) and 53 ± 11 years (control) Patient drop out: 9 after 7 months (15%)	Upper quadrant problems, i.e. loss of strength and range of motion, following breast cancer treatment. Intervention during radiotherapy	Intervention: usual care (independent exercise programme of gentle shoulder range of motion exercises) and a programme to stretch the pectoral muscles Control: usual care	Primary: passive range of movement for horizontal extension Secondary: passive movement for forward flexion and external rotation, active range of movement for abduction, strength of shoulder muscles, arm swelling and QOL	At completion of radiotherapy (after ca. 6 weeks) and 7 months after radiotherapy	There was no difference in any outcome between groups. The pectoral stretching programme did not influence the outcomes measured because the symptoms reported by patients were not a consequence of contracture.	More patients in the control group (n=27) had axillary surgery than in the stretch group (n=19)	Moderate

Study	Sample	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Lauridsen et al. 2005 (47), Denmark	N = 139 were randomized to; Group 1: control group (N=72), or Group 2: (N= 67), Median age: 52 (29-79) Patient dropout :14 (10%)	Breast cancer with conserving therapy (BCT) and modified radical mastectomy including axillary dissection of level I and II Intervention during radiotherapy	Group 1: Standard ward treatment and postoperative physiotherapy. 12 1-hour sessions, two sessions per week starting between the sixth and eighth postoperative weeks Group 2: same as above but the physiotherapy treatment started after the 26th postoperative week.	Shoulder function was assessed by the Constant Shoulder Score (CSS)	Follow-up at weeks 7, 13-15, 25-27, and 55-56.	Team instructed physiotherapy instituted at the sixth to eighth postoperative week, improved shoulder function significantly. After 6-8 weeks the Median ∆constant shoulder score (quartiles) was 4 (CI 0;11) vs 9 (CI 4;17) p=0,001 in controls. The same treatment was shown to improve shoulder function significantly when instituted as late as six months postoperatively.	CSS is a score which combines both subjective and objective measurements of shoulder function. The reliability and validity of the score is not given.	Moderate
Jansen et al. 1990(46), Netherlands	N=144 were randomized to: Group 1, control group (N=78), and Group 2, intervention (N= 66); mean age:59.2 (range 28-81) Patient dropout: N/A	Women undergoing primary surgery of breast carcinoma	Group 1: Shoulder exercises, immediately after surgery (day 1) Group 2: Shoulder exercises starting the eighth day after operation	Shoulder function (ROM), wound drainage volume, wound complication rates	Follow-up at 1 and 6 months	No significant difference in shoulder motion and drainage volume between groups at 1 and 6 months after intervention.	The duration and intensity of supervised physiotherapy are not given. Measurement of ROM differed between hospitals.	Moderate

N/A not available, CI= 95 % confidence interval

Appendix 5b. Physiotherapy after primary treatment of breast cancer

Study	Sample	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Didem et al. 2005(45) Turkey	N=53 randomized to Group 1: control group) (N = 26) or Group 2: experimental group (N = 27) Patient dropout 5 (9,4%)	Development of unilateral arm lymphedema one year after breast cancer surgery	Group 1: Standard treatment, e.g. minus MLD Group 2: Complex decongestive physiotherapy (CPD); e.g. manual lymph drainage (MLD), compression bandage, elevation, exercises and skin care, or standard physiotherapy (SP). once a day, three days a week for 4 weeks,	Reduction in lymphedema (circumference and volumetric measurements) and increase in shoulder mobility	No follow-up except for pre post intervention	Mean reduction in edema was 55.7% in the CDP group and 36% in the SP group. The reduction was significantly better in the CDP group ($p<0.05$). Only 45.2% of the patients had limitated shoulder mobility (48.1% in the CDP group vs 42.3% in the SP group). Shoulder flexion, abduction movements in both groups increased after treatment ($p< 0.05$). No significant difference was found in shoulder external rotation in either group. Shoulder mobility was not significantly different between the two groups	Measurement errors with respect to ROM and volumetric measurements were not given	Moderate
Mc Neely et al. 2004(48) USA	N=50 were randomized: to Group 1: control group (N=25) or Group 2: intervention group (N= 25), mean age: 60,5 years (range 33-87) Patient drop-out: 7 (14 %)	Breast surgery with axillary node dissection, medical diagnosis of lymphedema	Group 1: Compression bandages, standard education, and skin care Group 2: Compression bandages, standard education, and skin care. Manual lymph drainage 45 min daily for 4 weeks.	Primary endpoint: reduction of arm lymphedema volume (circumference and volumetric measurements)	No follow-up except for pre post intervention	No significant difference in lymphedema with or without MLD. Compression bandage alone was effective intervention in reducing lymphedema ($p<0.001$)		Moderate

Study	Sample	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Andersen et al. 2000 (44) Denmark	N=44 were randomized to Group 1:. control (N = 21), mean age: 53 (25-77) and Group 2 : intervention (N = 23), mean age: 53 (25-73) Patient drop-out: 6 (13,6)%) after 12 month	Development of unilateral arm lymphedema 4 months after breast cancer surgery	Group 1: Standard therapy, i.e. i) custom-made compression sleeve-and-glove garment (32-40 mmHg), ii) educational information about lymphoedema, iii) instruction in physical exercise, iv) skin care education Group 2: i) Standard therapy, ii)manual lymphatic drainage (MLD) 8 sessions over two weeks, iii) training in self massage	Primary endpoints: Change in volume in ipsilateral arm. and patient reported symptoms possibly related to lymphedema	Post intervention (3 month). 6, 9 and 12 month measurement not reported here.	No statistically significant difference in reduction of lymphedema over time between the two groups after 3 month (48% vs 60 %)(p = 0.66). No difference in patient reported lymphedema symptoms. MLD in addition to standard therapy did not improve treatment outcome	10 of the subjects in the standard care group changed intervention group after 3 months	Moderate

N/A not available, CI= 95 % confidence interval

Appendix 5c. Physical activity during primary breast cancer treatment.

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Mutrie et al. 2007 (56) UK	N = 203 randomized to supervised 12 week group exercise programme in addition to usual care (n=101), compared with usual care (n=102) Drop-out: 26 (at 6 months) (13%)	Women with stage 0-III breast cancer during treatment with chemotherapy or radiotherapy	The exercise programme ran for 12 weeks and participants were encouraged to attend 2 classes and 1 additional exercise session at home each week. The classes were led by specifically trained exercise specialists. The class lasted for 45 min in total and consisted of a warm-up of 5-10 min, 20 min exercise, and a cool-down and relaxation period.	QOL (FACT-G, FACT-B) Fatigue (FACT-Fatigue) Depression (BDI) Mood	12 weeks and 6 months	There was an effect on QoL after exercise intervention on FACT-B scale (effect estimate 2.5 (CI 1.0-3.9), p=0.0007) while no significant effect on QoL on FACT-G scale which were the primary outcome. At six month these effect were maintained. No differences were found between groups for other outcomes.		High
Courneya et al. 2007a (51) Canada	N = 242, randomized to usual care (UC) (n=82), supervised resistant exercise (RET) (n=82), supervised aerobic exercise (AET) (n=78) Patient dropout: 19 (9%)	Non pregnant women ≥ 18 years old with stage I-IIIA breast cancer who were beginning first line adjuvant chemotherapy	Training beginning 1-2 weeks after starting chemotherapy and ending 3 weeks after chemotherapy. AET group trained 3 times a week on ergometer, treadmill or elliptical beginning at 60 % of max ox consumption (week 1-6), 70 % (week 7-12) and 80 % (beyond week 12). Beginning at 15 min (week 1-3) then increase by 5 min every 3 weeks until reached 45 min at week 18. RET group: 3 times a week performing 2 sets of 8-12 rep of 9 diff exercises at 60-70 % of 1RM. UC group: asked not to start any exercise programme	Cancer-specific QoL (FACT-Anemia) Fatigue (FACT-An) Depression (CES-D) Anxiety (STAI) Psychososial functioning (RSES) Lymphedema	Median 17 weeks (95% CI 9-24 weeks)	Improved self-esteem subscale was superior in the AET (Mean cange 1.3 (CI 0.2-2.3), p=0.015) and RET (Mean cange 1.3 (CI 0.3-2.4), p=0.018) groups compared with UC. All other changes in patient-related outcomes favoured the exercise groups but did not reach statistical significance. Neither intervention caused lymphedema or significant adverse events.		High

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Courneya et al. 2007b (52) Canada	Same study as Courneya et al. 2007a	6 months follow up of Courneya et al. 2007a	Same study as Courneya et al. 2007a	Questionnaire that assessed QoL, self-esteem, fatigue, anxiety, depression and exercise behaviour.	6 months No follow-up except for pre post intervention	RET group reported significantly higher self-esteem than the UC group (adjusted mean diff 1.6, 95% CI 0.1-3.2, p=0.032) . AET group reported significantly lower anxiety than the UC group (adjusted mean diff -4.7, 95% CI -9.3-0.0, p=0.049). All other changes in patient-related outcomes favoured the exercise groups but did not reach statistical significance, thus no differences between groups.	Same study as Courneya et al. 2007a	High
Mock et al. 2005 (55) USA	N = 119 randomized to supervised 6 week home based exercise programme (n=60 compared with usual care (n=59 Drop-out: 11 (9%)	Women with stage 0-III breast cancer pot-surgery prior to any adjuvant theraphy. Exercising less than 45 min per week.	Exercise: home-based walking programme during treatment. 5 to 6 times/week at ~50 to 70 HR max. 15 mins per session initially increasing to 30 min. Booklet and video provided. Contacted fortnightly. Control: usual care, no intervention	Fatigue (PFS- total score) Physical function (MOS SF-36) 12-min walk Activity levels (PAQ)	No follow-up except for pre post intervention	The ITT analysis revealed no significant group differences on fatigue or physical functioning. When exercise participation was considered an effect of exercise on fatigue was demonstrated.	39% of the usual care group exercised and 28% of the exercise group did not exercise.	High
Segal et al., 2001 (63) Canada	N = 123 randomised to Group 1: usual care (n = 41) mean age 50.3, Group 2: home based exercise (n = 40) mean age 51 or Group 3: supervised exercise (n = 42) mean age 51.4 Patient dropout: 24 (20%)	Stage I – II breast cancer patients undergoing radiotherapy, hormonal therapy or chemotherapy	Both interventions: 26 weeks 5 days a week with walking exercise. Group 2: Home-based exercise: 5 days a week at 50-60 % of predicted maximal oxygen uptake Group 3: Supervised exercise: exercise specialist led a 7-10 minutes warmup 3 days a week and the patients completed walking exercise at a prescribed speed, in addition to exercise at home 2 days a week.	Primary endpoint: physical functioning (subscale I SF-36) Secondary endpoint: QOL (all the other subscales in SF-36) and maximal oxygen consumption	No follow-up except for pre post intervention	Significant and clinically important difference in physical functioning between control group and home-based exercise group (9.8 points on a 0-100 scale, p = 0.01) in favour of home based exercise group but no significance between supervised and control group (6.3 points, p = 0.09). No significant difference between groups in QOL and maximal oxygen consumption	A total of 99 patients completed; 24 patients dropped out during the intervention	High

CI= 95 % confidence interval, SF-36 = medical outcome survey short form - 36, FACT-G = functional assessment of cancer therapy - general , PFS=Piper Fatigue Scale, PAQ= physical Activity Questionnaire

Appendix 5d. Physical activity after primary breast cancer treatment.

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Milne et al. 2008 (54) Australia	N = 58 randomized to an immediate exercise group (IEG, n=29) or a delayed exercise group (DEG, n=29) Patient dropout: 1 (2%)	Breast cancer survivors within 2 years of completing adjuvant therapy	Three times a week for 12 weeks. The sessions were supervised by to exercise physiologists who ensured every participant received one-to-one contact during session. The programme included an aerobic component of 20 min with 5 min cool down. The resistant training component consisted of 12 different exercises of 10-15 repetitions. 5 min of stretching was performed in the beginning and end of each session.	Primary: overall QOL measured by the FACT-B and FACT-G scale. Fatigue (SCFS) Social physique anxiety (SPAS-7)	12 weeks No measurement after cross over.	QOL increased and Fatigue and anxiety decreased in the IEG from baseline to 12 weeks; FACT-B: (IEG: 110.5 (±10.3) vs DEG 82.6 (±14.3), p<0.001), FACT-G: (IEG: 86.4 (±8.3) vs DEG 64.1 (±11.2), p<0.001), Fatigue (IEG: 11.9 (±3.2) vs DEG 17.4 (±4.7), p<0.001), Anxiety (IEG 15.3 (±6.2) vs DEG 21.0 (±5.7), p<0.001),		High
Vallance et al. 2008 (57) Canada	Same as Vallance et al. 2007, 266 of 377 completed 6 months follow-up Patient dropout: 111 (29%)	Women with histological confirmed stage I to IIIA breast cancer, physician approval, freedom from chronic medical and orthopaedic conditions, completion of adjuvant therapy except hormone therapy and absence of current breast cancer	All groups received a standard recommendation to perform 30 min of moderate/vigorous PA 5 days a week. The SR group received no additional interventions material, the PM group received a copy of "Exercise for health: an exercise guide for breast cancer survivors". The PED group received a pedometer and a 12 week step calendar. The COM group received both interventions.	Same as Vallance et al. 2007	6 months	No differences were found between groups for QoL or fatigue at 6 months follow-up.	Primary endpoint is not relevant for our report on rehabilitation of breast cancer survivors	High

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Vallance et al. 2007 (58) Canada	N = 377 randomized to standard recommendations to physical activity (PA) (SR, n=96), printed material on breast cancer-specific PA (PM, n=94), step pedometer (PED, n=94), and PM plus PED (COM, n=93). Patient dropout: 39 (10%)	Women with histological confirmed stage I to IIIA breast cancer, physician approval, freedom from chronic medical and orthopaedic conditions, completion of adjuvant therapy except hormone therapy and absence of current breast cancer	All groups received a standard recommendation to perform 30 min of moderate/vigorous PA 5 days a week. The SR group received no additional interventions material, the PM group received a copy of "Exercise for health: an exercise guide for breast cancer survivors". The PED group received a pedometer and a 12 week step calendar. The COM group received both interventions.	QoL by FACT-B scale, Fatigue (Fatigue Scale)	12 weeks	The COM group reported significantly improved QOL (mean diff 5.8, (CI 2.0–9.6), p=0.003) compared with PA group. The COM group reported significantly reduced fatigue (mean diff 2.3, (0.0–4.7), p=0.052) compared with PA group.		High
Daley et al 2007 (53) UK	N = 108 randomized to supervised aerobic exercise therapy (n=34) or exercise-placebo: body condition (n=36) and usual care (n=38) Drop out: 6 at 8 weeks, 12 at 24 weeks Patient dropout: 12 (11%)	Women who were not regularly active and who had been treated for localized breast cancer 12 to 36 months previously.	One-to-one sessions with an exercise specialist for 50 min, 3 times a week for 8 weeks. Moderate intensity (65 – 85 % of age-adjusted heart rate. Placebo-intervention included 24 one-to-one 50 min sessions during 8 weeks with light-intensity (below 40 % heart rate) body condition/stretching. Usual care group continued their lives as usual.	QoL measured by FACT-G and FACT-B. Fatigue(PFS) Depression (BDI) physiological and physical health outcomes (BMI)	8 weeks	Exercise therapy had short term benefit on QoL (FACT-G mean difference 9.8 (CI 2.2-17.4), p=0.004; FACT-B mean difference 13.14 (CI 3.4-22.8), p=0.002), A significant (marginal) effect on QoL and fatigue was observed at 8 weeks between exercise-placebo and usual care group. Depression decreased in both exercise and placebo–exercise groups vs usual care (mean difference -6 (CI -10 to -2) P=0.001 at 8 weeks). No diference were observed in physical health outcomes.		High

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Courneya et al. 2003 (50) Canada	N = 53 randomized to exercise (n=25) or control (n=28) Drop out: 2; intervention n=0, control n=2 Patient dropout: (2%)	Early stage breast cancer with no evidence of recurrent or progressive disease, completed surgery, radiotherapy and/or chemotherapy (with or without current hormone therapy use)	Training 3 times a week for 15 weeks in recumbent or upright cycle ergometers. Training intensity: 70 – 75 % of maximum oxygen consumption in untrained subjects. Exercise duration week 1-3 was 15 min, and then increased by 5 min for every 3 weeks to 35 min for weeks 13-15. Control group did not train.	Primary: changes in peak oxygen consumption and overall QOL (FACT-B and FACT-G) Fatigue (FACT)	15 weeks	Overall QoL increased compared control group (FACT-B mean diff 8.8 points (CI 3.6-14), p=0.001; FACT-G mean diff 5.2 (CI 1.0-9.3, p=0.016). Fatigue (subscale of FACT) decresed in the physical activity group (mean diff -7.3 (CI -12.2 to -2.3). No diference were observed in bodyweight and BMI	Exercise group had more severe fatigue in the baseline measurement.	High
Basen-Engquist et al. 2006 (49) USA	N = 60 randomized to lifestyle programme (n=35) and standard care (n=25) Drop out: 9; intervention (n=7), control (n=2) Patient dropout: 9 (15%)	Within 7 years of breast cancer diagnosis, no longer receiving treatment (except hormone therapy), and not engaging in focused moderate activity for 30 min or more a day	6-month, 21-session intervention to teach breast cancer survivors to incorporate short periods of moderate activity into their daily routines	Physical performance, QoL (SF-36) Body composition (BMI) Lymphedema (arm circumferences)	Post intervention (6 month)	QoL: lifestyle group reported better QoL in general health; Lifestyle 77.2 (SD 13), SC 67.1 (SD 14), p=0.006). No difference were observed after the intervention on Body composition between the two groups. No difference were observed after the intervention on lymphedema between the two groups.	Assessors were blinded to participants study condition	Moderate
Ahmed et al, 2006 (59) USA	N =46 randomised to Group 1: control (n = 23), mean age 51.7 or Group 2: intervention (n = 23), mean age 52.3 Same study as Schmitz et al. 2005 Patient dropout: 1 (2%)	Same study as Schmitz et al. 2005	Same study as Schmitz et al. 2005	Lymphedema (arm circumferences) Incidence and symptoms of lymphedema	No follow-up beyond pre post intervention	None of the intervention group participants experienced a change in arm circumferences after 6 months weight training (p=0.40). Self-reported incidence of lymphedema or symptom changes over 6 months did not vary by intervention status (P=0.22).	Only 13 of the 46 participants had prevalent lymphedema at baseline Same study or population as Schmitz et al. 2005, Ohira et al. 2006	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Ohira et al. 2006 (60)USA	Same study as Schmitz et al. 2005	Same study as Schmitz et al. 2005	Same study as Schmitz et al. 2005	Endpoint: QOL (CARES-SF) and depressive symptoms (CES-D) No defined primary or secondary endpoints	No follow-up except for pre post intervention	Physical global improved by 2.1 points in the exercise group vs a decrease by 1.2 points in the control group (p=0.006). Psychosocial score improved 2.5 points in the exercise group vs 0.3 points in the control group (p=0.02). No difference in depressive symptoms between the groups.	No power analysis. Same population as Schmitz et al, 2005, Amhed et al. 2006	Moderate
Schmitz et al. 2005 (62), USA	N = 86 randomized to Group 1: control group (n = 43), mean age 52.8 or Group 2: Intervention (n = 43),mean age 53.3 Patient dropout: 7 (8%) after 6 months	Early stage (0-II) breast cancer patients completed chemo/radiotherapy 4-36 months before baseline. Stage 0-II.	Group1: Control group (waiting list – cross over design) Group 2: Twice-a-week weight training over a 6 month period. 60 minute sessions. The first 3 months they met in groups of four.	Primary outcome: change in % body fat and lean body mass. Secondary outcomes: change in body weight, BMI, body fat, waist circumference, glucose, insulin resistance and IGF-axis proteins	No follow-up beyond pre and post intervention	Increase in lean body mass, 0.88 vs 0.02 kg (p=0.008) for immediate treatment Decrease in body fat, -1.15 % vs 0.23 % (p=0.03) for immediate treatment	Same population as Schmitz et al, 2005, Amhed et al. 2006	Moderate
Pinto et al. 2005(61) USA	N = 86 randomized to Group 1: Control (n = 43) mean age 52.8 or Group 2: Intervention (n = 43), mean age 53.4 Patient dropout: 4 (5%)	Early stage (0-II) breast cancer patients over the last 5 years who had undergone surgery, chemotherapy, and/or radiation therapy	Group 1: Received weekly telephone calls from research staff who filled out a symptom questionnaire based on each phone call. Group 2: Home based physical activity intervention group (PA) over a 12 week period. Starting with 10 minutes at least 2 days each week, with a goal of increasing over 12 weeks to 30 minutes per day at least 5 days per week	Self-report physical activity (7-Day PAR and objective activity monitoring), fitness (Rockport 1-mile walk test), mood and physical symptoms (POMS), and body esteem (Body Esteem Scale) (	Post intervention (12 weeks) and 6 and 9 months post baseline	Physical activity (PA) engaged in significantly more total minutes of PA and were able to walk 1 mile significantly faster than the control group, (Minutes: -1.11 vs 0.20 p = 0.001). Changes in PA were not reflected in objective activity monitoring. PA group reported higher vigor than controls (2.72 vs 0.48 p = 0.001). PA group reported reduced fatigue compared to controls (-15.39 vs 0.62 p = 0.001). Changes in BES did not differ between the two groups, except for a small difference favouring the PA group on BES physical condition (2.21 vs 6.76 p=0.02).	No power analysis. All dropouts were from the exercise group. Follow-up data at 6 and 9 months are not reported here	Moderate

CI= 95 % confidence interval, BMI= Body Mass Index, SF-36 = medical outcome survey short form - 36, FACT-G = functional assessment of cancer therapy - general FACT-B = functional assessment of cancer therapy – breast, POMS = Profile of Mood States, BES= Body esteem scale, QoL= quality of life, CARES-SF = cancer rehabilitation evaluation system short form, CES-D = Center for Epidemiologic Studies-Depression Scale

Appendix 5e. Psychoeducational information during breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Sandgren et al 2007 (72) USA	N=218 were randomized to Group1: Control group (n=55) Group2: Intervention group 1 (n=78) Group3: Intervention group 2 (n=89) Mean age (SD): 54,5 (11,8) Follow up study of Sandgren 2003. Patient dropout: 19 (8 %)	Follow up study of Sandgren 2003.	Follow up study of Sandgren 2003.	QoL (FACT-B,) Mood States (POMS,) Knowledge (Preventing lymphedema) Perceived control (PSS) Self-efficacy (CBI) Social constraints	At 13 months	No treatment effects were obtained for QoL (FACT-B) or mood (POMS) after interventions after 13 month follow up.	Random assignment was based on 2.2.1 ratio, fewest into standard care condition Power analysis. Follow up study of Sandgren 2003.	Moderate
Sandgren et al 2003 (81) USA	N=222 were randomized to Group1: Control group (n=55) Group2: Intervention group 1 (n=78) Group3: Intervention group 2 (n=89) Mean age (SD): 54,5 (11,8) Patient dropout: 13 (6 %)	Stages I-III breast cancer 1-3 months after diagnosis. Undergoing adjuvant treatment.	Group1: Standard care Group 2: Health education (Structured curriculum presented by the nurse about understanding the disease, treatment, and side effects). Group 3: Emotional expression (Talks about thoughts and feelings about breast cancer). In addition: Group 2 and 3 recieved in addition five weekly 30-min phone calls and one follow-up call made 3 months later.	QoL (FACT-B,) Mood States (POMS,) Knowledge (Preventing lymphedema) Perceived control (PSS) Self-efficacy (CBI) Social constraints	At 5 months	No treatment effects were obtained for QoL (FACT-B) or mood (POMS) after interventions. Group 2 reported greater knowledge and perceived control than group 1; SMD 0.38 (CI 0.0.3-.073), F(1,218)=4.78, p=0.03. No differences between the three groups on self-efficacy or social constraints were observed after interventions.	Random assignment was based on 2.2.1 ratio, fewest into standard care condition Power analysis.	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Coleman et al. 2005 (74), USA	N=106 were randomized to Group1: Control group (n=52), age:58 Group2: Intervention group (n=54) age:57 Range of age or SD not reported. Patient dropout: 13 (14 %)	Nonmetastatic breast cancer, stage 0, I, II or III. Entering 2-4 weeks post-surgery	Group1 and 2: Educational materials via mailed resource kit. In addition in group 2: 13 months of telephone social support and education.	Social support (the effectiveness of a telephone social support and education intervention to promote emotional and interpersonal adaptation to breast cancer) Mood (POMS) Cancer related worry (VAS-W) Changes in relationship with significant others (RCS) Loneliness (UCLA-3) Symptoms relevant to breast cancer (SES)	At 3, 5, 8 and 13 months after surgery, data collected by mail.	No significant differences between the groups. Mailed educational resource kit alone appeared to be as effective, and cost-effective, as the telephone social support provided by oncology nurses.	Power analysis. Women in the experimental group were more likely to have stage II tumor. Women in the control group were more likely to have stage I tumor. A greater proportion of women in the experimental group received chemotherapy at the end of phase II.	Moderate
Yates et al. 2005 (85) Australia	N = 109 patients were randomized to Group 1: control (n = 51) and Group 2 intervention (n = 48). Mean age for each group not given Patient dropout: 12 (11 %)	Stage I-II breast cancer receiving adjuvant treatment	Group 1: The control group received general cancer education equivalent in number and timing to the intervention group. Group 2: Psychoeducational intervention given at the clinic and by phone over three 10-20 minutes sessions 1 week apart for the intervention group.	Cancer related fatigue measured by fatigue-management behaviors (developed from the literature?), confidence with managing fatigue, fatigue experience (RPFS and FACT-F). In addition cancer self-efficacy (instrument from unpublished report), QoL and psychological well-being (EORTC-QLQ-C30 Anxiety and Depression (HADS)	Three follow-ups after 7, 10 and 13 weeks after the intervention Data collected in relation during hospital visits for radio/chemotherapy	The intervention group received significant short time benefits (post intervention 7 weeks) in minimization of intensity and impact on fatigue on daily life compared to the control group mean change 1.0 (SD 2.8) vs 2.6 (SD 2.8), p=0.01). Piper inference subscale mean change 0.5 (SD 2.8) vs 2.1 (SD 2.8), p=0.01). FACT-F mean change 0.1 (SD 0.7) vs 0.3 (SD 0.7), p=0.04). However, no differences were observed between baseline and later assessments (week 10 and 13). There were no significant effects of the intervention on cancer self-efficacy, quality of life, anxiety or depression.		Moderate

CI= 95 % confidence interval, SMD= standardized mean difference, QoL= quality of life, FACT-B = functional assessment of cancer therapy – breast, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, EORTC-QLQ-C30 = The European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire, RPFS = Revised Piper Fatigue Scale, CBI = Cancer Behavior Inventory, VAS-W= Visual Analogue Scale-Worry, SES= Symptom Experience Scale, UCLA-3=University of California, Los Angeles, Loneliness Scale- version 3 , RCS= Relationship Change Scale, MSAS= memorial Symptom Assessment scale, PSS= Perceived Stress scale.

Appendix 5f. Psychoeducational information after primary breact cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Menenses et al. 2007 (71) USA	N= 261 were randomized into Group 1 Experimental: n= 129, , and Group 2 wait control: n= 132, Mean age 54.5 (SD 11.58). (Both groups together) Patient dropout: 5 (2 %)	Stage O-II breast cancer patient within one year of diagnosis. Finishes adjuvant treatment except hormonal therapy	Group 1: Experimental group: Psychoeducational support every month either face to face or telephone support: Group 2: Waiting list control Cross-over of waiting list control to intervention after 6 month.	QoL –Breast cancer survivor. The tool is scored from 0-10, with lower scores indicating better QoL	At 3 and 6 months after baseline	The experimental group showed a better overall QoL score (-0.309 (SD 0.834)) vs waiting list control group (0.042 (SD 0.752), compared to baseline scores (equal for the groups), p<0.001. After 6 month still a higher overall QoL for the experimental group, but less pronounced, p<0.001. Generalized estimating equation (GEE) analysis showed significant differences inn psychological and social wellbeing scores between the groups (P<0.001), values within the overall QoL scores.	No table of characteristics of the different groups, stated that no baseline differences were found	Moderate
Owen et al. 2005 (80) USA	N= 62 were randomized into Group 1: control group n= 30, mean age 51.3 (SD 10.5), and Group 2: intervention group n= 32, mean age 52.5 (SD 8.6). Patient dropout: 9 (15 %)	Stage 0-3 (original intention was to only include stage 1 and 2).	Group 1: Waiting list control and Group 2: 12 weeks with "Self guided internet coping". Cross-over of waiting list control to intervention after 12 weeks.	QoL (FACT-B), QoL (EuroQol-5D "feeling thermometer" of overall health) Distress (IES). Physical well-being (MSAS).	No follow-up except for pre post intervention	No significant main effects after intervention were observed for QoL, IES, or MSAS assessments. A treatment effect was observed for self reported health status (Euro QoL 5D) for participants with a low self-reported health status: SMD 1,03 (CI 0.5-1.56), F(1,39) =16.4, P<0.001	Participants in the treatment conditions had significantly more chemo therapy than control groups.	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Stanton et al. 2005 (84) USA	N = 558 were randomized to 3 groups: Group1: Control (CTL) (n=187), mean age (SD): 59.4 (11,.8) Group 2: Intervention (VID),(n=187), mean age (SD) 56,9 (11.4) Group3: (EDU) Intervention group(n= 177), mean age (SD) 57,9 (10.3) Patient dropout: 159 (28 %)	Primary surgery within the last 6 weeks. Invasive epithelial cancer histology, any tumor size, any nodal status.	Group1: Only standard National Cancer Institute print material (NCIPM). Group2: NCIPM and peer-modeling videotape Group3: NCIPM, videotape, two sessions with a trained cancer educator and informational workbook.	Primary endpoints: Energy/fatigue (SF-36). Cancer-specific distress (IES-R) Secondary endpoints: Depressive symptoms spanning one week (CES-D) Post-traumatic growth,(PTGI).	Post intervention-scores (6 months) and follow-up at 12 months	No significant effects on cancer-specific distress, depressive symptoms or post-traumatic growth were observed after intervention or at follow-up (12 months). Group2 (VID) produced significant improvement in energy/fatigue at 6 months relative to group 1 (CTL). Fatigue/vitality CTL mean change 3.35 (SD 18.09), VID mean change 9.17 (SD 18.12). EDU mean change 5.62 (SD 19.54). After 12 month the effect were no differences.	Randomization failed to equalize the groups on some psychological variables. Lost to follow-up:>20%. The women entered the trial at variable points after diagnosis. Power analysis.	Moderate

CI= 95 % confidence interval, SMD= standardized mean difference, QoL= quality of life, SF-36 = medical outcome survey short form - 36, FACT-B = functional assessment of cancer therapy – breast, CES-D = Center for Epidemiologic Studies-Depression Scale, IES-R=Revised Impact of Events Scale, PTGI= Posttraumatic Growth Inventory, EORTC-QLQ-C30 = The European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire, MSAS= memorial Symptom Assessment scale.

Appendix 5g. Cognitive behavioral therapy (CBT) during primary breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Kissane et al 2003 (78) Australia	N=303 were randomized to Group1: Control group (n=149),mean age (SD) 47,3 (8,3) Group2: Intervention group (n=154) mean age (SD): 45,4 (8,0) Patient dropout: 44 (14 %)	Early stage breast cancer (stage I and II) receiving adjuvant chemotherapy, age<65.	Group1: 3 relaxation classes (50 min) Group2: Cognitive-existential group psychotherapy (CEGT): 20 sessions (90 min) of weekly group therapy and 3 relaxation classes (50 min).	Mood and mental attitude to cancer. (MILP, ABS, POMS, HADS, MAC, FAD).	At 6 and 12 months	A trend toward improvement in anxiety for CEGT group vs control; HADS mean score -0.8 (SD 3.3) vs -0.1 (SD 3.4), p=0.05. There were no significant differences between the two groups on any of the other psychological variables.	Drop outs: n = 22 in each group.	High
Cohen et al. 2007 (69) Israel	N=114 were randomized to two Interventions groups: CB group: (n=38),mean age (SD) 55,9 (10,4) RGI group: (n=39) mean age (SD): 51,8 (11,6). Control group: (n=37),mean age (SD) 52,9 (11,8) Patient dropout: 26 (22 %)	Early stage breast cancer (stage I and II) receiving adjuvant chemotherapy or radiotherapy.	CB group: Cognitive-behaviour group focus on cognitive and behaviour learning techniques. RGI group: relaxation and guided imagery focus on relaxation and discussions afterwards. Both groups consist of 6-8 members who meet weekly for 90 min. Control group: received standard care in the oncology unit	Brief symptoms Inventory (BSI) Global Severity Index (GSI) to measure overall psychological distress Fatigue Symptom Inventory (FSI) Perceived Stress Scale (PSS)	Pre-Post intervention –scores and follow up at 4 month	Psychological distress and fatigue was reduced in both interventions group compared to control. GSI; SMD=0.59 (CI 0.19-0.99) F(2,111)=8.48, P<0.001 PSS; SMD=0.63 (CI 0.23-1,03) F(2,111)=9.68, P<0.001 Fatigue (FSI); SMD=0.82 (CI 0.41-1.23) F(2,111)= 16.45, P<0.001. There were no significant differences between the two groups on BSI. Psychological distress was still reduced in both interventions group compared to control after 4 month follow up,. Fatigue were only lower in the RGI group after 4 month follow up.		Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Antoni et al. 2006a (65) USA	N=199 were randomized to two Interventions groups: CBT group: (n=92),mean age (SD) 49.6 (9.1) Control group: (n=107),mean age (SD) 50.8 (9.0) Patient dropout: 44 (21 %)	Breast cancer patient (stage I, II and III) who had surgery within the past 8 weeks.	CBT group: CBT stress management techniques including anxiety reduction, cognitive restructuring and coping skills training (10 meetings (2hr) over 10 weeks). Control group: received condensed educational version of the intervention, but lack of therapeutic group environment and emotional support (5-6 hours)	Though intrusion and avoidance (IES) Interviewer-rated anxiety (Hamilton anxiety symptom score) Emotional stress (ABS)	Follow-up at 6 and 12 month after randomization. 3 and 9 moth after intervention ended	The CBT intervention reduced reports of thought intrusion, more than the control condition. IES; SMD=0.43, P<0.03 (6 month). And SMD=0.29, P=0.005 (12 month). Anxiety; no between group differences at any time. The CBT intervention reduced emotional stress more than the control condition only after 12 mth, ABS; SMD=0.43, P<0.01	The experimental group had higher anxiety ratings than control group at baseline. Same study population as Antoni 2006b	Moderate
Antoni et al. 2006b (66) USA	N=199 were randomized to two Interventions groups: CBT group: (n=92),mean age (SD) 49.6 (9.1) Control group: (n=107),mean age (SD) 50.8 (9.0) Patient dropout: 44 (21 %)	Breast cancer patient (stage I, II and III) who had surgery within the past 8 weeks.	CBT group: CBT stress management techniques including anxiety reduction, cognitive restructuring and coping skills training (10 meetings (2hr) over 10 weeks). Control group: received condensed educational version of the intervention, but lack of therapeutic group environment and emotional support (5-6 hours)	Different QoL outcomes; Positive outcomes; Positive states of mind (PSOM) Stress managements; Measure of current status (MOCS) QoL (FACT-G)	Follow-up at 6 and 12 month after randomization. 3 and 9 moth after intervention ended	The CBT intervention reduced emotional stress more than the control condition only after 12 mth, PSOM; SMD=0.39, P<0.04 The CBT intervention reduced emotional stress more than the control condition only after 12 mth, MOCS; SMD=0.33, P<0.004 No interventions effect on QoL by FACT-G total score, only on subscales.	Space constrains preclude a full description of FACT-B measurements in the article. Same study population as Antoni 2006a	Moderate

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale, MILP= Monash Interview for Liaison Psychiatry, ABS= Affects Balance Scale , FAD=Family Assessment Device, IES= Impact pf Event scale, PSOM= Positive states of mind, MOCS=Measure of current status, PSS= Perceived Stress scale, BSI= Brief Symptom Inventory, GSI= Global Severity Index, FSI= Fatigue symptom Inventory, FACT-G = functional assessment of cancer therapy – general.

Appendix 5h. Cognitive behavioral therapy (CBT) after primary breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Dirksen et al. 2007 (70) USA	N=81 were randomized to two Interventions groups: CBT-I group: (n=40),mean age (SD) 57.2 (9.8) Control group (CC): (n=41),mean age (SD) 59.2 (10.7) Patient dropout: 9 (11 %)	Breast cancer (stage I, II and III) , 3 month post completions of primary treatment	CBT Insomnia intervention (CBT-I); received stimulus control instructions, sleep restriction therapy and sleep education. Component control group (CC); received sleep education and hygiene only. The 10 weeks study consists of 2 weeks pretreatment, 6 weeks of treatment and 2 weeks of posttreatment. Both groups received the same attention and number of contacts hours.	Fatigue (POMS-subcale) Anxiety (STAI-S) Depresseion (CES-D) QoL (FACT-B)	Pre-Post intervention –scores	CBT-I intervention group had improvements in Fatigue and QoL (group-time interaction) compared to CC group. Fatigue by POMS:, SMD=0.61 (CI 0.14-1.09) F(1.70) =6.54, P=0.01 QoL by FACT-B:, SMD=0.56 (CI 0.09-1.03), F(1.70)=5.42, P=0.02		Moderate
Savard et al. 2005 (82), Canada	N=57 were randomized to Group1: Control group (n=30) Mean age (SD): 53,37 (7,72) Group2: Intervention group (n=27) Mean age (SD): 54,81 (7,01) Patient dropout: 12 (21 %)	Stage I-III breast cancer patients with chronic insomnia secondary to cancer. Completed radiotherapy and chemotherapy at least 1 month prior to enrollment.	Group1: Waiting-list control condition Group2: Cognitive-behavioral therapy (CBT). Multimodal approach combining cognitive, behavioral and educational strategies described in a manual given to all participants (stimulus control, sleep restriction, cognitive therapy, sleep hygiene, and fatigue management). Eight weekly sessions of 90 min in groups of 4-6 patients.	Current and past psychiatric disorders (SCID), Depression and anxiety (HADS), fatigue (MFI), and QoL (QLQ-C30+3)	8 week waiting list design, later outcomes excluded. At 3, 6, and 12 months	Participants who received the CBT treatment had significant better QoL and Moods Post treatment CBT group vs pretreatment waiting list control group Anxiety, between group-time interaction SMD 0.60 (CI 0.07-1.14), $F_{1,45}$= 5.19, P<0.05 Depression between group-time interaction SMD 0.54 (CI 0.01-1.07), $F_{1,48}$= 4.14, P<0.05 Quality of life between group-time interaction SMD 0.63 (CI 0.10-1.16), $F_{1,48}$= 5.69, P<0.05 No statistically significant differences were observed for fatigue compared to waiting list control group	The waiting list control condition did not control for nonspecific therapeutic ingredients. Power analyses (a priori) .	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Simpson et al 2002 (86) Canada	N=89 were randomized to Group1: Control group (n=43), mean age 48.9 (SD = 6.8) or Group2 Intervention group (n=46), mean age 50.0 (SD = 8.4) Patient dropout: 27 (30 %)	Completed treatment for stage 0, I, or II breast cancer. Below 70 years of age at the time of study entry	Group1: Information package. Therapy not including professionally led psychological group therapy, were open to them. Group 2: Six weekly 90 minute sessions with cognitive behavioral psychosocial meetings (relaxation, stress management, mental imagery, goal setting, planning and achieving change).	ISSI (Interview schedule for social integration) with subgroup ADAT (adequacy of close relationship), among others	1 and 2 year follow-up assessment	One year after intervention there was no statistically significant difference between the two groups in the different ISSI subcales. Social support measured by ISSI, (subgroup: "adequacy of close relationships" i.e. ADAT) was better at two-year follow-up ($p<0.10$).	Same study population as Simpsons 2001	Moderate
Simpson et al 2001 (83) Canada	N=89 were randomized to Group1: Control group (n=43), mean age 48.9 (SD = 6.8) and Group2: Intervention group (n=46), mean age 50.0 (SD = 8,.4) Patient dropout: 35 (39 %)	Completed treatment for stage 0, I, or II breast cancer. Age under 70 years at the time of study entry	Group1: Information package. Therapies not including professionally led psychological group therapy, were made available. Group 2: Six weekly 90 minute sessions with cognitive behavioral psychosocial meetings (relaxation, stress management, mental imagery, goal setting, planning and achieving change).	Primary endpoints: Psychiatric symptoms (SCID) Mood (SCL-90-R, POMS) Depression (BDI) Coping strategies (MAC, DWII) QoL (QLI) Secondary endpoints: Health care utilization (amount billed per person)	Post intervention – scores (6 weeks). Follow-up at 1 and 2 years	Intervention group had less depression vs control measured by BDI (6.5 vs 10.4; $p<0.01$), less mood disturbance by POMS (4.0 vs 20.4, $t=2.15$; $p<0.05$), and better overall QoL global score (23.0 vs 20.6, $p<0.01$). One year after intervention there was no statistically significant difference between the two groups. Two years after intervention, improved total functioning was measured by GAF compared to control (85.7 vs. 82.3), also less depression by BDI, less overall mood by POMS and better QoL compared to the control groups. There was a tendency towards less psychiatric morbidity by SCID after both one and two year follow-ups.	All women regardless of group membership improved on the scales over the course of the 2- year follow-up period. Women in group 2 were less likely to use avoidance and more likely to use active-behavioral strategies than women in group 1. No power analysis. Same study population as Simpson 2002	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Edelman et al 1999 (75), Australia	N = 60 were randomized into Group 1: supportive therapy n=31, mean age = 47.1 (SD = 9.6) and Group 2: Cognitive behavioral therapy (CBT) n=29 (SD = 9.8). Patient dropout: 23 (39%)	Primary stage (1 or 2) breast cancer diagnosed the last 12 months. Not concurrently receiving adjuvant or psychological treatment	Group 1 = Supportive therapy vs Group 2 = CBT. Both interventions comprised groups of eight to nine participants who met for 2 hours a week for 12 weeks.	Mood (POMS subscales: anxiety, depression, anger, and vigor). QoL (FLIC) Social support (7-points Likert scale) Self esteem (RSES).	Post intervention-scores (12 weeks). Follow-up at 4 months	CBT group intervention showed improved self esteem (-2.27, p=0.024) and QoL (-12.07 p=0.027) These differences between groups were no longer apparent at the 4 month follow-up. There were no significant differences between the two groups with respect to any of the other psychological variables	No “no-therapy” control group. Subscales of FLIC should have been reported better.	Moderate

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, SCID= Structured clinical interview for DSM-III-R, SCL-90-R= Symptom checklist, MAC= Mental adjustment to cancer scale, DWII= dealing with illness inventory, QLI= Quality of life index, FLIC = Functional Living Index, RSES = *Self esteem* (Rosenberg Self-Esteem Scale), MFI= Multidimensional Fatigue Inventory , QLQ-C30+3= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, FACT-B = functional assessment of cancer therapy – breast, CES-D = Center for Epidemiologic Studies-Depression Scale, STAI= State-Trait Anxiety Inventory (STAI).

Appendix 5i. Social and emotional support during primary breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Classen et al. 2008 (68) USA	N=357 patients were randomized to Group 1: standard care (SC) n=179, mean age 49.7 (SD =10.6) and Group 2: intervention =177, mean age 49.8 (SD = 10.9). Patient dropout: 31 (9%)	Early stage breast cancer, patients who had undergone surgical treatment. Cancer stage I, II or IIIa breast cancer.	Group 1: Standard care (SC) with educational control condition. Group 2 : Intervention 12 weekly 90 minute sessions included supportive-expressive group therapy supposed to reduced distress.	Total mood disturbance (POMS) Depression (HADS) Anxiety (HADS) Helpless/hopeless (MAC) Distress (IES) Distress (Yale informational support)	Post assessment after intervention; 3 month after randomization. Follow-up at 6, 12, 18 and 24 month after randomization	There were no significant differences between the two groups on the POMS scale. There were no significant differences between the two groups on the HADS, MAC, IES scales or Yale informational support for the secondary outcomes. However, small significant effects were observed on these scales when the analysis included an extreme outliner in the control group.	Baseline characteristics significantly differ in stage 3 disease. Control group had less stage 3 breast cancer patients. One extreme outliner in the control group was excluded in the analysis.	Moderate
Arving et al. 2007 (67) Sweden	N= 179 patients were randomized to Group 1: INS n=60, mean age 55(range 34-72) . Group 2: IPS n=60, mean age 55 (range 23-75) Group 3: SC n=60, mean age 55 (range 25-87) Patient dropout: 50 (28 %)	Breast cancer stage I - III patients about to start adjuvant treatment.	Group 1 Individual psychosocial support by a specially trained oncology nurse (INS). Group 2 Support by psychologist (IPS). Both groups used relaxation, distraction, activity scheduling, derived from CBT (4 month intervention) Group 3 standard care (SC).	QoL (EORTC QLQ-C30) Depression and Anxiety (HADS) Distress (IES) Anxiety (STAI-S)	Assessment at 1, 3 and 6 month from the week post intervention. Follow-up at 6thmonth post intervention.	Intervention group had better scores on global QoL/health status (Group by time); INS 67 (SD 23), IPS 68 (SD 21) and SC 60 (SD 24); P<0.05. In addition, more patients in the intervention groups improved clinically on distress; INS 4 (SD 4), IPS 4 (SD 4) and SC 6 (SD 4); P<0.05. There were no significant group differences between the two groups on the other scales.	High drop out rate in all three of the groups	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Andersen et al. 2007 (64), USA	N= 227 patients were randomized to Group 1: control n=113, mean age 51.1(SD=10.9) and Group 2: intervention n=114, mean age 50.6 (SD=10.7) Patient dropout: 26 (11 %)	Stage II or III breast cancer patients surgically treated and awaiting adjuvant therapy.	Group 1: Assessment only vs. Group 2: Psychosocial intervention with stress reduction, coping, problem solving and disease information (18 sessions of 1.5 hours over 4 months)	Stress (IES), Emotional distress (POMS)	12 month follow up	Intervention group had better scores on the POMS scale after 12 month follow up (three-way interaction effect of time x group x cancer stress); SMD 0.27 (CI 0.01-0.53), F(1,179) = 4.02, p<0.05. There were no significant differences between the two groups on IES scale after 12 month.	Follow up study of Andersen 2004.	Moderate
Andersen et al. 2004 (73), USA	N= 227 patients were randomized to Group 1: control n=113, mean age 51.1(SD=10.9) and Group 2: intervention n=114, mean age 50.6 (SD=10.7) Patient dropout: 29 (13 %)	Stage II or III breast cancer patients surgically treated and awaiting adjuvant therapy.	Group 1: Assessment only vs. Group 2: Psychosocial intervention with stress reduction, coping, problem solving and disease information (18 sessions of 1.5 hours over 4 months)	Stress (IES), Emotional distress; Total Mood Disturbance scale (POMS) Social adjustment (SNI and PSS) Health behaviors (food habits, exercise and smoke) Adherence to chemotherapy	No follow-up except for pre post intervention	Intervention group had better scores on the POMS scale at post-scores as a three-way interaction effect of time x group x ”high initial cancer stress” SMD 0.27 (CI 0.01-0.53), F(1,193) = 4.13, p<0.05. Reduced anxiety (subscale of POMS) as a two-way time x group interaction effect SMD 0.27 (CI 0.01-0.57),F(1,193) = 4.15, p<0.05. Some significant improvements in subscales of PSS were observed on the two-way time x group interaction. SMD 0.31 (CI 0.06-0.57), F= 5.36, p< 0.05 There were no significant differences between the two groups on IES, SNI, or health behavior. No significant difference in fatigue scale (subscale of POMS).	The use of interaction-effects instead of main-effects seems to be posthoc-analyses, e.g. 2-factor (Time x Group) & 3-factor (Time x Group x ”IES) Andersen 2007 has 12 month follow up data.	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Manne et al. 2005 (79), USA	N=238 couples were randomized to Group 1: standard care (UC) n=118, mean age 49.8 (SD = 10.5) and Group 2: intervention =120, mean age 49.2 (SD = 10.4). Patient dropout: 75 (31%)	Early stage breast cancer, patients who had undergone breast cancer surgery within the last 6 months and were also married or cohabitants Cancer in situ or stage 1, 2 or 3a breast cancer	Group 1: UC. Group 2 : Six weekly 90 minute sessions with couple-focused group-intervention (CG) to increase coping skills	Psychological adaptation to breast cancer was measured as: general distress (MHI-18 subscale), event specific distress (IES), partner unsupportive behaviors (PUS) physical impairment (CARES), treatment expectancy (treatment evaluation rating form), treatment evaluation (BNS), and psychosocial care usage (counting by care events)	Post assessment at 1 week post intervention. Follow-up at 6thmonth post intervention.	Couple-focused Group (CG) intervention had less depressive symptoms at post-scores (MHI); SMD 0.27 (CI 0.02-0.53) F(1,226)= 4,37, p=0.0376, These differences were no longer significant 6 month after intervention. There were no significant differences between the two groups on the other general distress scales or IES. Women with unsupportive partners and/or with more physical impairment benefited most from the intervention. Subgroup-analyses: Less distress in intervention group with real attendees.	High dropout rate Group differences were reported as F-values for "rates of change" in growth curves, i.e. slope differences, but the t-value difference between the intervention and the control-group slopes was not reported.	Moderate

CI= 95 % confidence interval SMD = standardized mean difference, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale, IES = Impact of Event Scale, SNI = Social Network Index, PSS = Perceived social support scale, MHI-18 = Mental Health Inventory-18, BEC= Loss of behavioral and Emotional control, Yale=Yale Social Support Index, QLQ-C30+3= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, STAI-S= State-Trait Anxiety Inventory – State, CARES= Cancer Rehabilitation Evaluation System.

Appendix 5j. Social and emotional support after primary breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Fukui et al 2000 (76) Japan	N=50 were randomized to Group1: Control group: (n=25) Mean age (SD): 54.3 (7.5), and Group2: Intervention group (n=25) Mean age (SD): 52.6 (6.8). Patient dropout: 4 (8 %)	Breast carcinoma, treated surgically. Lymph node metastasis positive and/or histologic or nuclear Grade 2-3, undergone surgery within the previous 4-18 months. < 65 years. Higher risk of recurrence. No ongoing or completed chemotherapy.	Group1: Waiting list control group. No contact with therapist until the intervention began. Group2: Experimental group. A 6 week, 1.5 hours weekly, structured psychosocial group intervention. (health education, coping skills training, stress management, and psychological support)	Psychological distress and coping (POMS) Mental adjustments to cancer (MAC) Clinical anxiety and depression (HADS)	Post intervention-scores (6th week), follow-up at 6th month.	There were no significant differences between the two groups on the HADS scale and MAC scale (except for "fighting spirit".) However, small significant effects were observed on the POMS-scale. Improvement in Total mood disturbance (TMD); 24.6 (SD 27.5) in the control group vs 13.8 (SD 21.3) the intervention group (p=0.003). Women who had undergone chemotherapy treatment benefited more from the intervention on TMD (POMS scale) SMD 0.88 (CI 0.30-1.47), F=9.73, p=0.003. These differences between groups were also present at the 6 month follow-up.	Small sample. No power analysis. Impossible to blind the participants to treatment allocation.	Moderate

CI= 95 % confidence interval SMD = standardized mean difference, POMS = Profile of Mood States, HADS= Hospital Anxiety Depression Scale, MAC= Mental adjustment to cancer scale.

Appendix 5k. Nutrition

Study	Population	Clinical info	Intervention	Out-comes	Follow-up	Results	Comments	Study Quality
Saquib et al. 2008 (87) USA	Participants from the Women's Healthy Eating and Living (WHEL) Study. N = 2718 randomized to intervention (n=1363) and control (n=1355) Mean age (SD): 53.4 (8.8). Patient dropout: 572 (21 %)	Breast cancer survivors stage I-IIIA aged 26-74 years, with baseline mean body mass index of 27.3 kg/m^2 (SD=6.3). Dietary intake was assessed through 24-h dietary recalls.	The intervention group were encouraged to have a daily consumption of 5 vegetable servings, 16 ounces of vegetable juice (or equivalent vegetable servings), 3 fruit servings, 30 g of fiber (18 g/1000 kcal) and 15-20 % energy from fat. They got telephone counseling, monthly cooking classes and newsletters. The control group received print materials that included dietary guidelines from the US Department of Agriculture and the National Cancer Institute, and a monthly newsletter with general health and nutrition information unrelated to the intervention group's dietary goals.	Body weight	1 and 4 year	The intervention group had a small but significant weight loss at 1 year (intrevntion; -0.05 ±0.12 vs control; 0.71±0.11, P<0.0001), but no between-group weight differences was observed at 4 years.	The intervention group significantly reduced dietary density compared to controls and maintained it over 4 years, but total energy intake and physical activity did not vary between groups.	Moderate
Thompson et al. 2005 (88) USA	A participant sample from the Women's Healthy Eating and Living (WHEL) Study. N = 77 randomized to intervention (n=21) mean age (SD): 55.5 (9.2). and control (n=31 mean age (SD): 52.3 (9.0). Patient dropout: 25 (32 %)	Breast cancer stage I-IIIA aged 18-70 years, completed conventional therapy.	The dietary intervention aimed for eight servings of fruit and vegetables, 30g fiber, ≤20% total energy from fat per day, as well as daily intake of vegetable juice. The comparison group was advised to follow general dietary guidelines for cancer prevention.	Body weight, BMI (body mass index)	Follow up at 6,12, 24 or 36 and 48 month	There were no significant difference in body weight and BMI during measurement, at 6, 12, 24 or 36 and 48 months.	Authors concluded a short term benefit on body weight, but the group difference were not significant (P=0.07). Many drop outs in both groups	Moderate

Appendix 5l. Complemetary interventions during primary breast cancer treatment

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Deng et al. 2007 (90), USA	N= 72 patients were randomized to Group 1: sham acupuncture n=42, mean age 55 (interquartile range 48-59) and Group 2: true acupuncture intervention n=30, mean age 56 (interquartile range 49-59) Patient dropout: 5 (7 %)	Breast cancer patients with more than 3 hot flashes in 1- week period.	Group 1: Sham acupuncture vs. Group 2: true acupuncture. Cross over study at 6 weeks (Twice weekly for four weeks)	Incidence of hot flashes; frequency of hot flashes per day	No follow-up except for post intervention at 6 weeks due to cross over study.	There were no significant differences between the two groups on the number of hot flashes after 6weeks.	There was a reduction of hot flashes for the intervention group after 6 weeks but the effect was not significant different.	High
Banerjee et al. 2007 (89)India	N= 68 patients were randomized to Group 1: control; supportive counseling group n=33, mean age 43 (SD 1.3) and Group 2: Yoga intervention n=30, mean age 47 (SD 1.1) Patient dropout: 10 (15%)	Breast cancer stage II and III patients surgically treated and undergoing radiotherapy.	Group 1: Control supportive counseling group vs. Group 2: Yoga intervention (6 weeks intervention)	Depression and anxiety (HADS) Self report measurements of psychological stress (PSS)	No follow-up except for post intervention at 6 weeks.	Intervention yoga group had a decrease in anxiety (42,8 %) and depression (57.5 %) from baseline measurements vs control groups had an increase in anxiety (28 %) and in depression (24 %) from baseline measument, p<0.001. Intervention yoga group had a decrease in perceived stress (25.9 %) from baseline measuments vs control groups had no change in perceived stress from baseline measurements, p<0.001.	Control group participants had less cycle of chemotherapy at baseline.	Moderate

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Walker et al. 1999 (93) UK	N= 96 patients were randomized to Group 1: control condition (SC); supportive counseling group n=48, mean age 50.1 (SD 11.3) and Group 2: Relaxation training and imagery n=48, mean age 49.3 (SD 10.8) Patient dropout: 3 (3%)	Locally advanced breast cancer (T_{2-4}, or T_xN_x and M_0) patients surgically treated and undergoing radiotherapy.	Group 1: control condition standard care (C); vs. Group 2: Experimental group; Relaxation training (E); consisting of one lesions instructions (audio taped) for continuing individual practice (during chemotherapy treatment)	Coping with stress (EPQ and CECS) QoL (GQOL) Mood (MRS) Psychiatric disorders (SCID and HADS)	Measurements: pre-, during and post- intervention. Reporting post interventions results.	Intervention group reported improved psychological wellbeing: Intervention group had an decrease in mood rating scale (MSR E; 73.29 (SD 44.77) vs C; 70.19 (SD 41.30), P=0.01), and the had higher QoL (GQOL: E; 3.29 (SD 0.80) vs C; 2.90 (SD 0.66),P=0.03) The intervention also reduced emotional suppression (CECS total E; 47.58 (SD 10.64) vs C; 52.13 (SD 9.63), P=0.02) There were no significant differences between the two groups on the other scales.	Low level of clinically anxiety or depression in the study population.	Moderate

CI= 95 % confidence interval SMD = standardized mean difference, QoL= quality of life, HADS= Hospital Anxiety Depression Scale, PSS= Perceived Stress scale , EPQ= Eysenck Personality Questionnaire - revised, CECS= Courtauld Emotional Control Scale, GQOL=Global self-rated Quality of Life, MRS= Mood Rating Scale, SCID= Structured clinical interview for DSM-III-R.

Appendix 5m. Complementary treatment after primary breast cancer treatments.

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Fenlon et al. 2008 (91), UK	N= 150 patients were randomized to Group 1: control n=76, mean age 54.9 (median and interquartile range 51.9-59.0) and Group 2: relaxation intervention n=76, mean age 55.4 (median and interquartile range 51.6-60.3) Patient dropout: 57 (35 %)	Primary breast cancer, HT excluded except if patients taking tamoxifen.	Group 1: control standard care vs. Group 2: Relaxation training by occupational therapist; a single 1 hour one-to-one session, following by self relaxation by audiotapes at home.	Incidence of hot flashes (severity descriptions) Distress caused by hot flashes; Hunter menopause scale QoL (FACT-ES) Anxiety (STAI)	1 and 3 month follow up after intervention.	Intervention group had a small reduction in the incidence of hot flashes (median difference; 7 (CI 4-11), severity of hot flashes (median difference; 0.54 (CI 0.11-1.01) and distress caused by hot flashes (median difference 1 (CI 0-2), after 1 month follow up. All p<0.01. There were no significant differences between the two groups on these outcomes after 3 month. There were no significant differences between the two groups on QoL and anxiety.	High drop out rate in both groups	Moderate
Öster et al. 2006 (92) Sweden	N= 55 patients were randomized to Group 1: control; group n=21, mean age 43 (SD 1.3) and Group 2: Art therapy, mean age 47 (SD 1.1) Patient dropout: 13 (24%)	Breast cancer patient with non-metastatic cancer	Group 1: Control group vs. Group 2: individual art therapy intervention to reflect over her situation and use nonverbal methods to express her self (Five session during 5 weeks)	Coping Resources Inventory (CRI)	Post assessment at 2 month post intervention. Follow-up at 6thmonth post intervention.	There were no significant differences between the two groups on total coping resources inventory scales. A significant higher scores were obtain by the study group on social domain subscale of CRI (p<0.05)	High drop out rate.	Moderate

CI= 95 % confidence interval, QoL= quality of life, FACT-ES= Functional Assessment of cancer Therapy – endocrine subscal, STAI= State-Trait Anxiety Inventory, CRI= Coping Resources Inventory

Appendix 5n. Complex interventions

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Denmark-Wahnefried et al. 2008 (94) USA	N = 90 randomized to calcium-rich diet (CA), n=29, CA + exercise (EX), n=29, and CA + EX + high fruit and vegetable, low-fat diet (FVLF), n=32 Drop-outs: 8 (9%)	Newly diagnosed breast cancer patients stage I-IIIA on adjuvant chemotherapy	All participants received mailed materials and telephone counseling on calcium rich food. CA+EX: CA intervention + participants were encouraged to pursue aerobic exercise ≥ 30 min per day ≥ 3 times a week and to perform strength training every other day. CA+EX+FVLF: CA and EX intervention + maintain an FVLF diet to reduce the energy density of the diet; ≤ 20% energy from fat and ≥ 5 servings of FV per day.	Primary: body composition, weight status, BMI, waist circumference, dietary intake, physical activity, QoL (FACT-G), anxiety and depression (HADS), and different blood parameters	6 months	QoL, anxiety and depression: no differences between groups observed Body composition, weight status, and waist circumference: no significant changes were detected among arms on lean body mass, significant decrease in the CA+EX+FVLF-group on percentage of body fat compared to other groups (+0.7% ± 2.3% (CA), +1.2% ± 2.7% (CA+EX), and +0.1% ± 2% (CA+EX+FVLF, p=0.047)	Measures effect of exercise and diet density	Moderate

CI= 95 % confidence interval, QoL= quality of life, FACT-G= Functional Assessment of cancer Therapy – general, HADS= Hospital Anxiety Depression Scale.

Appendix 5o. Complex interventions

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results	Comments	Study Quality
Hartmann et al. 2007 (95) Deutschland	N = 197 randomized to group A (n=98) mean age (SD): 55.4 (9.2) and group B (n=99) mean age (SD): 57.2 (8.9) Drop-outs: 29 (14.7%)	Women age 25-75 years with breast cancer diagnosis confirmed by histology not longer than 5 years ago	Group A: 3-week rehabilitation + 1-week sojourn 4 and 8 months later Group B: 4-week rehabilitation programme Both groups underwent a standardized step by steps rehab.programme with emphasis on psycho-oncological interventions including physiological interventions single and in groups, relaxation techniques, educational lesions and different types of activating physiotherapy.	Primary: global quality of life (gQoL) using ECORT-QoL-C30 Secondary: other dimensions of QoL	End of 3-4 week stay and 12 months after end of study	Patients from group B showed greater increase in gQoL, emotional function and cognitive function after 4-weeks of rehabilitation than patients from group A after 3-week of rehabilitation, although not statistically significant. After 12 months cognitive function improved in group A, but diminished in group B. For a subgroup of patients with impaired cognitive function at baseline, this difference between groups became significant (p=0.0098).	Intervention during and after treatment, the time interval between diagnosis and randomization ranged from 6 to 217 weeks.	Moderate
Cho et al. 2006(96), South Korea	N = 65 were randomized to 2 groups: Group1: Control (n=27), mean age (SD): 48.7 (9.1) Group 2: Intervention (n=28), mean age (SD) 49.6 (6.2) Patient dropout: 159 (28 %) N = 65	Breast cancer stage I – II within 2 years after mastectomy; the completion of chemotherapy and/or radiotherapy with or without hormone therapy. No mental disease or systemic disease.	Comprehensive rehabilitation for 10 weeks (psychology based education, exercise, and peer support group activity) vs standard control. To reduce attrition, the control group participants were offered the same intervention after the study.	Range of motion (ROM) Psychosocial adjustment QoL (measured by a 10 cm visual analog scale)	No follow-up except for pre post intervention	ROM was significantly increased in the intervention (11.5±7.8 %) compared to the control group (1.3±4.8 %) (p=0.000). Psychosocial adjustment were increased in the intervention by 2.9±6.3 points while decreased in the control group by 3.0±6.3 points (p=0.000). QoL was increased in the intervention by 0.9±1.3 points, while decreased in the control group by 0.1±1.0 points (p=0.002).		Moderate

CI= 95 % confidence interval, QoL= quality of life, ROM= Range of motion, EORTC-QLQ-C30 =The European Organization for Research and Treatment of Cancer – Quality of Life Que