PhD thesis

Corpus callosum in aging and dementia

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Body & Cancer

– The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

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The papers are referred to in the text by their Roman numerals.
SUMMARY

Background: Physical exercise has recently been suggested to reduce symptoms and side-effects from treatment in cancer patients. Very few studies have researched the effect of physical exercise in cancer populations undergoing adjuvant chemotherapy or treatment for advanced disease. The research took place within the framework of the Body & Cancer exercise intervention study (n=357) which was a multi-disciplinary trial investigating physical training for oncological and haematological patients undergoing chemotherapy. The Body & Cancer exercise intervention was originally developed as a clinical controlled trial in three phases (I, II and III) (2001-2007) and involved a heterogeneous cancer population at different stages of the disease. On January 1, 2007 Body & Cancer exercise intervention was implemented as a specialized rehabilitation at Rigshospitalet, Copenhagen University Hospital. Participants were allocated to groups comprising 8-16 individuals and the training was carried out four times weekly (9 hrs/week) for a six week period. The four components of the exercise intervention are high-intensity physical training (cardiovascular and heavy resistance training), relaxation- and body awareness training and massage. This thesis focuses on those studies that include data from Body & Cancer exercise intervention Phase II (n=54) (January 2002 – February 2003) and Phase III (n=213) (March 2004-March 2007), as well as data from the Body & Cancer rehabilitation intervention (n=15) (August 2011- February 2012). Quantitative and qualitative research methods are used in the three papers constituting in the present thesis. The thesis furthermore describes the functions and tasks that the Nurse-Coach is responsible for the Body & Cancer exercise intervention as well as important principles and competencies of the nurse’s role in the multidisciplinary team. The Body & Cancer exercise intervention is a collaborative between The University Hospitals Centre for Health Research (UCSF) and Oncology and Haematological Clinics of Rigshospitalet and Herlev Hospital, Copenhagen University Hospitals.

Aim and hypotheses: The aim of the thesis is to investigate whether a six week multimodal physical exercise intervention can reduce symptoms and side-effects during chemotherapy. The following three hypotheses are discussed in three separate papers: The intervention leads to; 1) Reduction in the intensity of 12 disease- and treatment induced symptoms and side-effects (heterogeneous sample, one group design, pre- and post-intervention study) (Paper I); 2) Reduction in the level of cancer related fatigue (CRF) (heterogeneous sample RCT) (Paper II), and 3) Changes in perception and management of chemotherapy-related muscle and joint pain (homogeneous sample, descriptive and qualitative study, pre- post interview) (Paper III).

Methods and population: The research was carried out as a, hypothesis-generated, prospective, clinical trial (phase II) and randomized controlled clinical trial (phase III) intervention studies with pre- and post-tests, as well as a descriptive and qualitative study. Quantitative and qualitative research methodologies were used. Participants (n=54) completed semi-structured diaries daily for six weeks allowing a continuous registration of 12 pre-specified symptoms and side-effects (loss of appetite, nausea, vomiting, diarrhoea, constipation, sensory impairment, mental fatigue, physical fatigue, treatment-related fatigue, muscle pain, joint pain and other pain). Patients scored each symptom and side-effect on a scale of 0 to 4 - 4 the most pronounced. Measurements of CRF were taken of 213 randomized patients divided between the Intervention group (n=106) and the control group (n=107). CRF was evaluated by using the Functional Assessment Questionnaire, a Cancer Therapy Anaemia Questionnaire (FACT-An fatigue score). Pre- and post-interviews (n=15) were carried out with a sample of operable breast cancer patients undergoing adjuvant chemotherapy using a semi-structured interview guide and including a description of the patient level, duration and management of muscle and joint pain.
**Results, study 1 results.** The first study (n=54) showed that during exercise intervention, the patients experienced a reduction in the average diary score in 10 of 12 identified symptoms and side-effects. No reduction was observed in the vomiting score and the score for nausea increased. In parallel, a significant decline (p= 0.036) was seen in the sum of symptom and side-effects burden. In total, 36 (67%) patients experienced a reduction in the sum of symptoms and side-effects burden, while 13 (24%) increased and 5 (9%) remained without change. From the first day to the last day of the intervention, the total scores for pain significantly improved (p = 0.046).

**Study 2 results.** In study 2 (n=213) a significant reduction in the patients’ experienced CRF levels was observed, as seen by a clear improvement in the FACT-An Fatigue score by 3.04 (effect size at 0.44, 95% CI 0.17-0.72) (p = 0.002) in the intervention group compared with the control group. Furthermore, there was a significant effect from baseline to six weeks in the intervention group when the ‘anaemia scale’ was included. Substantial improvements were seen in the FACT-An score of 5.40 (effect size at 0.34, 95% CI from 0.07 to 0.6), (p = 0.015), the FACT-An Toi score of 5.22 (effect size of 0.37, 95% CI 0.1-0.65) (p = 0.009) and anemia-ANS by 3.76 (effect size at 0.44, 95 CI 0.17-0.71) (p = 0.002) in comparison with the control group. There was no statistically significant effect (p = 0.21) on the General Quality of Life score (FACT-G) or on any of the individual wellbeing scores; Physical (p= 0.13), Emotional (p=0.87), Social (p= 0.83) and Functional (p=0.26).

**Study 3 results.** Experience and management of muscle and joint pain during the intervention period was in the third study described by 15 women during adjuvant Docetaxel (D) and hematopoietic growth factor support (G-CSF). During the phenomenological analysis process and attempts to grasp the phenomenon’s essence, five categories of findings were identified: ‘Abrupt pain - a predominant side-effect’, ‘Cogitated Pain Management’, ‘The adapted training’, ‘Non-immediate exacerbation of pain’, and condensed the essence of phenomena, ‘Exercise despite pain’. The chemotherapy-related muscle and joint pain was not aggravated by participation in the intervention.

**Conclusion:** This study documents that a six week structured, combined high- and low-intensity exercise intervention led to a reduction in the intensity of identified symptoms and side-effects (diarrhoea, constipation, diminished appetite, myalgia, arthralgia, other pains, physical fatigue, treatment-related fatigue and mental fatigue) in a heterogeneous group of cancer patients undergoing chemotherapy (one group design). Despite an accumulated dose of chemotherapy and the intensity of the training programme (9 hours weekly), the patients experienced a reduction in their CRF level (RCT design). In a homogenous group of operable breast cancer patients in adjuvant chemotherapy (D+ (G-CSF)) the results indicated that the patients’ perception of sudden onset of chemotherapy-related muscle and joint pain was not aggravated by training (descriptive and qualitative study).

**Perspectives:** In contrast with the concerns patients and therapists may have that exercise may exacerbate existing symptoms and side-effects in patients receiving chemotherapy, the results of this study support the argument for regular training with monitoring, guidance and supervision of an interdisciplinary exercise team that can support cancer patients receiving chemotherapy from impaired physical function and worsening overall burden of symptoms and side-effects. Further diagnosis specific exercise intervention studies in cancer patients receiving chemotherapy are needed to clarify the symptoms and side-effects complexity as well as to investigate whether an early supportive exercise intervention at diagnosis can reduce the patients’ total side-effect burden and prevent problems such as chronic fatigue and pain, which in the long-term might have physical, psychological, social and economic consequences for the patient.
DANSK RESUMÉ


Formål og hypoteser: Afhandlingens formål er at undersøge, hvorvidt en seks ugers multimodal træningsintervention kan reducere graden af symptomer og bivirkninger hos kræftpatienter, som får adjuverende kemoterapi eller er i kemoterapi for avanceret sygdom. Følgende tre hypoteser er afhandlet i tre separate publikationer: Interventionen medfører; 1) Reduktion af intensiteten af 12 sygdoms- og behandlingsinducerede symptomer og bivirkninger - (heterogen population, one-group design, pre- og post interventions studie), 2) Reduktion af niveauet af cancer relateret træthed (CRF) (heterogen population, RCT), 3) Ændringer i opfattelse og håndtering af kemoterapirelaterede muskel- og ledsmerter under deltagelse i Krop & Kræft (homogen population, deskriptivt og kvalitativt studie).

Metoder og population: Forskningen er gennemført som et hypotese- generende, prospektivt, klinisk kontrolleret Fase II og III- interventionsstudie med pre- og post test, samt som et deskriptivt og kvalitativt interviewstudie. Der anvendes kvantitative og kvalitative forskningsmetoder, inklusiv anvendelse af standardiserede dataindsamlingsmetoder udviklet af Krop & Kræft gruppen. For at opnå en kontinuerlig registrering af patienternes (n=54) 12 udvalgte symptomer og bivirkninger (appetitløshed, kvalme, opkastning, diarré, forstoppelse, føleforstyrrelser, mental træthed, fysisk træthed, behandlingstræthed, muskel- og ledsmerter) under interventionen, udfyldte patienterne dagligt i seks uger på en semi-struktureret dagbog. Patienterne scorede hvert symptom og bivirkning på en skala fra 0 til 4, hvor 4 var højest. Målingerne af CRF er foretaget på 213 randomiserede patienter fordelt imellem (n=106) intervention - og (n=107) kontrolpatienter. CRF blev evalueret ved hjælp af spørgeskemaet Functional Assessment Questionnaire (FACT-An Fatigue score). Pre - og post-interview (n = 15) blev gennemført på baggrund af en semistructureret interviewguide for at kunne beskrive patientens opfattelse og håndtering af deres muskel- og ledsmerter.
Resultater, resultater fra studie 1: Det første studie (n=54) viste, at i løbet af de seks ugers træningsintervention oplevede patienterne et fald i deres gennemsnitlige score på 10 ud af 12 udvalgte symptomer og bivirkninger. Resultaterne viste ingen reduktion i opkastningsscoren mens kvalmescoren steg. Samtidig sås der et signifikant fald (p= 0.036) i patienternes samlede bivirkningsbyrde. I alt oplevede 36 (67 %) patienter en reduktion i deres samlede symptomer og bivirkningsbyrde, mens 13 (24 %) havde en stigning og 5 (9 %) ikke oplevede nogen ændring. Fra den første til den sidste uge i interventionen blev den totale smertescore signifikant forbedret (p=0.046).

Resultater fra studie 2 (n=213) viste en signifikant reduktion i patienternes oplevede CRF-niveau, idet der sås en betydelig forbedring på FACT-An -Fatigue scoren på 3.04 (effektstørrelse på 0.44, 95 % CI 0.17-0.72) (p = 0.002) i interventionsgruppen sammenlignet med kontrolgruppen. Desuden var der en signifikant effekt fra baseline til seks uger til fordøj for interventionsgruppen, hvor ”anæmiskalaen” blev inkluderet. Markante forbedringer blev set i FACT-An scoren på 5.40 (effektstørrelse på 0.34, 95 % CI fra 0.07 til 0.6), (p = 0.015), i FACT-An Toi scoren på 5.22 (effektstørrelse på 0.37, 95% CI 0.1-0.65) (p = 0.009) og i anæmi-ANS på 3.76 (effektstørrelse på 0.44, 95 CI 0.17-0.71) (p = 0.002) sammenlignet med kontrolgruppen. Der var ingen statistisk signifikant effekt på den generelle livskvalitet score (FACT-G) (p = 0.21) eller på nogen af de enkelte livskvalitets subscore, Fysisk (p = 0.13), Emotionel (p = 0.87), Social (p = 0.83) og Funktionelle (p = 0.26).

Resultater fra studie 3 (n=15) viste, hvordan kvinder med operabel brystkræft i adjuverende kemoterapi med Docetaxel (D) og vækstfaktorstøtte (G-CSF) opfattede og håndterede deres kemoterapirelaterede muskel- og ledsmarter under de seks ugers træningsintervention. Under den fænomenologiske analyseproces og i søgningen efter fænomenets essens, blev der identificeret fem kategorier: ”Den pludselige smerte - en dominerende bivirkning”, ”Den Fokuserede smertehåndtering”, ”Den tilpassede træning”, ”Ingen umiddelbar forværring af smerten”, kondenseret i fænomenets essens: ”Træning trods smerter”. De kemoterapirelaterede muskel- og ledsmarter blev ikke forværret af deltagelsen i interventionen.


Perspektiver: Resultaterne i denne afhandling støtter argumentet for, at regelmæssig træning, under monitorering, guidning og tidning af et tværfagligt træningsteam, kan understøtte kræftpatienter i kemoterapi til ikke at få en forringet fysisk funktion og til at forebygge en forværring af patienternes samlede symptom- og bivirkningsbyrde. Yderligere diagnose-specifikke træningsinterventions-studier for kræftpatienter i kemoterapi er nødvendige for at undersøge symptom- og bivirkningskompleksiteten, samt for at undersøge om en tidlig understøttende træningsintervention yderligere kan bidrage til at mindske patienternes samlede bivirkningsbyrde og forebygge kroniske gener, som kronisk træthed og smerter, hvilket på længere sigt kan have fysiske, psykiske, sociale og økonomiske konsekvenser for patienten.
ABBREVIATIONS

ACSM - American College of Sport Medicine
Adj - Adjuvant
BFI - Brief Fatigue Inventory
CE - Cyclophosphamid and Epirubicin
CEF - Cyclophosphamide, Epirubicin and 5-Fluorouracil
CRF - Cancer Related Fatigue
DBCG - Danish Breast Cancer Group
D - Docetaxel
ED - Evidence of Disease
EORCT-QLQ-C30 - European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FACT - Functional Assessment of Cancer Therapy
FACT-F - Functional Assessment of Chronic Illness Therapy- Fatigue scale
FACT-An - Functional Assessment of Cancer Therapy-anaemia Questionnaire
MET - Metabolic Equivalent of Task
MOS-SF 36 - Medical Outcomes Study Short Form
NED - No Evidence Disease
PFS - Piper Fatigue Scale
POMS - Profile Of Mood States
PMR - Progressive Muscle Relaxation
RCT - Randomized Control Trial
r-PFS - revised Piper Fatigue Scale
RM - Repetition Maximum
SAS - Symptom Assessment Scale
SD - Standard Deviation
VO₂ Max - Maximum oxygen consumption
DEFINITIONS

**Body & Cancer exercise intervention:** Used in the thesis for both Body & Cancer project (April 2001 - March 2007) and Body & Cancer specialised rehabilitation (April 2007 - January 2012). The intervention consists of: supervised exercise, comprising high-intensity cardiovascular and heavy resistance training, relaxation- and body awareness training and massage, four times weekly (9 hrs/week) for a six week period.

**Specialised rehabilitation:** Rehabilitation in a supervised hospital setting with clinical monitoring by an interdisciplinary team (1).

**Physical activity:** Physical activity is any muscular effort, which increases energy metabolism in skeletal muscles and consists of both unstructured and at more deliberately targeted regular physical activity (2) (p. 21).

**Level of physical activity:** In the Body & Cancer exercise intervention the level of physical activity was defined as the leisure time physical activity level and was explored by questionnaire. The participants were classified as: sedentary (completely inactive); walking or cycling for pleasure; regular physical exercise at least 3 hours a week; or intense physical activity more than 4 hours a week (3).

**Exercise:** Exercise is defined as physical activity performed in a systematic and planned manner (a specific frequency, intensity and duration) in order to improve or maintain health-related outcomes as fitness and muscular strength. The level of intensity should be at least 55 % to 65 % of maximum heart rate. An exercise programme may include various forms of activity as swimming, resistance training, running or ball games (4).

**Symptoms:** A symptom is defined ‘a subjective experience reflecting changes in the bio-psychosocial functioning, sensations or cognition of an individual’, whereby it is only the patient alone who can decide whether the symptom control is reached (5).

**Side-effects:** A side-effects is defined as an adverse effect and unintended response to a drug (6).

**Cancer related fatigue:** Cancer related fatigue is defined as a consistent burdensome feeling of physical, psychological and/or cognitive tiredness related to cancer or cancer treatment that affects patients’ normal functional level and that is not relieved by rest or sleep (7).
**Pain**: Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (8).

**The chemotherapy-related muscle and joint pain**: The term of “muscle and joint pain” refers to toxicity related to the adjuvant chemotherapy regime consisting of 3 cycles of Epirubicin 90 mg/m² plus Cyclophosphamide 600 mg/m² every 3 weeks followed by 3 cycles of Docetaxel 100 mg/m² every 3 weeks + hematopoietic growth factor support (G-CSF). Muscle pain is defined as ‘pain and tenderness in muscles’ and joint pain is defined as ‘pain at the end positions; reduced mobility and instability of joints’.

**Definitions on symptoms and side-effects used in the semi-structured diary**

- **Lack of appetite**: Ranging from eating like before (100%) to reduced appetite (<50% compared to before).
- **Nausea**: Ranging from no nausea to ability to eat, to oral intake significantly decreased, and finally to no significant intake, requiring IV fluids.
- **Vomiting**: Ranging from no vomiting to one episode in 24 h, to two to five episodes in 24 h, to >six episodes in 24 h or need for IV fluids, and finally to requiring parenteral nutrition.
- **Diarrhoea**: Ranging from none to increased frequency of <4 stools/day, to increases of 4–6 stools/day or nocturnal stools, to increase of >7 stools/day or incontinence or need for parenteral support for dehydration and finally to increase of >10 stools/day haemodynamic collapse.
- **Paraesthesia**: Examples of paraesthesia can be any sensation, such as pins and needles, burning, prickling etc. in fingers or toes, pain under feet or other forms of numbness.
- **Constipation**: Ranging from none to disabling.
- **Physical fatigue**: The sense of fatigue that follows physical exercise and other forms of physical activities, characterized by, e.g. relaxed sense and energy.
- **Treatment-related fatigue**: This sense of fatigue can be related to the chemotherapy (and perhaps radiation therapy) and may be characterized by influenza–like symptoms unrelieved by rest or sleep.
- **Mental fatigue**: The sense of being unconcentrated and lacking energy to carry out any activities.
- **Myalgia**: Ranging from none to disabling.
- **Arthralgia**: Ranging from none to disabling.
- **Other pain**: Other pain (apart from arthralgia and myalgia) could be headache, back pain or pain caused by an operation scar.
INTRODUCTION
This dissertation was developed within the context of the Body & Cancer exercise intervention (April 2001-March 2007) (n=357), a prospective, longitudinal, clinically controlled trail carried out in three phases. Body & Cancer exercise intervention was conducted as an interdisciplinary exercise intervention for groups of oncological and haematological cancer patients who were undergoing adjuvant chemotherapy or treatment for advanced disease at the Copenhagen University Hospitals, Rigshospitalet and Herlev Hospital. The principal aim of the Body & Cancer exercise intervention was to increase physical, functional and emotional capacity and reduce symptom and side-effects while the patients were undergoing chemotherapy (9-17). The programme included a so-called 'body package', the four components of the exercise intervention are; high-intensity physical training (cardiovascular and heavy resistance training), relaxation- and body awareness training and massage. Training was carried out in groups of 8-16 participants, four times weekly (9 hrs/week), and took place in the Copenhagen University Hospital's fitness training rooms. In 2007 the Body & Cancer exercise intervention in 2007 was instituted as a specialized rehabilitation for cancer patients undergoing chemotherapy in Denmark’s metropolitan region. The Body & Cancer exercise intervention is a collaborative project between The University Hospitals Centre for Health Research (UCSF) (Rigshospitalet) and Oncology and Haematological Clinics of Rigshospitalet and Herlev Hospital, Copenhagen University Hospitals. The author (CA) of this dissertation participated as clinical nurse specialist in the development and the Body & Cancer exercise intervention in 2001 and until date. This thesis includes data from Phase II (n=54) (January 2002-February 2003) and Phase III (n=213) (March 2004 – March 2007) of the Body & Cancer exercise intervention as well as data from the Body & Cancer specialised rehabilitation (n=15) (April 2011-January 2012).

AIMS AND HYPOTHESES
The primary aim of the thesis is to investigate whether a six week multimodal exercise intervention can reduce cancer patient’s symptoms and side-effects during chemotherapy. The dissertation in addition describes the functions and tasks undertaken by the Nurse-Coach when supporting patients during their participation in the intervention. It was hypothesized that the intervention would:
• Reduce the intensity of 12 disease- and treatment-induced symptoms and side-effects (heterogeneous sample, single one-group design, pre- and post-intervention study) (Paper I).
• Reduce the level of cancer related fatigue (CRF) (heterogeneous sample, RCT) (Paper II).
• Change the perception and management of chemotherapy-related muscle and joint pain during the intervention (homogeneous sample, descriptive and qualitative study) (Paper III).
The main objectives of the research (Paper I–III) include:

- Investigating the effects of the six week supervised, combined high- and low-intensity exercise intervention on 12 selected symptoms and side-effects (i.e., lack of appetite, nausea, vomiting, diarrhoea, paraesthesia, constipation, physical fatigue, mental fatigue, treatment related fatigue, muscle pain, arthralgia and other pain) (Paper I).
- Evaluating in detail whether the intervention programme, as an adjunct to chemotherapy and standard supportive treatment, could lead to a reduction in cancer related fatigue (Paper II).
- Exploring the perception and management of chemotherapy-related muscle and joint pain experienced by women with operable breast cancer while undergoing adjuvant chemotherapy with docetaxel (D) and hematopoietic growth factor support (G-CSF) (Paper III).

BACKGROUND

Incidence and treatment of cancer in Denmark

The age corrected incidence of new cancer cases in Denmark has diminished over the past few years (3.4%) from 36.815 new cancer cases in 2009 to 35.562 new cases in 2010. Every third Dane will contract cancer during his/her lifetime, and thus cancer will impact almost all Danish families. With the exception of non-melanoma skin cancer, the most prevalent form of cancer in Denmark is breast cancer for women and prostate cancer for men, while lung cancer for both genders is the second most prevalent form of cancer — and most prevalent cause of death by cancer (18). Data from the Danish National Board of Health show that the one year relative survival rate after diagnosis, for the majority of the eight major cancer forms (breast, prostate, lung, ovarian, rectal, colon, cervix and uterine) increased from 1997 to 2008 (19). With respect to breast cancer, improved treatment options have led to a five year relative survival rate of 79% (20). An increasing number of cancer patients are offered chemotherapy either as treatment for advanced stages of cancer or as adjuvant treatment following surgery and/or in connection with radiation treatment (21).

Common symptoms, side-effects and late effects of chemotherapy

It is well-documented that chemotherapy is accompanied by significant symptoms and side-effects such as fatigue (22;23), pain (24), nausea and vomiting (25;26), diarrhoea and constipation (27), anaemia, infections and bleeding due to decreased bone marrow function (21), hair loss (28;29), neuropathies (30), anxiety and depression (31-34), sleeplessness (35), low self-esteem (36) and weight gain (37), all of which impact the cancer patient’s physical capacity and quality of life (38-40). Late effects such as diminished respiratory and heart capacity and muscle strength and psychological effects such as depression, anxiety and fatigue are well-known amongst cancer patients and for some patients these effects can last for months and years.
following treatment (41-43). Recent studies of patients with breast, colon and prostate cancer indicate that regular physical activity can reduce the risk of relapse and mortality (44-47).

**Treatment of patients with breast cancer in Denmark - symptoms and side-effects**

Treatment of early operable breast cancer is multidisciplinary and includes surgery, radiation- and medical therapy. Axillary sampling or clearance combined with breast conserving surgery or mastectomy is universally recommended (48). Adjuvant medical therapy is recommended to more than 90% of the patients. HER2 targeted therapy is recommended to patients with HER2 positive tumours and endocrine therapy is recommended to patients with oestrogen receptor (ER) positive tumours. Chemotherapy is recommended to patients with HER2 positive tumours, to patients with ER negative tumours and to patients with ER positive tumours with a poor prognosis despite optimal endocrine therapy (48;49). When the Body & Cancer exercise intervention was launched in 2001, the Danish Breast Cancer Cooperative Group’s (DBCG) recommended seven series of Cyclophosphamide 600 mg/m², Epirubicin 60 mg/m² and 5-Fluorouracil 600 mg/m² (CEF), given intravenously, with 3 weeks between treatments, if chemotherapy was indicated (50;51). In 2007, the DBCG changed its recommendation to three series of Epirubicin 90 mg/m² and Cyclophosphamide 600 mg/m² (EC), followed by three series of Docetaxel 100 mg/m²(D), both regimens given intravenously with three week intervals. From 2008 it was recommended to administer growth factor support (G-CSF) immediately after D (50;51). The most frequently documented side-effects/symptoms of EC+ D + (G-CSF) include: alopecia, neutropenia, thrombocytopenia, hypersensitivity, peripheral sensory and motor neuropathy, nausea, vomiting, stomatitis, nail disorders, fluid retention and myalgia (52-54). The literature varies on its description of side-effects of sequential EC-D but not in relation to the side-effects described for EC and D, and myelosuppression is indicated to be dose limiting (50;51). Following introduction of treatment with D and G-CSF in clinical practice, pain predominantly in the form of myalgia and arthralgia became frequent. The pain typically commences two days after D series and lasts 2-3 days. The etiological background for taxane-induced pain is unknown and effect of analgesics is sparsely described. The incidence is reported in two published studies to be 33% and 79% respectively (24;55).

**Change in side-effect burden in the Body & Cancer exercise intervention**

When adjuvant chemotherapy changed from 7 series of CEF to sequential EC followed by D, a major change in side-effect burden was observed and noted among participating patients in the Body & Cancer exercise intervention. The patients indicated to the exercise team members a high intensity of muscle, joint and bone pain in connection with their training. This observation was substantiated by a reduced participation rate and smaller progress in strength and fitness aims in the group of patients with breast cancer under EC-D and G-CSF treatment (n=17) compared to the group of patients undertaking the CEF treatment (n=18) (unpublished data). This observation was the basis for the qualitative study (Paper III) in this dissertation. In the Body & Cancer exercise intervention, the patients with operable breast cancer were included following their first
cycle of chemotherapy with CEF or EC respectively and with a minimum of six weeks after surgery in order to minimize risks prior to high intensity strength training of the breast musculature (15).

![Diagram of treatment schedule](image)

**Cancer Related Fatigue**

Cancer Related Fatigue (CRF) is a common complaint of cancer patients undergoing chemotherapy and is associated with the disease itself and the treatment (56;57). The term CRF refers to a consistent burdensome feeling of physical, psychological and/or cognitive tiredness that affects the patient’s functional level and is not relieved by rest or sleep (7). CRF is associated with physical inactivity, a lower functional level and lack of energy (38;58-60). The prevalence of CRF in patients undergoing chemotherapy has been reported as being as high as 60-90% in the weeks following treatment (22;57;61). Patients undergoing chemotherapy experience that fatigue diminishes with time up to the next chemotherapy session (62-64). Duration of fatigue varies from months while under treatment to years following treatment and if defined as chronic fatigue the duration should be six months or more (22;23;65-67). Studies of breast cancer patients have shown that 11-35% reported significant fatigue 5-10 years following diagnosis (68;69). CRF may be regarded as a multifactoral and multidimensional symptom, where interactions between different etiological mechanisms are complex and only partially understood (70-72). Mustian et al. (73) describe the complexity of CRF in four dimensions; Direct cancer burden, Cancer treatment burden, Cancer and treatment psychosocial burden and Comorbid conditions burden (Figure 2) (73). Cancer patients with CRF often describe...
a combination of bio-psychosocial symptoms that are associated with cancer or the treatment-related side-effects (5;74;75).

CRF is detected through physiological signs and symptoms such as anaemia, infection, muscle dystrophy, poor physical condition, diminished nutritional intake, breathing difficulty, sleep disturbances and pain, mental symptoms such as depression and anxiety as well as cognitive symptoms that are manifested as diminished memory and lack of ability to concentrate (57;76). CRF has a significant impact on the cancer patient’s socialization ability as it is generally seen to reduce the patient’s ability to participate in recreational activities and activities with the family as well as the ability to work (76;77).

Figure 2: Multiple bio-psycho-social dimensions of cancer related fatigue (73) (p. 53)

**Exercise oncology**

Interest in physical training for cancer survivors has increased substantially over the past 20 years. Prior to that, there was a tendency to safeguard these patients from physical activity whilst today it is recommended to patients, including those undergoing cancer treatment (78;79). This increased interest in physical training occurred in parallel with the fact that more patients outlive cancer today as well as there being more focus on managing symptoms and side-effects and sequelae following initial cancer treatment. From the late 1990s, international research on physical training of cancer patients under treatment was launched and was only introduced in 2001 in Denmark in conjunction with the Body & Cancer exercise intervention (9;12;15).

**Guidelines for physical training for cancer survivors**

In 2010, the American College of Sports Medicine (ACSM) (40) published guidelines for physical training for
cancer survivors. The guidelines were based on the same recommendations as those for the healthy population (40). The Danish Health and Medicines Authority recommends a minimum of 30 minutes of moderate to intense physical activity per day for adults as a supplement to daily activities. In addition, The Danish Health and Medicines Authority recommends that high intensity training for 20 minutes be done at least twice weekly in order to maintain/improve fitness and muscle strength (bone strength; agility) (2).

Based on the literature from interventions, the ACSM concludes that it is safe for cancer patients to participate in physical training programmes, while undergoing cancer treatment. A few studies have reported adverse effects from the training. However, an expert panel highlighted that only half of the studies that include participants undergoing cancer treatment actually focused on the participants’ safety while in training. It was furthermore highlighted that physical training must be adjusted to the individual patient’s cancer diagnosis, illness status, cancer treatment and general health status (80-82). To date, no formal guidelines for physical training for cancer patients undertaking chemotherapy have been published in Denmark. In order to improve the competencies of health professionals in the field of oncology tasked with this training, the ACSM recommends that the trainers (the team) acquire a training certificate that qualifies them to focus on the cancer patients’ need for guidance and knowledge about specific symptoms and side-effects related to the individual’s illness and treatment process (40).

The literature

An intervention during the late 1990s, conducted by two American cancer nurses, Winningham og MacVicar, was the first research to show a significant positive effect (p=0.03) on nausea in the intervention group patients (83). They researched the effect of a ten week supervised fitness training programme using ergometer bicycles in patients with breast cancer and who were undertaking adjuvant chemotherapy (n=17). In 2001, when the Body & Cancer exercise intervention was initiated, there were few studies that had tested exercise as an instrument to reduce symptoms and side-effects. Today, the literature on oncology exercise is much more comprehensive, however, apart from fatigue, patient symptoms and side-effects during chemotherapy remain unexplored. A literature search was carried out (April 2012 and October 2012) with a broad search profile that included the words: Cancer, Exercise, Cardiovascular training, Resistance training, Relaxation training, Body awareness training, Massage, Symptoms, Side-effect, Fatigue, Pain, Paraesthesia, Myalgia, Arthralgia, Neuropathy, Constipation, Diarrhoea, Vomiting, Nausea, Lack of appetite and During chemotherapy (appendix 1a). 181 studies were identified of which 28 were reviews and/or meta-analyses, and the distribution of which matched the components of the Body & Cancer exercise intervention as follows: cardiovascular training: 47, resistance training: 16, relaxation training: 65, body awareness training: 11 and massage: 42. No studies found used all five exercise components at once as did the Body & Cancer exercise intervention. The majority of the published studies researched the effect of an exercise intervention on physical capacity maximum oxygen consumption (VO₂ Max) as the primary outcome measure. Typically, quality of life questionnaires were used as well as a limited number of symptom and side-effect sub-scales to...
shed light on psychosocial aspects. The majority of the studies did not describe with any precision what point in the patients treatment course did the patients actually participate in the interventions. Most of the existing exercise intervention studies included breast cancer patients which limited the generalization value for other cancer diagnosis groups. The literature is characterized by heterogeneity with regard to study design, methods and side-effects. As such, it is difficult to recommend an optimal combination of physical training components or intensity, frequency and duration of training. In order to get a basis for comparison with the results of Body & Cancer exercise intervention, the literature review was framed by the following components: 1) RCT, 2) diagnosis groups comparable with those in Body & Cancer exercise intervention, 3) studies in which exercise target patients undergoing chemotherapy, and 4) outcome measure on symptoms and side-effects, including: appetite loss, paresthesia, fatigue, muscle and joint pain, nausea, vomiting, diarrhoea and constipation.

**Cardiovascular and resistance training**

Only a few RCT studies have researched the effect of aerobic exercise on patients' reported symptoms and side-effects (84-89). The interventions comprise either hospital-based, structured, supervised exercise programmes or home-based exercise programmes, aerobic or resistance training or both, with varying degrees of duration, frequency and intensity (walking/cycling, 3-5 hours/weekly, 30-45 minutes, for a minimum of 5 weeks). The studies include primarily small samples of women with breast cancer who were undergoing adjuvant chemotherapy and haematological patients undergoing high-dose chemotherapy (81;90;91). Few RCTs targeted nausea and pain as outcome (92;93), however, some RCT have researched the extent to which patients undergoing chemotherapy can reduce their CRF during exercise interventions (85;94-96). The studies do not show a clear effect of cardiovascular and/or resistance training. Some studies have documented significant positive effects on CRF (89;97-100) while other studies did not find any significant CRF effect (100-102). The two largest RCT studies, Courneya et al. (2007) (n=242) and Adamsen et al. 2009 (n=269) found the opposite effect on CRF. Courneya et al. (94) did not find a significant effect with 17 weeks of supervised aerobic exercise/resistance training in women with breast cancer undergoing adjuvant chemotherapy, while the Body & Cancer exercise intervention saw a significant positive effect on CRF measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORCT-QLQ -30) (15).
Massage, Relaxation and Body-awareness Training

Few RCTs (103-107) have investigated the effect of massage on symptoms and side-effects in patients undergoing chemotherapy (CRF, peripheral neuropathy, pain, nausea). There is no evidence of any specific type of massage, frequency, intensity and duration that would be optimal to use as an intervention. No RCTs in cancer patients undergoing chemotherapy have investigated the effect of body-awareness training with the aim to reduce symptoms and side-effects. Some RCTs (93;108;109) have used progressive muscle relaxation training either as an isolated intervention or in combination with other interventions. The studies primarily researched nausea as an outcome focus. A more recent comparative study by Sawada et al. (110) that included patients undergoing chemotherapy (n= 75) in parallel with 24 weekly relaxation sessions (visualization and acupuncture), found statistically significant effect on fatigue (p = .009) and appetite loss (p= .009) in the intervention group, measured on the EORCT-QLQ 30-3 pre- and post test. A meta-analysis by Leubbert et al. (111), including 15 RCT (n=742), shows a significant positive effect on the patients’ self-reported nausea and pain, however, there was no significant effect on CRF from the relaxation training.

Central Reviews and meta-analysis: CRF, Pain, Nausea

Reviews and meta-analyses were identified based on their inclusion of patients during treatment as well as inclusion of CRF, pain and nausea as outcome foci. Two reviews, i.e. Speck et al. (112) and Leubbert et al. (111), undertook a meta-analysis with pain and nausea as foci. Speck et al. (112) found no significant positive effect on pain while Leubbert et al. (111) found significant positive effect of relaxation training on nausea and pain in patients undergoing treatment. Velthuis et al. (113), Kangas et al. (114), Cramp & Daniel (115), McNeely et al. (39) and Brown et al. (82) found significant positive effect on patients’ self-reported CRF during or post treatment while other reviews, i.e., Speck et al. (112), Jacobsen et al. (116) and Markes et al. (81) did not find statistically significant effect on CRF from exercise interventions (Table 1).
Table 1: Selected reviews and meta-analysis

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Study design</th>
<th>Sample</th>
<th>Author</th>
<th>Type of Intervention Frequency, Duration</th>
<th>Instrument used to assess CRF, Pain, Nausea</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed cancer diagnoses - during or post cancer treatment</td>
<td>83% breast cancer</td>
<td>66 studies high internal validity</td>
<td>Meta – analysis / CRF</td>
<td>Aerobic or combined activity interventions Moderate to vigorous intensity Frequency: 3-5 times/week Length min/session: 30-45min. Duration: a least 5 weeks</td>
<td>Information not provided</td>
<td>Meta-analysis/CRF: No significant results reported on CRF during cancer treatment No significant results reported on Pain during cancer treatment</td>
</tr>
</tbody>
</table>
| | | | Speck et al. 2010 (112) | All types of exercise, single or combined interventions Home based - supervised Aerobic exercise, cycle or walking, 40-80% Resistance training, intensity 60-70% /2x12 repetition Flexibility exercises Frequency day/week: a least 2 Length min/session: 10-90 min. Duration: a least 3 weeks | BFI FACT-An FACT-F PFS POMS r-PFS SAS | Meta-analysis/CRF: CRF ↓ 
A significant result reported on CRF in breast cancer patient during treatment on all exercises Effect-size 0.29 No significant results reported on CRF in breast cancer patient during treatment on home-based exercise A significant results reported effect on CRF in breast cancer patient during treatment on Aerobic exercise |
| Mixed cancer diagnoses - during or post cancer treatment | Total 18 studies (n= 1109) 12 studies/breast cancer 1 study/acute myelogenous leukaemia 1 study multiple myeloma 4 studies prostate cancer | Meta – analysis / CRF | Velthuis et al. 2010 (113) | All types of exercise interventions Moderate intensity Aerobic exercise, cycle or walking, 40-60% Resistance training, intensity 60-70% /2x12 repetition Average Frequency day/week: 3.5 Length min/session: 48.5 Duration: 11.5 weeks | FACT PFS EORTC QOL-C30 BFI Linear analogue scale Other | Meta-analysis/CRF: CRF ↓ 
A significant result reported on CRF among cancer survivors Effect-size 0.31 A significant result reported on CRF among breast cancer survivors Effect-size 0.39 CRF is primarily reduced in moderate intensity exercise programmes (p = 0.01), in strength training programmes among old cancer survivors (p = 0.04) and when supplemented with theoretical interventions (p < 0.001). |
| Mixed cancer diagnoses - during or post cancer treatment | Total 44 RCT (n= 3254) | Meta – analysis / CRF | Brown et al. 2010 (82) | Activity - based interventions Aerobic or resistance exercise Involved exercise recommendations - at least 150 min/week Cycle or walking | Information not provided | Meta – analysis/CRF: 
No significant results reported on CRF on activity-based intervention. |
| Mixed cancer diagnoses - during or post cancer treatment | Total 41 RCT 24 RCT /psychological interventions 17 RCT /activity-based interventions | Meta-analysis/CRF – 30 RCT | Jacobsen et al. 2007 (116) | Activity - based interventions Aerobic or resistance exercise Involved exercise recommenda- tions - at least 150 min/week Cycle or walking | Information not provided | Meta – analysis/CRF: 
No significant results reported on CRF on activity-based intervention. |
| Mixed cancer diagnoses – during or post cancer treatment | All types of exercise interventions | FACT-An, FACIT-F, PPS, SAS, EORTC QOL-C30 – fatigue sub-scale, The Schwartz Cancer fatigue | Meta-analysis/CRF: CRF ↓
A significant result reported on CRF during or post cancer treatment
**Effect-size 0.23**
A significant result reported on CRF during or post cancer treatment for breast cancer patient
**Effect-size 0.34**

Cramp & Daniel, 2008 (115)

| All types of exercise interventions | Home based - supervised
Aerobic exercise - cycle or walking
Strength training
Flexibility exercises : yoga - Relaxation
Frequency day/week: a least 2
Length min /session: 10-75
Duration: 3-32 weeks |

<table>
<thead>
<tr>
<th>Mixed cancer diagnoses - during or post cancer treatment</th>
<th>Aerobic or Aerobic and resistance exercise interventions</th>
<th>FACIT-F, PFS Visual analogue Scale for fatigue</th>
</tr>
</thead>
</table>
| Total 14 RCT (n=717) during or post cancer treatment | Frequency day/week: a least 2
Length min /session: 10-60
Aerobic exercise:
10 - 60 min cycle or walking
Resistive exercise:
Intensity : 10- 15 repetitions or at least 40%- 75% 1RM | Meta-analysis/CRF: CRF ↓
A significant result reported on CRF during adjuvant therapy or post treatment for breast cancer patient.
**Effect-size 0.46**

McNeely et al. 2006 (39)

<table>
<thead>
<tr>
<th>Mixed cancer diagnoses - during or post cancer treatment</th>
<th>ALL types of exercise interventions</th>
<th>POMS, FACIT, EORCT-QLQ-C30 – sub scale MOS-SF-36</th>
</tr>
</thead>
</table>
| Total 119 RCT and non – RCT | Multimodal exercise programmes
Walking intervention
Bicycle / cycling programmes
Cardiovascular, flexibility and/or strength training and resistance training. | Meta-analysis/CRF: CRF ↓
A Significant result reported on CRF during or post cancer treatment
**Effect-size 0.42**

Kangas et al. 2008 (114)

<table>
<thead>
<tr>
<th>Breast cancer - during adj. therapy</th>
<th>Aerobic or resistance exercise or both</th>
<th>PFS, SAS, F-36 vitality reversed</th>
</tr>
</thead>
</table>
| Total 9 studies (n=452) during adj. therapy | Aerobic exercise: 20- 60 min cycle or walking at least 3 days/week at least 6 weeks
Resistive exercise:
Intensity : 10-15 repetitions or at least 60% / 1RM At least 1 set Frequency 2-3 - day /week at least 6 weeks | Meta-analysis/CRF:
No significant results reported on CRF on breast cancer patient during adj. therapy.

Markes et al. 2006 (81)

<table>
<thead>
<tr>
<th>Mixed cancer diagnoses – during medical treatment</th>
<th>Progressive Muscle relaxation +/- Guided imagery +/- instruction to practice home (audio cassette)</th>
<th>Visual analogue Scale for nausea and pain</th>
</tr>
</thead>
</table>
| Total 15 RCT studies/ meta – analysis (n=742) | Number of session: Mean 3.6 – range 1.7
Duration of session : Mean 40 min - range 15-90 min
Intensity : Mean 149 min -range 15-360 min | Meta-analysis/nausea/pain/CRF: Nausea and pain ↓
A significant result reported on nausea during medical treatment
**Effect-size 0.45**
A significant result reported on pain during medical treatment
**Effect-size 0.43**
No significant results reported on CRF during medical treatment |

Leubbert et al. 2001 (111)

During treatment : Chemotherapy, radiation or hormonal therapy or a combination
During medical treatment : Chemotherapy, radiation , bone marrow transplant and hyperthermia
The Body & Cancer exercise intervention

The project was a prospective, longitudinal, clinically controlled trial in three phases: Phase I (feasibility study) included 23 patients and was completed in November 2001, confirming that the programme was safe and well tolerated (9). Phase II (diagnostic testing) included 88 patients and was completed in July 2003 (10;12;14;117;118). Phase III (randomization with intervention; and wait list control group) included 269 patients and was completed in December 2006 (15). The intervention demonstrated positive effects on depression (17), aerobic capacity, muscular strength, physical and functional activity, vitality, emotional wellbeing and fatigue (15). The Body & Cancer exercise intervention was continued in January 2007 as a specialized rehabilitation for cancer patients in the metropolitan area and as of January 2013, 1280 cancer have completed participation in the intervention.

The intervention: high- and low-intensity exercise

The intervention took place in a fitness facility located at the Copenhagen University Hospital and was carried out over a six week period, nine hours per week, in the mornings (Mondays, Tuesdays, Wednesdays and Fridays). The exercise intervention consisted of high- and low-intensity activities, including: (1) high-intensity physical training (119;120); (2) relaxation training (121;122); (3) body-awareness training (123;124); and (4) massage (125).

Table 2. Multimodal exercise intervention, weekly schedule (values: hours)

<table>
<thead>
<tr>
<th></th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
</tr>
</thead>
<tbody>
<tr>
<td>High intensity training*</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low intensity training</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body awareness</td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relaxation</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Massage</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Comprising: warm-up exercises, heavy resistance and cardiovascular training

In total high- and low-intensity activities were equivalent to a total of 43 Metabolic Equivalent of Task (MET) hours per week (126). The participants trained in mixed groups (i.e. non-discrimination of gender, diagnosis or stage of disease) consisting of 8 to 16 participants. Physiotherapists and Nurse Coaches specialists supervised the programme and participated in the physical training component. During physical training, the participants’ heart rates were continuously monitored by means of a wireless heart rate transmitter. The different components of the intervention constituted a total package implying that the high-intensity physical training did not allow participants to be selective of any one particular activity over another.
**High-intensity physical training (heavy resistance- and cardiovascular training)**

The fitness training involved 10-min. interval efforts on stationary bicycles at an intensity of 150-250 W, corresponding to 10.5 METs or 85%-95% of each patient’s maximum heart rate. Warm-up and cool-down exercises comprised dynamic actions with the large muscle groups (8 METs), stretching and coordination training (2.5 METs). In total the high intensity activities corresponded to 33 MET-hours per week. During heavy resistance training, patients trained at 85%-95% of one repetition maximum (1RM) corresponding to 6 METs (15;126).

**Low- intensity physical training**

This part of the programme comprised three components; A) *Relaxation training in groups (121;122).* Groups of patients were instructed in the use of relaxation techniques, using principles of progressive relaxation, i.e. tensing and relaxing major muscle groups. The patients used audio-tapes with recorded instructions and relaxing background music; (B) *Body-awareness training (123;124).* This part of the training focused on developing the patients’ awareness, recognition and control of their bodies as well as stretching, breathing, yoga and Pilates techniques. *Massage (125):* (C) Massage was provided on an individual basis and either induced relaxation or was therapeutic. Classic scar tissue and venous pump massage were administered as well as ultrasound (9) (p.709). In total the low intensity activities corresponded to 10 MET-hours per week.
The Nurse-Coach and related tasks and functions in the Body & Cancer exercise intervention

The Nurse-Coach

This description of the Nurse-Coach’s tasks and functions in the training component of the Body & Cancer exercise intervention is based on the author’s clinical experience and competences as a cancer nurse specialist educated as a nurse supervisor and who holds a Master’s degree in Public Health (MPH) sciences, as well as long term exercise experiences. Since initiation, the author (CA) has worked as a nurse in the Body & Cancer exercise intervention’s multidisciplinary team along with other members including physiotherapists, psychologists, sociologists and physicians.

The Nurse-Coach actively participates in the training sessions alongside the patients and performs investigative functions at Rigshospital’s Haematological and Oncological clinics, assessing potential patients for inclusion in the Body & Cancer exercise intervention. The Nurse-Coach builds collaboration between the clinic and the Body & Cancer exercise intervention’s multidisciplinary team.

The role of the Nurse-Coach is to carry out the following tasks and functions:

- Screening, recruiting and inclusion of patients in the Body & Cancer exercise intervention.
- Daily pre-screening for inclusion in the high intensity training.
- Motivational interviewing – ad hoc meetings.
- Coaching in management of symptoms and side-effects during the intervention period.
- Instruction in relaxation training (a component of the training programme).
- Facilitation of social processes among peers.

Screening, recruiting and inclusion of patients in the Body & Cancer exercise intervention

During the author’s (CA) thesis preparation period, 250 journals were screened and 130 ‘face-to-face’ meetings were held with patients in the oncology and haematology ward as well as the outpatient unit or by phone as part of the screening process for inclusion of patients in the Body & Cancer exercise intervention (from 2001-2006) and Programme (from 2007-2012) (appendix 2a +b). With uncertainty regarding the extent that the inclusion criteria could be met in the Body & Cancer exercise intervention – Phases I-III, the professors, both responsible for the cancer patients’ treatment (Professor, oncologist Mikael Rørth and Professor, haematologist Niels Borregard) were consulted. Daily presence in the oncology and haematology ward and the outpatient unit allowed for the distribution of folders about the project to patients as well as orienting patients receiving cytostatic treatment that physical training was an option for them despite their cancer, chemotherapy regimen, side-effects and symptoms such as fatigue. In order to underscore an exercise oriented context during the recruitment process, it was decided that the Body & Cancer exercise intervention team would be dressed in training clothing in the training facility as well as in the hospital ward.
**Daily pre-screening for inclusion in the high intensity training**

In 2001, when the Body & Cancer exercise intervention started, there were no national or international guidelines for preventing the risk of adverse events when providing physical activity options to cancer patients undergoing treatment (38;127). Initial international recommendations for exercise in the cancer patient population were made in 2006 and highlighted treatment complications such as thrombocytopenia, infection and serious disease related symptoms (40;128).

In order to prevent adverse events during the pre- and post-physiological max-tests (VO$_2$Max) and during high-intensity training, patients are excluded from training on any day on which he/she experiences one or more of the following symptoms:

1. Pulse at rest > 100.
2. Diastolic blood pressure < 45 or >95.
3. Temperature >38 degrees Celsius.
4. Respiration frequency at rest >20.
6. Leukocyte value < 1 mia/l.
7. Thrombocyte value < 50mia/L.

The intervention’s pre-exercise screening takes place in a separate room from the training facility to allow the screening and for the Nurse-Coach and patient to have an open dialogue about the patient’s physical and mental status. Over and above ensuring that the patient meets the screening criteria, the pre-screening allowed discussion about the patient’s health related situation and experiences with symptoms and side-effects of treatment. Throughout the intervention period, concrete coaching is continuously offered to patients facing issues with symptoms or side-effects. Prior to each patient’s pre-exercise screening, their blood test values are reviewed and that allows a more meaningful dialogue with the patient when establishing aims as the patient’s specific point in the treatment trajectory can then be considered. If, for example, a patient has a low haemoglobin level, the patient is advised to be aware of any dizziness, difficulty breathing, palpitations and headaches while he/she trains. These may be signs of low oxygen level in the blood and the patients then have to train at a slower pace. If the patient is excluded from participating in the exercise session on a given day, the patient’s treating ward (oncological/hematological) is contacted and an acute physician-nurse consultation is arranged to ensure that the patient’s wellbeing and symptoms and side-effects are managed as well as to prevent further complications. If any patient has concrete practical questions about their treatment trajectory and participation in the intervention, the patient’s treating ward is contacted. In total, there were 25 queries.
Pre-exercise screenings held during the training process could be, for instance, with breast cancer patients in adjuvant chemotherapy using (EC+D +G-CSF), and dialogue can focus on specific side-effects of the cytostatic regimen (53) in relation to physical training, e.g.

- Immunological suppression (52)
- Cardiological symptoms (129)
- Nausea (130)
- Muscle and joint pain (54)
- Limited shoulder/arm movement (131;132)
- Development of lymphoedema (133;134)
- Menopausal symptoms (52;135)
- Sensory neuropathies in toes and fingers (136)
- Changes to finger- and toenails (137)

**Motivational interviewing – ad hoc meetings**

Patient pre-screening are structured and take place three times weekly. In addition, the Nurse-Coach can invite patients to ad hoc coaching meetings. The aim of these coaching sessions is to encourage the patient to reflect on own resources and possible actions to use in managing symptoms and side-effects (fatigue, muscle pain, dizziness) when training as well as on sustaining physical activity following chemotherapy in order to prevent long-term co-morbidity (138). The Nurse-Coach is inspired by the principles of motivational interviewing in her meetings with patients. These principles include: 1) expressing empathy, 2) developing discrepancy, 3) resistance, and 4) self-efficacy (139).

Within the field of cancer, there are few studies (140-142) that have researched the effect of Motivational Interviewing in connection with physical activity amongst inactive cancer patients. Bennett et al. (140), in their RCT of 56 cancer patients, found that interventions with Motivational Interviewing can be used as a way of increasing regular physical activity and that patients’ self-efficacy plays a role in its success. In contrast, a study by Campbell et al. shows no significant effect of Motivational Interviewing on the level of physical activity amongst colorectal cancer patients (141). Coaching to manage symptoms and side-effects during the Body & Cancer exercise intervention physical training takes place under the supervision of two coaches (a Physiotherapist-Coach and a Nurse-Coach). The Nurse-Coach is responsible for individual coaching with a focus on the patient’s physical aim regarding symptoms and side-effects (fatigue, muscle pain, nausea) while the Physiotherapist-Coach is the instructor and responsible for implementing the group-based physical training and pre- and post-programme physical tests (VO₂Max). A coaching effort by the nurse may take the form of being a training partner to a patient who admits to feeling some discomfort (e.g. dizziness, nausea, difficulty breathing). The Nurse-Coach’s central role is to observe and monitor a patient’s functioning during training. The Nurse-Coach’s function ensures safety by having knowledge about each
patient’s disease and treatment and simultaneously being a motivator and ‘enforcer’ for the patients in the training context. The literature describes the patients’ treatment-related symptoms and side-effects as the greatest barrier for not participating in the exercise intervention during chemotherapy (143). If a patient does not feel well during training and needs to lie down, it is the Nurse-Coach’s responsibility to observe the patient’s level of consciousness, skin complexion, respiration, pulse and blood pressure, as well as to remain with the patient. The goal in this situation is to create a sense of safety for the patient as well as to lower the level of uncertainty that can spread to other patients. At the same time, it is the Nurse-Coach’s task to identify the patient’s discomfort (e.g. dehydration, medicinal, pain, fatigue, etc.). Depending on the situation, the patient is coached to rejoin the training session when he/she feels better; however, the patient would remain under intense observation.

Instruction in relaxation training
Based on the American physician and physiologist, Edmund Jacobsen’s principles for the progressive muscle relaxation technique, the Nurse-Coach instructor is responsible for conducting relaxation training sessions four times weekly (144;145). The relaxation session context is the training facility in which lights are dimmed and unnecessary noise minimized, including turning off mobile telephones and heart pulse watches. Patients lay on mats on the floor. Tight clothing and shoes are loosened and the patients are provided with pillows and blankets. Patients are instructed on how to take deep breaths to relieve tense muscles and about large muscle groups and each muscle within each group, and then while breathing deeply, to flex and relax each muscle. Relaxation starts with the lower extremities, moving in a straight line up to the head and facial region. The aim of this technique is to give the patient a physical consciousness about when relaxation increases while simultaneously creating a sense of deep relaxation in the body (144). Tapes/CDs that both instruct patients and provide background music (new age) accompany the relaxation session and increase the treatment’s integrity and uniformity. The patients borrow tapes/CDs to take home so that they can familiarize themselves more with the relaxation technique. During the entire relaxation session, the Nurse-Coach is present and guides patients in managing potential somatic problems (nausea/vomiting, muscle cramps) and emotional reactions.

Facilitation of social processes among peers
A central principle in the Body & Cancer exercise intervention is to focus on a context of group-oriented training. It is for this reason that the intervention comprises common warm-up activities such as ball games and aerobics, strength-training with ‘mates’, common bike training on stationary bicycles and body awareness and relaxation in groups. Our earlier qualitative findings demonstrate that being in a group is useful to attaining high adherence to the training programme (16;117). When new cancer patients start their participation as a team in the Body & Cancer exercise intervention, the first training session offers breakfast and a short round of presentations during which each participant’s expectations of the training programme
are highlighted. On the last training day, the team holds a smaller sports competition in which each participant receives a training diploma that documents his/her participation percentage and physical test results. The Nurse-Coach functions as an initiator and facilitator of social processes together with the physiotherapists in that they creates an optimistic atmosphere that is marked with humour, play, confidence in patient expectations and attention to the individual. These are contributing factors to creating the basis for the participants’ own management of their change processes, including management of their symptoms.

THEORETICAL INSPIRATION

Theory of Symptom Management

The Theory of Symptom Management was developed by nurse researchers at the University of California at San Francisco Symptom Management Center (5;146;147) and has been the inspiration for this thesis on physical activity’s potential influence on symptoms and side-effects in cancer patients undergoing chemotherapy. Theory of symptom management is a broad and comprehensive model that allows studying a symptom from both subjective and objective perspectives. In the model, symptom management is seen as a dynamic process between the patient’s experienced symptoms and the interactive effect of those in the same environment. According to Dodd et al., a symptom is defined as ‘a subjective experience reflecting changes in the bio-psychosocial functioning, sensations or cognition of an individual’, whereby it is only the patient alone who can decide whether the symptom control is reached (5).

Figure 3 The Symptom Management Conceptual Model (5),

The model comprises three essential concepts: 1) Symptom experience; 2) Components of symptom management strategies; and 3) outcomes of symptom status, and where the arrows in the model indicate the interaction between the three concepts (see figure 3). The concepts that are framed within the dimensions of nursing science (Person, Health & Illness and Environment) serve as a reminder of the contextual considerations for nursing. The symptom experience concept includes three interconnected
concepts; the patient’s perception of symptoms (frequency, intensity, distress), personal evaluation of each symptom; and response to the symptoms. The Symptom outcome concept includes, in principle, multiple outcomes such as functional status, emotional status, morbidity and co-morbidity, quality of life and self-care as well as economic losses. The Components of symptom management strategies are used to evaluate the intervention’s ability to 1) reduce the frequency of the symptom; 2) minimize the degree of the symptom; and 3) help to relieve the anxiety and uncertainty associated with the symptom (148).

It is not possible to identify studies that have tested the model in its entirety. Empirical studies have focused on highlighting patients’ symptom experience and symptom management strategies in different clinical settings (149-151). Carrieri-Kohlman et al. (150) used effective symptom management strategies such as a dyspnoea self-management programme in patients with chronic obstructive pulmonary disease. In clinical nursing practice, Ahlberg et al. used the model to illustrate a framework for the treatment of cancer-related fatigue in uterine cancer patients receiving radiotherapy (152).

The Theory of Symptom Management was seen as an inspiration to highlight the complex symptom and side-effect dimensions that can arise in patients undergoing chemotherapy during our intervention. The four components of the Body & Cancer exercise intervention together can be seen as a Symptom Management Strategy framework that integrates Symptom Management Strategies. Each of the components has equal potential to have an effect on the patient’s management of symptoms. The ‘Symptom experience dimension’ inspired Papers I and III.

Social Cognitive Theory and Self-efficacy

According to Albert Bandura, the Social Cognitive Theory is based on the fundamental assumption that behaviour is learned from one’s environment. Self-efficacy is a central component of the social cognitive theory and Bandura describes self-efficacy as: ‘Belief in one’s capabilities to organize and execute the courses of action required to produce given attainments’ (153) (p. 3). According to Bandura, the degree of self-efficacy is proportional with the opportunity to succeed. This is not an innate competency but one that needs to be learned (Bandura 1997). A person’s assessment of self-efficacy controls how he/she acts and what actions will be used. If one experienced success earlier on with overcoming a challenge then self-belief increases that one is capable of succeeding in a new circumstance (153).

Several observational and intervention studies have used Bandura’s Social Cognitive Theory as a framework for understanding cancer patients’ behaviour in connection with physical activity, as well as some intervention studies that used the theory in practice as a motivational strategy in cancer patients with sedentary behaviour (142;154;155). In studies of breast cancer patients, an association is seen between self-efficacy and motivation for positive behaviour in connection with physical activity, and which showed that women with high self-efficacy were more likely to be motivated to sustain their levels of physical activity (156;157). It has been an important principle that the Body & Cancer team use a resource and motivational
oriented approach with the patients, inspired by self-efficacy thinking (Paper I, II, III). This is done through encouraging and guiding patients to challenge their own physical abilities and simultaneously create awareness of physical limitations (16;158).

Coaching

Coaching in sport, psychology, business and nursing have been reported as being successful in motivating individuals towards personal and professional development (159). Stelter describes coaching as follows; ‘Coaching is a form of conversation which always shall be related to a specific context and situation in which the focus person is experiencing something significant and challenging - challenging in the sense that the focus person is governed by a desire for an in-depth reflection, understanding and change of him - or herself and certain circumstances in their life or work’ (160) (p. 1).

Few studies (84;161-163) describe the nurse as a coach in the context of exercise interventions, however, other intervention studies show a positive effect of coaching towards healthy lifestyle changes by nurses in older adult groups (164) as well as amongst young adults at risk of developing diabetes (165). More recent RCT intervention studies in cancer patients with pain (166;167) show a positive effect of combining interventions in which coaching by nurses is seen in components of the interventions. An intervention study by Park et al. (166) of post-treatment breast cancer patients (n=48) with the intervention 1) individual face-to-face education, 2) telephone-delivered health-coaching sessions, and 3) small-group meetings, showed a significant improvement in life quality and an increased sense of emotional well-being in the intervention group compared with the control group.

The communication component in the Nurse-Coach function of the Body & Cancer exercise intervention is inspired by Gregory Bateson’s (1904 – 1980) and Humberto Maturan’s (1928-) systems theory communication that is based on the understanding that everything in the world should be understood from a communications perspective and relative perspective (168). Three central concepts: context, recognition and neutrality steered the Nurse-Coach communication with patients in the Body & Cancer exercise intervention. During coaching sessions, the context is what determined how the coach understands the individual’s expressed focus, recognition of this focus by the coach creates a fundamental feeling of self-esteem and confidence, and with neutrality reflecting the coach’s curiosity and active presence in the dialogue with the patient (169-173).

Phenomenological methodology approach

The qualitative study (Paper III) in this thesis takes a phenomenological approach and it focuses on each patient’s experiences and actions in relation to muscle and joint pain, chemotherapy and physical activity. Phenomenology is based on Edmund Husserl’s (1859-1938) philosophic tradition that has been further developed by others including Martin Heidegger (1889-1976) and is an approach that analyzes the individual’s life experiences. Phenomenology takes two directions, i.e. descriptive phenomenology that
describes the meaning of an individual’s experiences and the interpretive phenomenology (hermeneutics) that interprets these experiences (174). Polit, describes the phenomenological approach as ‘... that lived experience gives meaning to each person’s perception of a particular phenomenon.’ - .... ‘that human existence is meaningful and interesting because of people consciousness of that existence. The phase being-in – the- world (or embodiment) is a concept that acknowledges people physical ties to their world – they think, see, hear, feel and are conscious through their bodies interaction with the world’. (175) (p. 253). In phenomenological studies, the focus is typically to draw a description of the lived experience and perceptions that the study raises. The American psychologist Amedeo Giorgi (176) highlights that the meaning of phenomenon or phenomena will surface without being dominated by the researcher’s understand or interpretation (176). Insight and understanding requires data that is based on the participants’ subjective description of the phenomenon (177;178). The method of analysis mainly makes use of a phenomenon’s four basic characteristics: ‘the descriptive’, ‘the reductive’, ‘Searching for the essence’ and ‘Focus on the intentionality’ (179)

MATERIALS AND METHODS

Design

The thesis applied method triangulation by combining quantitative and qualitative research methods (180;181). Including interview, standardized data collection and psychometric questionnaires developed by the Body & Cancer exercise intervention team. The research was carried out as a hypothesis-generated, prospective, clinical trial (phase II) with a one-group design, and a randomized controlled clinical intervention trial (phase III) with pre-and post-tests, as well as a descriptive and qualitative interview study.

Recruitment and inclusion criteria

All patients were initially attracted to the study by posters and pamphlets made available in the outpatient clinic or at oncology and haematology wards at the Rigshospital (Paper I, II, III) and Herlev Hospital, (Paper II and III) Copenhagen University Hospitals. Recruitment was carried out through efforts made by nurses and physicians in informing patients about the Body & Cancer exercise intervention and by the Nurse-Coach who likewise recruited and included the patients to the intervention. The patients were eligible to participate in the Body & Cancer exercise intervention (Paper I, II) if they had received at least one cycle of chemotherapy for advanced disease or as adjuvant treatment; had a WHO performance status of 0 or 1; were aged 18 to 65 years. Patients with brain or bone metastases, thrombocytopenia (<50x109 /l), myocardial infarction within the past three months, or uncontrolled hypertension (diastolic pressure >95 mm Hg.) were excluded (9). The breast cancer patients (paper III) were selected from a population of cancer patients undergoing chemotherapy and concurrently included in the Body & Cancer exercise intervention. A criterion sampling method was used. Patients who met the following criteria were eligible to participate in the qualitative study:
Operable breast cancer patients, aged >18 years. WHO performance status of 0 or 1, Participating in the Body & Cancer exercise and undergoing adjuvant chemotherapy regimen EC+D+ (G-CSF), had received at least three cycles of (EC) and were undergoing D+(G-CSF) during the six week study period.

Sample and excluded patients

The hypothesis-generated, prospective, clinical trial (phase II) - (Paper I)

Eighty-eight (n=88) patients gave written informed consent during the study period (January 2002- February 2003). Eleven patients dropped out, i.e. six patients due to progressive acute illness and two because they did not feel that they belonged to the group, and three patients were excluded because their treatment schedules had changed. Thus, 77 patients completed the six week intervention. Twenty-three patients were excluded from the data set. Nine patients were excluded because their chemotherapy schedules had changed or treatments had terminated, and a further 14 patients were omitted due to the fact that they had not completed all six semi-structured diaries. The characteristics of these patients did not differ from those included with regard to age, education, previous exercise history, diagnosis or treatment (Figure 4).

The Randomized controlled clinical trial (phase III) - (Paper II)

A total of 1956 cancer patients between 18-65 years of age were referred to chemotherapy at the oncological and haematological wards during the study period (March 2004 – March 2007). 506 patients attended pre-screening and 269 of these met the inclusion criteria and agreed to participate in the study. After written informed consent and baseline measures were obtained, the patients were randomized by computer (Clinical Internet Trial Management System: CITMAS) to the intervention group or to the wait-list control group. The patients were stratified by gender, cancer diagnosis (breast, bowel, other solid tumours, haematological malignancies) and disease status. Patients with No Evidence of Disease (NED) received adjuvant chemotherapy after radical local treatment for their cancer disease. Patients with Evidence of Disease (ED) had residual or advanced disease after the initial diagnosis of cancer was made by biopsy or local treatment. Participants assigned to the wait-list control group received conventional medical care and were allowed to undertake unrestricted physical activity and they completed outcome measures identical to those of the intervention group. The wait-list control group patients were invited to participate in the intervention programme after their participation in the study period. Allocated to the intervention group were 135 participants and 134 to the control group. Post-intervention data after six weeks were obtained from 106 intervention group participants (78.5%) and 107 in the control group (79.8%) (n = 213), using the FACT-An Questionnaire. After the six weeks study period, 57% of the wait-list control group patients in this study subsequently elected to participate in the Body & Cancer exercise intervention and therefore it was not possible to report relevant follow-up data.
The descriptive and qualitative interview study - (Paper III)

Eighty-two (n=82) patients agreed to attend the Body & Cancer exercise intervention (August 2011 - January 2012). Sixty-seven patients did not meet the inclusion criteria, 45 had other cancer diagnoses, 20 breast cancer patients were not undergoing adjuvant chemotherapy (D+G-CSF) and two patients were medically treated for muscle and joint pain. All 15 (n=15) surveyed breast cancer patients provided written and verbal consent prior to their participation.

Data collection

The thesis included two quantitative methods, a semi-structured diary study and a questionnaire study. The semi-structured diary method was developed based on the assumption that cancer patient's symptoms and side-effects patterns continuously change concurrently the patient's individual disease status, chemotherapy regimen and to demonstrate the impact of the intervention on selected symptoms and side-effects. The questionnaire Fact-An was selected to highlight several dimensions of CRF, and to compare results with exercise studies (182;183). The qualitative method was applied to get multifaceted knowledge (184;185) of the interventions impact on the patients’ perception of pain.

Quantitative data collection

Medical, demographic and physical activity level data (Paper I, II, III)

Medical, Demographic data and Leisure time physical activity level (pre-illness, baseline, post intervention) were collected through self-report questionnaires (pre- and post-test) (Appendix 2c) and medical data (diagnosis, disease status, relapse of disease, chemotherapy regime, chemotherapy cycles before the study period and chemotherapy during the study period) were drawn from patient records. The participants completed the questionnaires baseline, before the randomization, and after the six week study period (pre- and post-test).
The Body and Cancer trial Phase II  
(January 2002 - February 2003)  
One group design, Heterogeneous sample  
(n=64)

Written informed consent to enter the study  
(n=88)

Drop-outs (n=11)  
Progressive acute illness (n=6)  
Not feel belonged to the group (n=2)  
Treatment schedules had changed (n=3)

Excluded (n=237)  
Did not meet inclusion criteria: Performance status ≥ 2 (n=44), 
Health problems (n=77), Chemotherapy completed (n=43), Other reasons (n=71)

Not assessed at 6 Weeks (n=27)  
Not contactable (n=3), Absent from test (n=8), Infections (n=2), Bone marrow suppression (n=1), Failed to complete FACT-An and symptom assessment questionnaire (n=10)

Allocated to control Group (n=134)

Control group (n=107)

Allocated to intervention Group (n=135)

Not assessed at 6 Weeks (n=29)  
Never started the programme (n=2), Infections (n=7), Bone marrow suppression (n=4), Excluded (n=1) Other health problems (n=3), Failed to complete FACT-An questionnaire (n=12)

Pre-post intervention study
Primary outcome: 12 selected symptoms/side-effects; lack of appetite, nausea, vomiting, diarrhea, paraesthesia, constipation, physical fatigue, mental fatigue, treatment related fatigue, muscle pain, arthralgia and other pain evaluated by semi-structured diaries
Sample: n=54

Pre-post test
Primary outcome cancer related fatigue evaluated by Functional Assessment of Cancer Therapy-Anemia Questionnaire (FACT-An).
Sample: n=213

Figure 4: Patients flow chart

The Body and Cancer trial Phase III  
(March 2004 – March 2007)  
RCT-design - Heterogeneous sample  
(n=213)

Agreed to Attend Pre-screening (n=506)

Excluded (n=237)  
Did not meet inclusion criteria: Performance status ≥ 2 (n=44), Health problems (n=77), Chemotherapy completed (n=43), Other reasons (n=71)

Randomised (n=269)

Allocated to control Group (n=134)

Allocated to intervention Group (n=135)

Pre and post Semi-structured Interviews  
Focus on: Perceptions and management of muscle and joint pain experienced by women with operable breast cancer undergoing adjuvant chemotherapy EC+D (G-CSF) during the exercise intervention
Sample: n=15

The Body and Cancer rehabilitation (Paper III)  
(August 2011 - February 2012)  
Descriptive and qualitative study - Homogeneous sample  
(n=15)

Agreed to attend Body & Cancer  
(n=82)

Excluded (n=67)  
Did not meet inclusion criteria: Other cancer Diagnoses (n=45), Breast cancer pt. not undergoing adjuvant chemotherapy D+E+G-CSF during the 6 weeks (n=20) or pre-illness medically treated for muscle and joint pain(n=2)

Control group (n=107)  
Intervention Group (n=106)

Pre-post intervention study
Primary outcome: 12 selected symptoms/side-effects; lack of appetite, nausea, vomiting, diarrhea, paraesthesia, constipation, physical fatigue, mental fatigue, treatment related fatigue, muscle pain, arthralgia and other pain evaluated by semi-structured diaries
Sample: n=54

Pre-post test
Primary outcome cancer related fatigue evaluated by Functional Assessment of Cancer Therapy-Anemia Questionnaire (FACT-An).
Sample: n=213

Focus on: Perceptions and management of muscle and joint pain experienced by women with operable breast cancer undergoing adjuvant chemotherapy EC+D (G-CSF) during the exercise intervention
Sample: n=15
Semi-structured diaries (Paper I)

In order to obtain a detailed and continuous registration of the patient’s symptoms and side-effects during the exercise intervention a patient diary was developed by the Body & Cancer exercise intervention team and used throughout the six weeks of the intervention. The study outcomes were 12 individual symptom and side-effects and the sum of the participants’ symptom and side-effects. The diary comprised a structured part based on closed questions and a free text part. Each patient used one book per week that was then handed to the Nurse-Coach at the end of the week. The diary format comprised eight A4 pages. The patients recorded the date and hour of treatment in their respective diaries. The free text part comprised blank pages in which the patients could describe experiences and actions related to managing their symptoms and side-effects. The symptoms and side-effects categories in the diary were tested by reviewing diary entries of 11 of the patients. Interviews were then conducted by an external interviewer with these same patients to compare similarity of responses with those provided in the respective diaries. Each interview had duration of 10–15 min. This test gave rise to a few corrections in the diary categories: physical-, mental-, and treatment-related fatigue and other pain. We selected 12 symptoms and side-effects of chemotherapy in order to grasp a comprehensive picture of the total sum on the patients’ symptoms and side-effects. The side-effects and symptoms were selected from our clinical experience and with reference to reported data on frequency in the literature (186). We did not include symptoms and side-effects that had no direct link to physical activity (e.g. hair loss). Furthermore, the 12 symptom and side-effects served as a screening test for possible deleterious effects of the rather strenuous intervention. The following symptoms and side-effects were recorded daily: lack of appetite, nausea, vomiting, diarrhoea, paraesthesia, constipation, physical fatigue, treatment-related fatigue, mental fatigue, myalgia, arthralgia and other pains. The symptoms and side-effects were defined and based on the validated Common Toxicity Criteria (CTC) (187) and the patient scored each symptom/side-effect on a scale from 0 to 4 (0 = no symptoms, 1 = little, 2 = moderate, 3 = heavy, 4 = intolerable symptoms). The patients scored their nausea, lack of appetite and paraesthesia on a scale from 0 to 3 (appendix 2d).

Functional Assessment of Cancer Therapy – Anaemia Questionnaire (FACT-An) (Paper II)

The participants completed the Danish version of the well validated FACT-An questionnaire (Version 4) before randomization and after the 6 week study period (pre & posttest) (182;188). The primary outcome, Fatigue score (CRF), was assessed using the Fact-An Anaemia Subscale. FACT-An is a 47 item, cancer-specific questionnaire consisting of 27 items (FACT-General (FACT-G score)) that measures the four general domains of Quality of Life, and an additional 20 items related to anemia (FACT-An Anemia subscale) that measures 13 items related to fatigue (Fatigue score) and seven items indirectly related to fatigue (Anaemia - ANS Score) (189). The four general domains of Quality of Life measured in the FACT-G include: Physical wellbeing (PWB); meeting daily needs without physical symptoms (seven items), Social wellbeing (SWB); social or family
support (seven items), Emotional-wellbeing (EWB); sadness and degree of worry (six items), Functional wellbeing (FWB); enjoyment and fulfilment (seven items). The sum of PWB, FWB and FACT-An Anemia subscales form the Trial Outcome Index Anaemia (FACT-An Toi) (34 items) score and is regarded as a useful summary index to measure physical and functional capacity. All items on the FACT-An questionnaire range seven days back. Scores were registered on a 5-point Likert Scale ranging from 0 to 4 (‘not at all’ – ‘very much’) (182;188;189). The possible score ranges are as follows; Fatigue (0-52), FACT-An (0-188), FACT-G (0-108), FACT-An Toi (0-136), PWB (0-28), SWB (0-28), EWB (0-24) and FWB (0-28). Low scores indicate poor quality of life while high scores indicate good quality of life. Likewise, high fatigue scores indicate less fatigue, with a range from 0 to 52 (appendix 2e).

Qualitative data collection

The individual semi-structured (Paper III)

The individual semi-structured interviews were conducted on two occasions; before entering the intervention (pre –interview) and on completion of the intervention (post-interview after six weeks). The participants were interviewed individually by CA in an office close to the fitness facilities. The themes covered in the two interviews were: (pre-interview, baseline of Body & Cancer): the impact of cancer diagnosis/treatment (chemotherapy EC followed by D with G-CSF), prior experience with and interpretation of pain symptoms and expectations of the training programme on pain; (post-interview, completion of Body & Cancer): descriptions of the pain (intensity, management, compliance and correlation between expectations experiences), pain perception (intensity and amangement with supervised hith-and low physical training (warming-up, strength, fitness, relaxation and massage)), (appendix 2f). The average duration of the interviews was 50 minutes (35 minutes minimum to 100 minutes maximum), all interviews were tape-recorded. The interviews were transcribed verbatim using Microsoft Word (DSS Player Pro Transcription Module, version 5). Data saturation was reached after 13 participants had been interviewed but to ensure no further relevant themes could be derived from the interviews, two further interviews were performed (n = 15) (190).

DATA ANALYSIS AND INTERPRETATION

Quantitative data analysis (Paper I & II)

In Paper I data were entered into Excel using Microsoft Office 2000 Professional for Windows 2000. Patients with missing data were excluded from the data set using the following criteria: (1) consecutive periods of missing data for 6 days or more; or (2) more than 20% of total data missing. When data for included patients were missing, substitute values were calculated as the average of the values from the other days during that particular week. The total impact of symptoms and side-effects for each patient was calculated from the sum of the scores for the patient on that particular day. Each week the mean scores of the daily results were
calculated and depicted graphically. With regard to pain, individual scores for myalgia, arthralgia and “other pains” were calculated as well as the sum of these pain scores. Mental fatigue, treatment-related fatigue and physical fatigue were summed up as the total fatigue-related score; constipation and diarrhoea were summed up as the total score for gastrointestinal problems; and finally, vomiting, appetite and nausea were summed up as the total score for gastric problems. Statistical analyses were carried out using the statistics analysis software tool, Strategic Analysis System (SAS) for Windows (Version 9.1). The results were produced using PROC MIXED (the Mixed Procedure SAS software tool) by using the number of days from baseline as the explanatory variable and, where indicated, disease status as an additional, categorized, explanatory variable. Each patient’s daily scores were repeated, e.g. dependent observations with the following structure: the correlation between successive observations declines exponentially with time between the respective observations (AR = 1). The Satterweight method for approximation of degree of freedom was used as the basis for determining probabilities of significance.

In Paper II the baseline comparisons were performed using univariate analysis of variance for continuous variables and likelihood 2 analysis for categorical variables. Primary analysis was undertaken post hoc and we examined whether significant differences in outcome (mean differences) between baseline and six weeks existed between the intervention and control groups with respect to CRF measures (FACT-An questionnaire Fatigue scale). According to Cella et al. (183), the minimal clinically important difference on the Fact-An scales is estimated to be for the five targeted scores: Fatigue Score = 3.0, FACT-An score = 7.0, Fact-G score = 4.0 and the FACT-An Toi score = 6.0. We performed a forward stepwise regression analysis using differences in outcome between baseline and six weeks (in all outcome measures) as the dependent variable in a general linear model (GLM). The stepwise procedure was initiated by identifying the covariate that was most strongly related to the dependent variable. The next strongest related covariate was then selected after controlling for the first covariate, and so on. As such, only significant covariates were included in the model. The variable intervention/control was fixed and the following 13 covariates were tested: sex, age, cohabitation, educational level, baseline outcome score, relative change in B-haemoglobin, VO₂Max , one repetition maximum knee extension and the five disease related covariates; diagnosis, evidence of disease, relapse of disease, chemotherapy cycles before the study period and chemotherapy during the study period (15). All analyses were tested with a significance level of p<0.05 by using the ‘intention to treat’ principle. Available data for participants with missing data were included under the ‘missing at random’ assumption. Clinically important changes were estimated using Cohen’s guidelines, whereby a value of 0.2 denoted a small effect size, 0.5 a medium and 0.8 a large effect size (191;192). Effect size (ES) was calculated by the mean difference divided by the pooled standard deviation and the root mean square error was estimated using the general linear model (GLM).
**Qualitative data analysis (Paper III & I)**

The analysis in paper III was inspired by Giorgi’s phenomenological method of analysis, based on decontextualization and recontextualization, the study’s analytical process was carried out in four steps (176). This is to be regarded as an attempt to reach an understanding of each participant’s personal experiences and management of treatment-induced pain and to get an insight into the participant’s transformation from a ‘healthy life’ to a ‘painful life’. The first step consisted of reading the transcriptions in order to gain a comprehensive overview of the material and to pinpoint possible themes. In practice, each participant’s interview was read through several times (Segments). The next step involved reading the interview material again with the aim of identifying and framing important allegations from which themes could be extracted as general meaningful text heading (Meaning units). This was done to identify distinct thought segments in the interview transcripts and to underscore any common accounts given by the women. These meaningful text segments were then sorted by group and/or patterns and were copied onto a separate file and reread to identify central themes for each thought unit (176). The third step involved identifying specific meaningful text headings (theme) related to the study’s goals (Categories). According to Giorgi, it is at this step in the process that estimation should be made of the understanding of the phenomenon in order to avoid misinterpretation of the women’s accounts or being unable to see the phenomenon in an objective manner (176). An important development in this part of the analytical process was therefore to minimize and ‘put aside’ earlier knowledge about the phenomenon (phenomenological reduction). The final step of the process involved summarizing the sense of each category into a general analysis and entailed a comprehensive identification of ‘universal’ and ‘unique’ themes across all of the interviews, summing up each theme area to form a heading so that the essence of the phenomenon could be clearly identified (Essence). The analysis was carried out by the principal author (CA), in continuous collaboration with the co-author (LA). Throughout the analytical process and particularly in the final phase during which themes of the phenomenon’s essence were identified.

Description of the Analytical Process (appendix1 b).

In Paper I the qualitative data from the diaries was categorized in accordance with the thematically symptoms and side-effects. A few citations were selected by the authors (CA, LA) to illustrate the qualitative aspects of the symptoms and side-effects as they provide examples of the complexity of the intervention.

**ETHICAL CONSIDERATIONS**

The studies were approved by the Scientific Committees of the Copenhagen and Frederiksberg Municipalities (J.nr. 01-273/00) that evaluated both the ethical aspects and methodologies used in the research project. In addition, the study was approved by the Danish Data Protection Agency (J.nr. 2000-41-0-149) and Trial registration Current Controlled trials ISRCTN05322922 (Appendix 2 g).
In addition, the studies were carried out in accordance with the Helsinki II declaration and the participants provided informed oral and written consent in compliance with requirements of the Committee. After contacting The Scientific Committees of the Copenhagen and Frederiksberg Municipalities and the Danish Data Protection Agency, it was announced that the dissertation qualitative study did not require separate approvals, referring to previous approval (No. 01-273/00) (J. No 2000-41-0-149).

RESULTS

The effect of a multidimensional exercise programme on symptoms and side-effects in cancer patients undergoing chemotherapy - The use of semi-structured diaries- Paper I (published)

The aim of this paper was to evaluate the effect of the intervention programme on the cancer patients’ self-reported symptoms and side-effects while undergoing chemotherapy. This paper includes results from 54 patients (n= 54) who received antiemetic drugs: 5 HT3 receptor antagonists (Zofran, Kytril), Metoclopramide (Emperal), Metopimazin (Vogalene) and/or Prednisone according to the standards of the individual treatment regimens. The patients’ demographic and clinical characteristics are described in appendix 1c and 1d. The intervention group’s adherence rate to the intervention was 75%. During the intervention period a decrease in ten of the 12 symptoms and side-effects and in the sum of symptoms and side-effects were found (Figure 5). The individual symptoms and side-effects scores changed as follows; physical fatigue (from 0.95 to 0.74); treatment-related fatigue (from 0.83 to 0.55), mental fatigue (from 0.75 to 0.57), other pain (from 0.53 to 0.39), paraesthesia (from 0.53 to 0.43), lack of appetite (from 0.43 to 0.34), constipation (from 0.40 to 0.24), myalgia (from 0.36 to 0.17), arthralgia from 0.31 to 0.29) and diarrhoea (from 0.17 to 0.06). The myalgia scores (and other pain scores) changed significantly (p= 0.013 and 0.041, respectively). None of the other changes reached statistical significance at the 95% level. The score for vomiting was unchanged (from 0.04 to 0.04) and nausea in significance increased from 0.22 to 0.24. The sum of the symptoms and side-effects decreased by (27%) (p=0.036). A total of 36 (67%) of the patients experienced a reduction in the sum of the symptoms and side-effects, while 13 (24%) showed an increase in this sum and 5 (9%) did not change their sum of symptoms and side-effects (Figure 6). Patients with ED (n =26) had a significantly higher level of symptoms and side-effects than patients with NED (n=28) (p = 0.027). Both groups did experience a significant reduction in the sum of symptoms and side-effects during the intervention (Figure 7).
**Figure 5:** Scores of 12 side-effects at start of intervention and after 6 weeks Mean ± S.D, n=54.

**Figure 6:** The sum of symptoms and side-effects during the 6 week intervention.

**Figure 7:** Sum of the average scores of symptoms and side-effects in NED (n=28) and ED patients (n=26) during the 6 week intervention.

With regard to the individual symptoms and side-effects, the differences between ED and NED patients were particularly clear when looking at myalgia (p =0.002), physical fatigue (p = 0.001) and treatment-related fatigue (P =0.003). Patients with ED had significantly less nausea (p = 0. 038) than patients with NED. The total scores for pain (Myalgia, Arthralgia Other pain, Paraesthesiae) decreased significantly during the intervention (p=0.046) (Figure 8), while the sum of fatigue-related scores (physical fatigue, treatment-related fatigue, mental fatigue) decreased during the intervention from 2.53 to 1.87 (p =0.069) (Figure 9). The
combined gastrointestinal symptoms and side-effects (constipation, diarrhoea) were reduced from 0.57 to 0.30 (p = 0.60) (Figure 10). The combined score of symptoms and side-effects related to food intake (lack of appetite, nausea and vomiting) did not change (p = 0.083) over the intervention period (Figure 11). In a subsequent, randomized study of the same intervention including 213 patients with various cancer diagnoses the significant differences reported here could not be confirmed. Only non-significant changes in the 12 selected variables were found. The symptoms were recorded in semi-structured diaries.

Figure 8: Stacked average daily scores per patient for Myalgia, Arthralgia, Other pain and Paraesthesiae for each week during the intervention period. (n=54).

Figure 9: Stacked average daily score per patient for Mental fatigue, Treated related fatigue and Physical fatigue for each week during the intervention period (n=54).

Figure 10: Stacked average daily score per patient for Constipation and Diarrhoea for each week during the intervention period (n=54).
The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue- Paper II (published)

The aim of this paper was to evaluate whether the exercise intervention could reduce the level of the patient’s CRF. The cancer patients (n=213) were randomised into an intervention group (n= 106) or to a waiting-list control group (n=107). The patient’s demographic and clinical characteristics are described in appendix 1e and 1f. The intervention group’s adherence rate to the intervention programme was 73% (mean: 18 out of 24 training days; range 5-24). The results presented are based on the Fatigue Functional Assessment of CANCER Therapy-Anaemia Questionnaire (FACT-An) where the primary outcome was the Fatigue score. A clinical significant improvement on the Fatigue score by 3.04 (effect size of 0.44, 95% CI 0.17- 0.72) (p=.002) was seen in the intervention group compared with the control group. Furthermore, there was a clinical significant effect from baseline to six weeks in favour of the intervention group, where the ‘anaemia scale’ was included. Significant improvements were seen in the FACT-An score by 5.40 (effect size of 0.34, 95% CI 0.07 to 0.6), (p=.0145), the FACT-An Toi score by 5.22 (effect size of 0.37, 95% CI 0.1 to 0.65) (p=.009) and the Anaemia-ANS by 3.76 (effect size of 0.44, 95 CI 0.17 to 0.71) (p=.002) compared with the control group. In addition, there was no statistically significant effect on the General Quality of Life score (FACT-G) or on any of the individual wellbeing scores; Physical (p= 0.13), Emotional (p= 0.87), Social (p= 0.83) and Functional (p=0.26) (Table 3).

Figure 11 Stacked average daily score per patient for Vomiting, Lack of appetite and Nausea, for each week during the intervention period. (n=54).
### Table 3. FACT-An outcome variables intervention effect estimates

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean (SD) Baseline</th>
<th>6 Weeks</th>
<th>Test (Reference: Control) Mean Difference (95% CI)</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatigue score (0-52)&lt;sup&gt;b&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>35.34 (9.88)</td>
<td>36.34 (9.27)</td>
<td>3.04 (1.17 to 4.91)</td>
<td><strong>.002</strong></td>
</tr>
<tr>
<td>Intervention</td>
<td>36.86 (9.54)</td>
<td>40.24 (7.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FACT-An score (0-188)&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>135.27 (25.07)</td>
<td>139.14 (24.08)</td>
<td>5.40 (1.09 to 9.73)</td>
<td><strong>.015</strong></td>
</tr>
<tr>
<td>Intervention</td>
<td>140.43 (24.16)</td>
<td>147.60 (21.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FACT-G score (0-108)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>78.84 (13.97)</td>
<td>81.45 (13.33)</td>
<td>1.55 (-0.90 to 4.01)</td>
<td>.21</td>
</tr>
<tr>
<td>Intervention</td>
<td>81.14 (14.51)</td>
<td>84.41 (12.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FACT-An Toi score (0-136)&lt;sup&gt;d&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>93.81 (21.70)</td>
<td>97.11 (20.51)</td>
<td>5.22 (1.34 to 9.11)</td>
<td><strong>.009</strong></td>
</tr>
<tr>
<td>Intervention</td>
<td>98.80 (20.31)</td>
<td>105.08 (17.51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anaemia ANS Score (0-80)&lt;sup&gt;e&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>56.42 (12.76)</td>
<td>57.69 (12.28)</td>
<td>3.76 (1.42 to 6.10)</td>
<td><strong>.002</strong></td>
</tr>
<tr>
<td>Intervention</td>
<td>59.07 (12.06)</td>
<td>63.02 (10.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PWB score physical well-being (0-28)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>19.77 (5.44)</td>
<td>20.59 (5.19)</td>
<td>0.91 (-0.27 to 2.10)</td>
<td>.13</td>
</tr>
<tr>
<td>Intervention</td>
<td>20.64 (5.41)</td>
<td>21.92 (4.59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EWB Score emotional well-being (0-24)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>17.69 (4.32)</td>
<td>18.91 (3.73)</td>
<td>0.06 (-0.67 to 0.80)</td>
<td>.87</td>
</tr>
<tr>
<td>Intervention</td>
<td>18.14 (4.01)</td>
<td>19.25 (3.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SWB Score social well-being (0-28)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23.53 (3.77)</td>
<td>23.27 (3.73)</td>
<td>0.08 (-0.63 to 0.78)</td>
<td>.83</td>
</tr>
<tr>
<td>Intervention</td>
<td>23.38 (4.20)</td>
<td>23.25 (3.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FWB Score functional well-being (0-28)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>17.85 (5.81)</td>
<td>18.67 (5.10)</td>
<td>0.57 (-0.42 to 1.56)</td>
<td>.26</td>
</tr>
<tr>
<td>Intervention</td>
<td>18.93 (4.97)</td>
<td>19.92 (4.88)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; SD, standard deviation

<sup>a</sup>Based on general linear model adjusted for sex, age, cohabiting, educational level, baseline outcome score, relative change in B-haemoglobin, maximal oxygen uptake (VO2max), one repetition maximum knee extension, diagnose, NED (no evidence of disease) /ED(evidence of disease), Relapse of disease, chemotherapy prior and during intervention.

Effect size (ES) on significant outcomes:
- Fatigue ES<sup>b</sup>=<strong>0.44</strong> (CI:0.17-0.72)
- FACT-An ES<sup>c</sup>=<strong>0.34</strong> (CI:0.07-0.6)
- FACT-An Toi ES<sup>d</sup>=<strong>0.37</strong> (CI:0.1-0.65)
- Anaemia ANS score ES<sup>e</sup>=<strong>0.44</strong> (CI:0.17-0.71)
Using a criterion sampling strategy, 15 pre- and post exercise semi-structured interviews with operable breast cancer patients in the study period (six week) were included in this analysis and the patients’ perception and management of potential muscle and joint pain was explored on the days following the chemotherapy (D+ (G-CSF)). The patient’s demographic and clinical characteristics are described in appendix 1g. The participants’ adherence rate to the exercise intervention was 77% (mean: 18.5 out of 24 training days; range 9-22). The findings of the phenomenological analysis identified four categories. **Abrupt pain – a predominant side-effect, Cogitated pain Management, Adapted training, No immediate exacerbation of pain and Exercise despite pain** as a final expression of the phenomenon’s essence. The participants felt muscle and joint pain during 2-3 days after the chemotherapy infusion (D+ (G-CSF)). They were convinced that their pain was primarily caused by chemotherapy.

The pain was described as stabbing and nagging, growing pains primarily from muscle and joint in different parts of the body and shifting around in the body during the weeks that the pain persisted. With respect to the participants pre-illness ways of managing pain, e.g. headaches, menstrual pain, lower back pain, they used two strategies for pain management; physical activity (jogging or walking) or relaxation. During the Body & Cancer exercise intervention the majority of the study participants (n=12) used the same strategy for managing their pain as they had used prior to their cancer diagnosis. Few of the participants (n=3) who had expected that they could manage their chemotherapy related pain in the same fashion as they had with previously experienced pain, stated that it was not possible to maintain their strategy. A few of the women (n=3) actually attended all of the training sessions, even during those days when they experienced muscle and joint pain originating from chemotherapy, while the rest of the participants claimed that, at least twice (range 2-7) they had to cancel their participation in exercise as their muscle and joint pain was so disabling that they did not feel able to participate. However, the majority of the women (n=10) informed that their pain did not worsen during the training sessions. A consequence of the participants muscle and joint pain was that the patients had to diminish the intensity and frequency of training and needed to take several breaks during the training programme. In relation to the programme’s strength training component, the majority of the women (n=13) informed that despite having pain sensations they were able to carry out their respective strength training programmes. During the women’s training process, they have shown that they are aware that active participation in exercise can shift focus away from pain sensations. Using the physical exercise context (high music etc) made it possible for the women to better neglect their feeling of pain.
DISCUSSION

Introduction

This thesis presents results on the impact of an exercise intervention on selected symptoms and side-effects of cancer patients with different diagnoses, who are undertaking adjuvant chemotherapy or who are being treated for advanced stages of the disease. Quantitative and qualitative methods are used in this thesis. The quantitative method (questionnaires and diary registrations) is used to investigate the subjective goal (loss of appetite, nausea, vomiting, diarrhoea, paraesthesia, constipation, mental fatigue, treatment-related fatigue, physical fatigue, muscle pain, joint pain and other pain, CRF). The qualitative method provides insight into the breast cancer patient’s pain status during the treatment process with adjuvant chemotherapy (D+ (G-CSF)). Firstly, Paper I states the results of a one-group design study that investigates the effect of the patients’ (n=54) total burden of side-effects from 12 symptoms as well as side-effects during the six week study period. Secondly, the results of a RTC (n=213) are presented, that evaluate whether the intervention programme as a supplement to chemotherapy can lead to reduced patient reported CEF. Thirdly, Paper III presents a descriptive, qualitative study of 15 operable breast cancer patients’ experiences with chemotherapy related muscle and joint pain during the study period. Not least, insights are offered regarding the qualifications, competences and functions of the Nurse-Coach role with patients participating in the Body & Cancer exercise intervention.

Methodological considerations and limitations

Strengths and limitations in the study population and exercise intervention

The selection of patients for this study is subjected to bias as not all patients in chemotherapy were informed of the intervention. The selected patients were informed about the intervention by the doctors and nurses, who took care of their treatment and by posters in the departments and out-patient clinics. It is furthermore very likely that the included patients were a priori better motivated and more used to being physical active, than the population of patients as a whole. This was evident from a questionnaire, where 2/3 of the included patients reported, that they exercised regularly at least 3h/week (3). Our patients were relatively well-educated (2/3 had completed secondary school or higher), young (average age 45 years) and in good performance status (WHO 0-1). Therefore, the results of this study (Paper I and Paper II) are not generalizable to the total population of cancer patients in Denmark receiving chemotherapy. It has never been the intention to blind the professionals (physiotherapists and the nurse-coach) in the Body & Cancer exercise intervention team on the contrary it has been an important principle that the team should apply a resource and motivational oriented approach with the patients. The professionals in the exercise team conducting the daily exercise sessions supervised and motivated the patients during the exercise guiding patients to challenge their own physical abilities and simultaneously create awareness of physical limitations.
The quantitative data were keyed in and analysed by research assistants who were not involved in the intervention.

**Quantitative methods considerations and limitations**

**Validity, sampling and bias in the semi-structured diary study (Paper I)**

This study is one of relatively few studies that continuously records and evaluates symptoms and side-effects in cancer patients in chemotherapy undergoing a multimodal intervention like the one applied here. The use of the semi-structured diaries as a research tool can be time consuming for the patients undergoing chemotherapy. However, the diary can also prove to be a useful tool for the patient to assess whether exercising resulted in lessening/worsening of symptoms or side-effects and use of own resources for their management both during and following the intervention. A strength of the study was a rather high adherence rate to the exercise intervention of 75% (mean: 18 out of 24 training days), the response rate of 70.1% after six weeks of daily diary recording. The characteristics of the 23 patients excluded, did not differ from those included with regard to age, education, exercise level, diagnosis or treatment. Furthermore the use of semi-structured diaries can in this study be seen as strength, because the effect of daily fluctuations are minimized when data are collected over several days and recorded while the patient is still feeling the side-effect and thereby minimizing recall bias. At the same time the course of individual symptoms and side-effects can be tracked and the course of events can be depicted for each patient, conceivably revealing more details than looking only at the mean scores. As the diaries were completed at home, a possible negative or positive influence of the Body & Cancer exercise intervention team was probably a minor bias. The methodological limitations of the study were the non randomized design and the small sample size (n=54) which limited the study’s external validity. A limitation not to be ignored is the possibility that the long period (six weeks) of recording daily symptoms and side-effects could have led the patients to slacken their judgement in scoring, i.e. each patient continuously recording the same scores, and as such, this could negatively impact the overall results. A further limitation is the fact that data are missing for some of the patients at certain points in time (a total of 21 registrations). This could give rise to bias, as the patients could be in particularly bad shape on certain days when they did not make any diary entries. Finally an important consideration in this study is whether transforming answers in each category to a continuous variable is justifiable. If an answer in one category is interpreted as a continuous scale of the patients’ perception of symptoms and side-effects, this would imply that the difference between parallel categories would be the same for all categories. In order to improve the internal validity it would have been appropriate to use a well-validated semi-structured diary or questionnaire for recording daily symptoms and side-effects i.e. M.D. Anderson’s well validated Symptom Inventory questionnaire, measuring multiple symptoms assessment scale that consists of 13 items (pain, fatigue, nausea, disturbed sleep, distressed,
shortness breath, remembering, lack of appetite, drowsy, dry mouth, feeling sad, vomiting and numbness or tingling) and six interference items could with advantage have been used in the study (193).

Validity, sampling and bias in the RCT (Paper II)
The methodological strengths of the study were the randomized, controlled study design, and the evaluation methods using the well validated questionnaire (Fact-An) (182;183) with pre- posttest points. The patients were randomized by computer (Clinical Internet Trial Management System: CITMAS) to the intervention group or to the wait-list control group. The patients were stratified by gender, cancer diagnosis (breast, bowel, other solid tumours, haematological malignancies) and disease status (NED and ED). The control and intervention groups were well-balanced at baseline for both demographic and medical characteristics (appendix 1 e). A strength of the study is the size (n=213), including cancer patients of both genders with different cancer diseases and stages. By recording the primary outcome, CRF, only twice i.e. pre and post intervention, we have not identified possible nuances in the CRF as perceived by the participants during the six weeks of intervention. It is evident from the literature that significant variations in CRF occur typically with a high score in the weeks following chemotherapy (22;23;57;61). The option for patients in the control arm to participate in the Body & Cancer exercise intervention after the six weeks period, (which 57% made use of) obviously precluded meaningful long-term follow up studies.

The results of this study can to a limited degree be generalized to a group of cancer patients receiving chemotherapy with a good performance status (WHO), who are motivated for a supervised multimodal exercise programme. It is conceivable, that there are considerable differences between different diagnoses and treatments with respect to the specific effects triggered by the exercise intervention.

Qualitative methodological considerations and limitations
Validity and sampling in the qualitative interview study (Paper III)
The qualitative interview method was selected in order to gain a deeper insight into a defined issue, more specifically, how women with operable breast cancer experienced and managed their chemotherapy related muscle and joint pain throughout the six week exercise intervention. Using the criterion sample procedure, a target group with sufficient experience and knowledge were identified to contribute on this specific topic. All the surveyed breast cancer patients (n=15) accepted to participate in the interview study. The average attendance rate for the breast cancer patients in this study was 77.0% (mean: 18, 5 of 24 training days; range 9-22) which is comparable with an earlier reported attendance rate (70.8%) (15). The data saturation point was in the study reached within the first 13 interviews; however, two more interviews were
effect research have predominantly focused on one isolated symptom or side-effect, which can explain why occurring symptoms and side-effects could benefit from an exercise intervention. Most clinical intervention studies related to symptoms and side-effects, however, to distinguish whether the side-effects experienced during the intervention period were from treatment or whether they were associated with disease symptoms. It is well documented in the literature that cancer patients experience an average of 10 simultaneously observed at the arbitrary – derived sum of the scores for both symptoms and side-effects. It is difficult, to distinguish whether the side-effects experienced during the intervention period were from treatment or whether they were associated with disease symptoms.

Discussion of the results

Reduction of the sum of symptoms and side-effects during the Body & Cancer exercise intervention (paper I)

This part of the thesis focuses on the patients' total sum of symptoms and side-effects during their participation in the Body & Cancer exercise intervention. The results of the study indicate that cancer patients undergoing chemotherapy can reduce their sum of symptoms and side-effects as seen in 67% of the patients who experienced a reduction in the sum of their symptoms and side-effects during the intervention. A decrease in the scoring for 10 out of 12 side-effects was found and statistical significance (p= 0.036) was observed at the arbitrary – derived sum of the scores for both symptoms and side-effects. It is difficult, however, to distinguish whether the side-effects experienced during the intervention period were from treatment or whether they were associated with disease symptoms.

It is well documented in the literature that cancer patients experience an average of 10 simultaneously occurring symptoms and side-effects during treatment that have a significant impact on the patients’ physical and social functions (148;195). The present study focused on 12 symptoms and side-effects that could benefit from an exercise intervention. Most clinical intervention studies related to symptoms and side-effect research have predominantly focused on one isolated symptom or side-effect, which can explain why
interventions of this type do not necessarily improve the patient’s physical capacity or quality of life (40;193;196). The present study attempts to capture a daily image of the patients’ total side-effects burden during an intervention and as such we decided to add each patient’s symptoms and side-effects into a collective sum. Our results demonstrate that patients with ED had higher symptom and side-effect total scores than NED-patients during the intervention and that both groups experienced significant reductions in the sum of symptoms and side-effects. This conclusion is in line with the findings of Dimeo et al. (97) and Jarden et al. (197;198), who studied patients undergoing high-dose chemotherapy followed by bone-marrow transplantation and acute leukaemia patients in consolidation chemotherapy. A symptom cluster analysis (199) that documents the extent to which several of the patients’ symptoms and side-effects were related to each other without having the same etiology (5) may have been a good supplement to the results of the present study. However, we were only able to identify one study that used cluster analyses in conjunction with documenting patients’ chemotherapy side-effects burden during an exercise intervention (197).

Cancer related fatigue reduction during the Body & Cancer Exercise Intervention (Paper II)

The findings of the RCT study indicate that CRF decreases in patients with different cancer diagnoses as they progress through their chemotherapy cycles and simultaneously participate in the exercise intervention. We showed an effect size of 0.44 using the more detailed FACT-An questionnaire that suggested a small but clinically significant improvement of the fatigue dimension.

Several exercise intervention studies today (December 2012) (200) have evaluated fatigue using health related quality of life instruments, but only few RCT studies have evaluated fatigue, measured on the FACT-An questionnaire (89;90;201), with patients undergoing chemotherapy. Courneya et al. (201) did not find a significant change in the fatigue score with 17 weeks of supervised aerobic exercise and resistance training in women with breast cancer who were undergoing adjuvant chemotherapy, while Courneya et al. (89) found a minimally significant difference of 4.6 points on the Fatigue score following 12 weeks of a three times weekly, supervised aerobic exercise training programme with lymphoma patients. As previously described, these studies (90) are not conducive to comparison with our population as they included patients with Hematopoietic stem cell transplants and are thus quite different from our patients.

Our effect size of 0.44 on the Fatigue score is comparable to what McNeely et al. (39) report in a meta-analysis of 14 RCT exercise studies (n = 717) with breast cancer patients during or following cancer treatment. They found an improvement of 6.6 points on the FACT-Breast Scale and a Fatigue score effect size of 0.46. Likewise, Cramp and Daniel’s meta-analysis found based on a meta-analysis comprising in 22 RCTs exercise studies (n = 1662) a Fatigue score effect size of 0.23 in 56% of breast cancer patients during or post-cancer treatment while the effect size on fatigue for the breast cancer group alone was 0.34. CRF is a burdensome (57;60;64) and probably often under-reported symptom (202;203) in cancer patients.
undergoing chemotherapy, and there is no documented effects of pharmacological interventions. We think that our finding of a small and clinically significant improvement can be seen as a positive indication of the value of attempt to use an appealing, non-pharmacological intervention that targets patients’ most burdensome symptom; an effect which should be pursued and elaborated on. CRF is seen as a undoubtedly and multi-causal problem (70-72) and as such it cannot be ignored that other mechanisms such as changed health status and immunity may have influenced the patients’ reported reduction in CRF at the intervention’s post-test (128). The structure and intensity of the intervention, i.e. nine hours weekly of high intensity exercise, may have been significant factors in the patients’ attaining improved and sustainable physical function throughout the intervention. In a previous report on this patient population, we found a small clinically significant improvement (effect size of 0.37) on results from the (MOS SF-36) questionnaire on the physical functioning (15). This may have led to these patients achieving physical control and change in their CRF experiences despite concomitant chemotherapy. This conclusion is supported by our previous qualitative findings on transforming chemotherapy-induced fatigue, in which patients described their experience of fatigue during the intervention as having changed from chemotherapy-induced fatigue to exercise-induces fatigue (10;13;16). Similarly, the patients’ social interactions with other patients during training have had an indirect impact on their perceptions of changed CRF, as CRF is generally seen as an obstacle for the patient’s ability to participate in leisure time activities such as sports (76;77). One important factor in the discussion regarding the extent to which patients undergoing chemotherapy can reduce their CRF by means of exercise interventions is how CRF is defined and measured (204).

Muscle and joint pain experiences during the Body & Cancer exercise intervention (Paper III)
Based on descriptions in the present study, we found that 15 participants with breast cancer experienced muscle and joint pain as ‘the abrupt pain’ during adjuvant chemotherapy. This finding can be interpreted as an expression of a dominating side-effect that persists over a period of time, signifying that the women can be said to be experiencing ‘a life with pain’. The majority of the participants were able to continue exercise and their pain was not aggravated during the training. A retrospective Danish study similarly describes breast cancer patients (n= 1143) during adjuvant chemotherapy (EC and D) experiencing muscle and joint pain. In that study, 53% of the women reported muscle and joint pain conceivably caused by D and/or G-CSF (54). The pathophysiological background for taxane-induced muscle and joint pain is unknown and effects of analgesics are sparsely described. Based on the women’s descriptions of experiencing stabbing and nagging pain in the present study, it was not possible to distinguish between their pain characteristics or to clarify the extent of the interaction impact of D and G-CSF. Furthermore, it was not possible to distinguish whether the cause of pain experienced 2-3 days following chemotherapy was due to the discontinuation of Prednisone (post-treatment), or if the lack of pain on the day following chemotherapy was in fact due to the effect of
Prednisone. One explanation for why the women were able to continue training while experiencing muscle and joint pain may be due to both psychological and physical factors. Prior to their illness, the women were used to exercise. These patients furthermore took the initiative to sign up to the Body & Cancer exercise intervention, believing in advance that they would complete the training programme and as such achieve a positive effect from it. The study analysis of ‘Exercise despite pain’ indicates that the physically challenging exercise may have helped the women to neglect their experience of pain.

It cannot be ignored that exercise interventions throughout the breast cancer patient’s treatment period (adjuvant chemotherapy and irradiation) could have a preventive effect on patients’ treatment related pain (205).

The Nurse-Coach Role

The Nurse-Coach in the Body & Cancer exercise intervention has been a permanent member of the interdisciplinary team and has provided daily counselling to participants regarding their symptoms and side-effects, while simultaneously participating alongside them and dressed similarly to them during all workout sessions. As such, the role of the Nurse-Coach in this context is clearly distinguished from that of the traditional clinical nursing role. The extent to which cancer patients undergoing treatment felt the need and desire for physical training was as yet nebulous in 2001. However, a series of studies today from Norway (206;207), Sweden (208), Canada (209-212), USA (213) and the United Kingdom (214) confirms that cancer patients during and following treatment have a desire for such programmes. A Danish survey study (n=451) launched in the Finsen Center, Rigshospitalet similarly showed that patients undergoing chemotherapy were interested in physical activity. 68% of these patients felt that exercise would benefit them; 78% of them who were not physically active also showed interest while 74% reported fatigue as an obstacle for exercising (158). In addition, the literature shows that cancer patients during and following chemotherapy desire face-to-face exercise counselling (209;215) by a physical training specialist from their own oncology department, e.g. an oncologist cancer nurse or cancer nurse specialist (209;215;216) who is knowledgeable about their disease and treatment process. These unique trends confirm the patients’ desire and preferences for physical activity. The literature on exercise interventions in which cancer patients undergoing chemotherapy are included (94;95;217) is unclear regarding the extent to which the cancer patients are functionally independent during their participation. Winningham and MacVicar, described how nurses have a participatory role in a supervised physical training programme for breast cancer patients undergoing adjuvant chemotherapy and highlight that the nurse plays an important role in counselling and educating cancer patients in health promotion behaviour (83;84;218). Similarly, Anna Swartz, a nurse and coach and earlier cancer patient, describes step by step in her book ‘Cancer Fitness’ just how she provided exercise coaching to cancer patients during and following their treatment (163). Against the backdrop of her own
research as a coach, Schwartz concludes that ‘resting’ does not result in cancer patients’ improved physical wellbeing but rather that physical activity can provide them with a certain control of their bodies and as such management of their side-effects from fatigue and pain (163). The Nurse-Coach can have a central role in the patients’ disease and treatment-related pain management during the intervention period, as she has the opportunity to observe and recognize the patients’ pain. Likewise she can support and counsel patients in the management of their pain, in accordance with the demands and expectations described by hospitalized cancer patients with pain (219). The literature describes the patients’ treatment-related side-effects and symptoms during chemotherapy as being serious obstacles to physical intervention programmes (220). The Nurse-Coach role has two principal functions, i.e. an external function linked to the hospital’s clinical departments and an internal function within the training team; both functions of which use specific clinical experience and competencies within oncology care. The aim of the external function is partially to evaluate and identify potential cancer patients who are undertaking chemotherapy for inclusion in the exercise intervention. The external function also requires the Nurse-Coach to be the link between the patient and the haematology and oncology clinics of Rigshospitalet and Herlev Hospital. In order to support the patients’ desire of minimizing absences from the exercise programme and following agreement with the patients’ treatment departments, the Nurse-Coach assumes minor nursing related tasks (e.g. administering G-CSF injections, care of the central venous catheter, removal of sutures following surgery) that other members of the training team do not have (219). The Nurse-Coach’s internal functions and tasks within the training call for balancing between relational and nursing tasks (221), pedagogical principles (222) and principles of coaching (160;223).

Based on the author’s (CA) personal experiences, the role of the Nurse-Coach can be seen as a balancing act between promoting a secure environment for participants by having the relevant clinical competencies (i.e. being knowledgeable of the patients’ disease and treatment process, being observant of potential symptoms and side-effects and advising pragmatic strategies for symptom and side-effect management) and by being the motivator and ‘enforcer’ for the patient within the training context.

**The Body & Cancer exercise intervention - and implementation in Denmark**

To date (January 2013), 1280 cancer patients during chemotherapy have participated in the Body & Cancer exercise intervention. The patients’ positive acknowledgement of the training programme’s context, including the pre-screening, advice and counselling and the programme’s four components, and the positive results in a series of effect goals (i.e. physical capacity, muscle strength, vitality, physical function, emotional and mental health (15) anxiety and depression (11;17) as well as fatigue (10;15) has meant that only small adjustments have been made to the actual intervention. In line with a growing demand for physical training by cancer patients undergoing chemotherapy, the number of participants in each training group has
increased from 8 to 16 participants. The exercise intervention takes place at a fitness facility located at Rigshospitalet, Copenhagen University Hospital. There has been a progression through the six week relaxation programme, the mental training progresses near the end of the intervention period, where the principles of mindfulness based training is a part of the training in order to support the patients to achieve greater balance, ease and peace of mind (224;225). The exercise intervention frequency and high intensity training has proved not to be suitable for patients with poor performance (performance stage 2-4, WHO) and not suited for patients with long-term and intensive high-dose chemotherapy in semi-outpatient hospitalization. Therefore it is recommended that patients with bone or brain metastases, acute leukaemia and inoperable lung cancer do not participate in the intervention since it is difficult for these patient groups to carry out the intervention due to their disease or treatment related issues. This means the need to develop specific exercise intervention for these patients. As a consequence of the daily pre-exercise screening procedure, in total 12 patients (total of 30 times) (Paper I, Paper II) were excluded from the high intensity physical training component throughout the intervention programme (due to fever, infection requiring treatment, leucopenia and risk of bleeding). Half of the Body & Cancer exercise intervention Phase III population comprised breast cancer patients in adjuvant chemotherapy (n= 50) in 2012, a study was initiated to ascertain whether this patient group could develop breast cancer related lymphedema in connection with the training programme’s resistance training component ( > 80% 1 repetition maximum) Bloomquist et al. included breast cancer patients (n= 149) who had previously participated in the intervention during adjuvant chemotherapy (mean: 14 month after participation) in their cross-sectional, self-reported prospective study. The study showed that there was no association between the development of breast cancer related lymphedema and the women’s participation in the heavy resistance training component in the Body & Cancer exercise intervention (226). The Body & Cancer exercise intervention has furthermore created a basis for the Body & Cancer exercise intervention being implemented at other hospitals in Denmark, including the Aarhus University Hospital and the Vejle Hospital (227;228). A five year multidisciplinary research initiative, The Center for Integrated Rehabilitation of Cancer patients (CIRE) was launched in 2011, in Copenhagen at Rigshospitalet in collaboration with Institute of Public health, Copenhagen University, on the backcloth of clinical experience and research results from the Body & Cancer exercise intervention. The rehabilitation programme’s goal is to improve the cancer treatment process by supporting patients in sustaining their daily lives during and following the treatment process and drawing on several of the diagnosis groups who are excluded from participating in or who have been sparsely represented in the Body & Cancer exercise intervention population, i.e. patients with lung, testicular, prostate, breast and colorectal cancer with inactive lifestyle, patients with brain tumours and leukaemia as well as children with cancer (1).
CONCLUSIONS

This thesis indicate that the six week, nine hours weekly, structured, supervised combined high- and low-intensity Body & Cancer exercise intervention, provides an improvement in selected symptoms and side-effects patients undergoing chemotherapy.

In the semi-structured diary study (one-group design) (Phase II) a statistically significant reduction was shown in pain score (p = 0.046) and the arbitrary-derived sum of the scores for symptoms and side-effects (p=0.036). Out of the 12 symptoms and side-effects scores in cancer patients undergoing chemotherapy decrease in intensity was observed in 10 (diarrhoea, constipation, diminished appetite, myalgia, arthralgia, other pains, physical fatigue, treatment-related fatigue and mental fatigue) during the exercise intervention. Patients with advanced disease had the highest symptom and side-effect burden and they respond positively to the intervention as indicated from the sum of symptoms and side-effect scores.

In the randomized clinical trial study (RCT) (Phase III) we found a significant reduction (effect-size 0.44) with a small clinically significant improvement in the patients’ self-reported perception of cancer related fatigue (CRF) level during the intervention. However, we found no statistically significant effect on the patient’s self-reported General Quality of Life score or on any of the individual wellbeing scores; Physical, Emotional, Social and Functional.

The findings from the qualitative study in a homogenous group of fifteen operable breast cancer patients undergoing adjuvant chemotherapy with docetaxel and haematological growth factor support (D+(G-CSF)) indicate that muscle and joint pain started 2-3 days after chemotherapy, and continued for 6-14 days. Pain intensity peaked between 2 and 9 days after chemotherapy. The muscle and joint pain did not worsen during the exercise intervention. Despite pain the patients continued the multimodal exercise intervention, but often reduced the high intensity component of their physical training.

The Nurse-Coach has a central role in the Body & Cancer exercise intervention. The Nurse-Coach’s role can be seen as a balancing act between promoting a secure environment for participants by having the relevant clinical competencies and by being the motivator the patient within the training context.

The results of this thesis support in collaboration with the patients’ responsible oncologist/haematologist the assumption of that regular training with monitoring, guidance and supervision of an interdisciplinary exercise team can support cancer patients receiving chemotherapy from impaired physical function and worsening of overall burden of symptoms and side-effects.

PERSPECTIVES

Many cancer patients receive chemotherapy or other antineoplastic treatments for fairly long periods of
time (months or years). Furthermore, many of these treatments are hampered by significant side-effects, which are difficult to treat by conventional means. It is therefore quite essential to develop non-pharmacological interventions like physical exercise that potentially can reduce the patients' symptoms and side-effects.

Further exercise intervention studies in cancer patients receiving chemotherapy are needed to clarify the dose–response effects on symptoms and side-effects. Furthermore it is of interest to investigate whether or not an early intervention e.g. already at time of diagnosis can reduce the burden of patients' side-effect burden and reduce problems such as chronic fatigue, pain and other late-effects.

Studies indicate that three to five hours of physical activity weekly can positively impact the relapse rate and lower the general mortality risk in selected cancer populations (44;46). We find it therefore very relevant to focus in future studies on those patients, who prior to their cancer diagnosis were sedentary, unmotivated and therefore quite untrained.

Developments in cancer treatment have resulted in increased survival rates while the burden of symptoms and side-effects during and following treatment with chemotherapy continue to be a persistent challenge. Physical exercise is an evidence-based form of intervention in cancer rehabilitation, but there is still lacking knowledge regarding the extent to which unimodal or multimodal exercise interventions can positively impact specific symptoms and side-effects.

Based on the description in the present study of the Nurse-Coach's role, it is recommended that a Nurse-Coach should be present when cancer patients are in the initial treatment period during chemotherapy and are exposed to moderate to high intensity exercise training. The nurse can from her clinical competence and knowledge of the patient's diagnosis, disease status and treatment, help in evaluating the cancer patients exercise tolerance on a specific training day and ensure safety and security of the patient training situation and provide ad hoc guidance for patient self-management of their symptoms and side-effects.

The results of this thesis support the argument for regular training with monitoring, guidance and supervision of an interdisciplinary exercise team, in collaboration with the patient's oncologist and haematologist that can support cancer patients receiving chemotherapy in the fight against impaired physical function and the overall burden of symptoms and side-effects. Many patients undoubtedly fear that exercise as applied here, can exacerbate their symptoms and side-effects; we found no indication of such an effect.
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The effect of a multidimensional exercise programme on symptoms and side-effects in cancer patients undergoing chemotherapy—The use of semi-structured diaries

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Summary: The aim of this study was to evaluate the effects of a 6-week intervention with structured physical activity, relaxation, body-awareness techniques and massage on the symptoms/side-effects of cancer patients undergoing chemotherapy. The study was prospective and exploratory, and 54 patients completed assessments for all 6 weeks of the intervention. In order to obtain a continuous record of side-effects, a diary was developed for the patients’ use throughout the intervention. The patients scored their symptoms/side-effects on a scale from 0 to 4, using the Common Toxicity Criteria and reported these scores in questionnaires. Twelve possible symptoms/side-effects were registered daily: lack of appetite, nausea, vomiting, diarrhea, paraesthesia, constipation, physical fatigue, mental fatigue, treatment-related fatigue, muscle pain, arthralgia and other pain. During the intervention a decrease in the scoring for 10 out of the 12 side-effects was found. Statistical significance was observed in the pain score \((P = 0.046)\) and the arbitrary-derived sum of the scores for symptoms and side-effects \((P = 0.036)\) respectively. Patients with evidence of disease \((n = 26)\) had significantly higher levels of symptoms/side-effects than patients with no evidence of disease \((n = 28)\) \((P = 0.027)\). The results indicate that a six weeks multidimensional exercise intervention undertaken by cancer patients with or without...
residual disease while undergoing chemotherapy can lead to a reduction in treatment-related symptoms.

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Introduction

Clinical treatment is instrumental in changing cancer from a terminal to a chronic illness and chemotherapy has become a more prevalent and advanced treatment mode for this disease. An increasing number of cancer patients is offered chemotherapy to treat advanced stages of the disease and as adjuvant treatment after surgery or radiation (Cavalli et al., 2004). These advancements underscore the importance of helping people to live with a life threatening chronic disease and side-effects of arduous treatment is steadily growing (Baum and Andersen, 2001).

Chemotherapy is frequently accompanied by psychological and physical reactions that lead to psycho-social burden for the patient. It also carries with it symptoms/side-effects such as fatigue, diarrhoea, impaired bone-marrow function, hair loss and neurotoxicity. In addition, cancer patients experience disease symptoms that include pain and fatigue (Greene et al., 1994; Griffin et al., 1996). Management of this wide spectrum of side-effects and symptoms is compounded by the fact that they also affect quality of life.

Physical activity as a means to diminish side-effects in cancer patients is a relatively new research area in cancer nursing. Very few studies have looked into the effect of physical activity concomitant with the cytotoxic treatment (MacVicar et al., 1989; Courneya et al., 2003; Young-McCaughan et al., 2003). These studies have primarily been carried out in breast cancer and haematological patients (Winningham et al., 1989; Mock et al., 1994; Courneya et al., 2000; Segal et al., 2001; Dimeo et al., 2003; Kolden et al., 2002).

More recently, physical exercise has been tested in the treatment of cancer-related fatigue (Dimeo, 2001; Mock et al., 2004; Schwartz et al., 2001), and there is growing evidence that aerobic exercise programmes can reduce fatigue in cancer patients undergoing chemotherapy (Adamsen et al., 2004; MacVicar et al., 1989; Mock et al., 2001; Stricker et al., 2004). However, most available studies are small and have little control over the amount of physical activity participants do, rendering interpretation and comparison of results difficult (Ballard-Barbash et al., 2002).

In addition to physical activity, behavioural techniques have proven useful in the management
of chemotherapy-induced symptoms/side-effects. Massage and relaxation/visualization techniques have been reported to positively affect pain, nausea and vomiting (Weinrich and Weinrich, 1990; Lerman et al., 1990; Arakawa, 1997; Molassiotis et al., 2002).

A wide range of cancer treatment-related symptoms have been reduced through interventions that include relaxation training and massage, and which spanned patients with considerable variance in type of cancer, stage of the disease and/or treatment protocols (Arakawa, 1997; Molassiotis et al., 2002; Sloman et al., 1994; Weinrich and Weinrich, 1990; Syrjala et al., 1995). These interventions have also positively affected anxiety, depression (Bindemann et al., 1991; Luebbert et al., 2001) and mood disturbances in cancer patients undergoing chemotherapy (Bredin et al., 1999; Bridge et al., 1988). Similarly, sports science has shown that body awareness can be used to release tension and control anxiety (Pensgaard and Ursin, 1998). The above-mentioned research provides evidence that exercise relaxation, massage-and body-awareness training can each impact positively on physical and/or psycho-social well-being. The aim of this study is to evaluate the effect of a 6 week intervention with structured physical activity, relaxation, and body-awareness training techniques as well as massage on self-reported symptoms/side-effects of cancer patients concurrently undergoing chemotherapy.

Materials and methods

The study design was prospective and exploratory. Assessments of cancer-related symptoms/side-effects were made daily over a 6 week period using semi-structured diaries. The diaries were completed by the patients in the full knowledge that the contents would be analysed and written by the research team.

Participants

Cancer patients were initially attracted to the project by posters and pamphlets made available in the outpatient clinic or oncology and haematology wards at Rigshospitalet (Copenhagen University Hospital). Recruitment was carried out through efforts made by nurses and doctors in informing patients about the project, after which the patients contacted the project team directly.

Inclusion criteria: Age 18–65 years; with a diagnosis of cancer given at least 1 month before the recruitment. The patients were admitted to the oncological or haematological clinics for outpatient chemotherapy either as treatment for advanced disease or as part of an adjuvant treatment. The patients had received at least one series of chemotherapy and had a performance stage 0–1 (WHO).

Exclusion criteria: Documented brain or bone metastases; anticoagulation treatment; symptomatic cardiac disease including congestive heart disease, treatment for arrhythmia or myocardial infarction within the last 3 months; dementia and psychotic conditions, inability to write or read Danish (Adamsen et al., 2003, p. 709).

Ethical considerations: The study was approved by the Scientific Committees of the Copenhagen and Frederiksberg Municipalities (J.no. 01-273/00) that evaluated both the ethical aspects and methodologies used in the research project. In addition, the study was approved by the Danish Data Protection Agency (J.no. 2000-41-0-149).

Intervention

We developed a structured and supervised exercise intervention comprising the following components: resistance and fitness training, massage, and body-awareness training. The intention was to maximize the effect (Adamsen et al., 2006). According to the American College of Sports Medicine (ACSM, Position Stand, February 2002), 6–7 weeks of training is sufficient to obtain measurable muscle hypertrophy.

Furthermore, the ACSM Journal states that 2–3 times weekly is sufficient exercise frequency for both men and women. The programme took place in specially designed work-out rooms located at the hospital and was carried out over a 6 week period, 9 h per week, in the mornings. The patients trained in mixed groups (men and women) of 7–9 patients. During the programme, time was secured for patients to exchange experiences (work, family, illness and treatment). The programme was supervised by trained physiotherapists and a specially trained nurse, who participated in the physical training component (Adamsen et al., 2003 p. 709).

The patients undertook a total package of activities that were classified at either high or low intensity, and they could not select one activity in preference over another.

High intensity physical training (in groups): 1.5 h; 3 times weekly. Physical training comprised three components: warm-up exercises, heavy resistance training and fitness. Warm-up exercises included dynamic actions with the large muscle groups,
balance and coordination training (running, ball games and weight-lifting). Three machines were used for heavy resistance training (leg press, chest press, lat. machine, (Technogym Italy). The practical goal in the training component was to accomplish three continuous series of 5–8 repetitions at 85–95% of 1 RM (RM = repetition maximum). The fitness training comprised 10 min interval exertions in the form of cycling on stationary bicycles, with an intensity of 150–250 W equivalent to 80–100% of each patient’s maximum heart rate (Saltin and Gollnick, 1983; Fentem, 1994; Saltin and Pilegaard, 2002; Adamsen et al., 2003).

Low-intensity physical training: (A) Relaxation (in groups): 0.5 h, 4 times weekly. Groups of patients were instructed in the use of relaxation techniques, using principles of progressive relaxation (Lyles et al., 1982; Lerman et al., 1990). This involved switching from muscle tension to muscle-relaxation motions in each of the muscle groups. The patients used audio-tapes with recorded instructions and relaxing background music. (B) Massage (individual), 0.5 h, twice weekly. Massage could be relaxing, facilitative or therapeutic. Classic, scar tissue and venous pump massages were administered as well as ultrasound and exercise therapy (Bunkan and Schultz, 1998). (C) Body-awareness training: In groups, 1.5 h a week focused on balance/coordination; grounding and integration of the senses (Dychtwald, 1977; Hardy et al., 1999; Adamsen et al., 2003 p. 708–9).

In accordance with the guidelines and safety precautions determined by Winningham et al. (1986) and Dimeo et al. (1999), daily pre-exercise screening was performed. If one of the following criteria was met, the patient was excluded from the physical exercise component of the programme on that specific day: diastolic blood pressure <45 or >95; pulse at rest >100, body temperature >38 °C, respiration frequency at rest >20, infection requiring treatment by antibiotics, ongoing bleeding, fresh petechiae, B-thrombocytes <50 billion/litre, leucocytes <1.0 billion/litre (Adamsen et al., 2003, p. 709).

Adverse reactions: As a consequence of the daily screening procedure, seven patients in total were excluded from the physical exercise component throughout the intervention programme (i.e. three patients: one on three occasions; three patients: three on eight occasions; and one patient on eight to eleven occasions) due to fever, infection requiring treatment, and/or risk of bleeding. The patients did not show signs of unintentional physical reaction, cardiac or respiratory arrest, hypotension, etc.

Definitions

We selected 12 symptoms and side-effects of chemotherapy and of the disease itself in order to grasp a comprehensive picture of the total strain on the patients. The side-effects and symptoms were selected from our clinical experience and with reference to reported data on frequency (Faull and Woof, 2002). We did not include symptoms/side-effects that had no direct link to physical activity (e.g. hair loss).

An arbitrary sum of the symptoms/side-effects was calculated to give an indication of the total burden of the symptoms/side-effects over a 6 week intervention period. It is difficult to distinguish between side-effects from treatments and symptoms of the disease. The distinction, however, is unimportant for those patients, who experience a total burden of symptoms/side-effects. We looked at possible changes in 12 symptoms/side-effects in a population with heterogeneity of diagnoses as well as treatment regimens. Furthermore, the 12 symptoms/side-effects served as a screening test for possible deleterious effects of the rather strenuous intervention. The use of semi-structured patient diaries served to give a detailed record of the change progress throughout the intervention.

The following symptoms/side-effects were recorded daily: lack of appetite, nausea, vomiting, diarrhoea, paraesthesia, constipation, physical fatigue, treatment-related fatigue, mental fatigue, myalgia, arthralgia and other pains. The symptoms and side-effects were defined and based on the validated Common Toxicity Criteria (CTC) (Cancer Therapy Evaluation Program, 1999) and the patient scored each symptom/side-effect on a scale from 0 to 4 (0 = no symptoms, 1 = little, 2 = moderate, 3 = heavy, 4 = intolerable symptoms) (Table 1).

Diaries

In order to obtain a continuous registration of the patient’s symptoms/side-effects during the exercise intervention a patient diary was developed and used throughout the 6 weeks of the intervention. The diary comprised a structured part based on questionnaires and a free text part. Each patient used one book per week that was then handed to the project nurse at the close of the week. The diary format comprised eight A4 pages with various header questions. The questionnaires contained a registration form using the CTC (Cancer Therapy Evaluation program, 1999) (Table 1). The patients recorded the date and hour of treatment in their respective diaries.
The free text part comprised blank pages in which the patients could describe experiences and actions related to managing their symptoms/side-effects. The systems/side-effects categories in the diary were tested by reviewing diary entries of 11 of the patients. Interviews were then conducted by
an external interviewer with these same patients to compare similarity of responses with those provided in the respective diaries. Each interview had a duration of 10–15 min. This test gave rise to a few corrections in the diary categories: physical-, mental-, and treatment-related fatigue and other pain.

Data analysis

Data were entered into Excel using Microsoft Office 2000 Professional for Windows 2000. Patients with missing data were excluded from the data set using the following criteria: (1) consecutive periods of missing data for 6 days or more; or (2) more than 20% of total data missing. When data for included patients were missing, substitute values were calculated as the average of the values from the other days during that particular week. The total impact of symptoms/side-effects for each patient was calculated from the sum of the scores for the patient on that particular day. Each week the mean scores of the daily results were calculated and depicted graphically. With regard to pain, individual scores for myalgia, arthralgia and other pains were calculated as well as the sum of these pain scores. Mental fatigue, treatment-related fatigue and physical fatigue were summed up as the total fatigue-related score; constipation and diarrhoea were summed up as the total score for gastrointestinal problems; and finally, vomiting, appetite and nausea were summed up as the total score for gastric problems.

Statistical analyses were carried out using the statistics analysis software tool—Strategic Analysis System (SAS) for Windows (Version 9.1). The results were produced using PROC MIXED (the Mixed Procedure SAS software tool) by using the number of days from baseline as the explanatory variable and, where indicated, disease status as an additional, categorized, explanatory variable. Each patient’s daily scores were repeated, e.g. dependent observations with the following structure: the correlation between successive observations declines exponentially with time between the respective observations (AR = 1). The Satterweight method for approximation of degree of freedom was used as the basis for determining probabilities of significance.

In order to minimize bias, two researchers independently analysed the qualitative data from the diary texts (Malterud, 2001). The qualitative data from the diaries was transcribed and thematically categorized in accordance with the pre-established symptoms/side-effects categories. A few citations are selected to illustrate the qualitative aspects of the symptoms/side-effects as they provide particularly good examples of the complexity of the intervention’s aim.

Results

Eighty-eight patients gave written informed consent to enter the study. Eight patients dropped out, i.e. six patients due to progressive acute illness and two because they did not feel that they belonged to the group. A further three patients were excluded because their treatment schedules had changed. Thus, 77 patients completed the 6 week intervention. Twenty-three patients were excluded from the data set. Nine patients were excluded because their chemotherapy schedules had changed or treatments had terminated, and a further 14 patients were omitted due to the fact that they had not returned all six diaries. The characteristics of these patients did not differ from those included with regard to age, education, previous exercise history, diagnosis or treatment. The present study thus includes results from 54 patients (70.1%); i.e. 45 patients with solid tumours and 9 patients with malignant haematological diseases.

The patients’ characteristics, i.e., mean age, gender, marital status, educational background, and level of physical activity pre-illness and at the start of the intervention are provided in Table 2. Patients were primarily classified according to diagnosis and presence or absence of disease at the beginning of the intervention. Twenty-eight patients had no evidence of disease (NED), which meant that they received adjuvant treatment either after surgery or after having reached complete remission through radiotherapy or chemotherapy. Twenty-six patients had evidence of malignant disease (ED) while being treated with chemotherapy.

The diagnoses, disease status and different treatment regimens are described in Table 3. All patients in this study were undergoing chemotherapy during the intervention. Ten patients had previously received antineoplastic treatment: five patients (1 ALL, 1 AML, 1 NHL, 1 Ewing sarcoma and 1 ovarian cancer patients) had previously undergone chemotherapy. Two breast cancer patients previously received radiotherapy as well as chemotherapy (CMF or CEF); and 1 patient with cervical cancer had received concomitant radiotherapy and cisplatinum. Two further patients (1 with oesophageal and 1 with rhinopharynx
cancer) had received radiotherapy. At the beginning of the intervention all of the patients had received 1–10 series of chemotherapy (median 3) with 3–4 week intervals. All 54 patients received antiemetic drugs: 5 HT3 receptor antagonists (Zofran, Kytril), Metoclopramide (Emepal), Metopimazin (Vogalene) and/or Prednisone according to the standards of the individual treatment regimens.

Individual symptoms and side-effects

During the 6 week intervention a decrease in 10 of the 12 symptoms/side-effects and in the sum of symptoms/side effects were found (Fig. 1). The following reflect the score changes: physical fatigue (from 0.95 to 0.74); treatment-related fatigue (from 0.83 to 0.55), mental fatigue (from 0.75 to 0.57), other pain (from 0.53 to 0.39), paraesthesia (from 0.53 to 0.43), lack of appetite (from 0.43 to 0.34), constipation (from 0.40 to 0.24), malagia (from 0.36 to 0.17), arthralgia (from 0.31 to 0.29),) and diarrhoea (from 0.17 to 0.06). From the first to the last week the myalgia scores \( P = 0.013 \) and other pain scores \( P = 0.041 \) significantly changed. None of the other changes reached statistical significance at the 95% level. The score for vomiting was unchanged (from 0.04 to 0.04) and nausea increased from 0.22 to 0.24.

Sum of the symptoms and side-effects

A significant decrease (27%) in the sum of the symptoms/side-effects was found \( P = 0.036 \). A total of 36 (67%) of the patients experienced a reduction in the sum of the symptoms/side-effects, while 13 (24%) showed an increase in this sum and 5 (9%) did not change their sum of symptoms/side-effects (Fig. 2).

Influence of disease-status (NED versus ED)

Patients with ED \( n = 26 \) had a significantly higher level of symptoms/side-effects than patients with NED \( n = 28 \) \( P = 0.027 \). Both groups did
experience a significant reduction in the sum of symptoms/side-effects during the intervention (Fig. 3). With regard to the individual symptoms/side-effects, the differences between ED and NED patients were particularly clear when looking at myalgia ($P = 0.002$), physical fatigue ($P = 0.001$) and treatment-related fatigue ($P = 0.003$). Patients with ED had significantly less nausea ($P = 0.038$) than patients with NED.

### Pain

The total scores for pain decreased significantly during the intervention ($P = 0.046$) (Fig. 4).

The following citation describes a participant’s experience of pain

It has been a positive experience for me to be able to participate in the project even though

---

**Table 3** Patient characteristics: diagnosis, treatment and status ($n = 54$).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Treatment*</th>
<th>Status¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oncological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>20</td>
<td>17 CEF (adjuvant)</td>
<td>18 NED</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 CMF (adjuvant)</td>
<td>1 T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 T</td>
<td>1 T+G</td>
</tr>
<tr>
<td>Ovary cancer</td>
<td>11</td>
<td>5 Carbo+T (adjuvant)</td>
<td>5 NED</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 Carbo+T</td>
<td>1 Carbo+Topo+T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Carbo+V+Eto</td>
<td>1 Carbo+V+Eto</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 T</td>
<td>1 T</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>4</td>
<td>3 5FU+Lv (adjuvant)</td>
<td>3 NED</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 5FU+Lv</td>
<td>1 ED</td>
</tr>
<tr>
<td>Testis cancer</td>
<td>1</td>
<td>1 P Eto B</td>
<td>1 ED</td>
</tr>
<tr>
<td>Cervix cancer</td>
<td>1</td>
<td>1 P+T</td>
<td>1 ED</td>
</tr>
<tr>
<td>SCCL²</td>
<td>1</td>
<td>1 Carbo+G+Eto</td>
<td>1 ED</td>
</tr>
<tr>
<td>NSCLC²</td>
<td>1</td>
<td>1 P+VI</td>
<td>1 ED</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1 G+P+T</td>
<td>1 ED</td>
</tr>
<tr>
<td>primary tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophageus cancer</td>
<td>2</td>
<td>1 Cap+T+Carbo</td>
<td>2 ED</td>
</tr>
<tr>
<td>Ewings</td>
<td>1</td>
<td>1 5FU+P</td>
<td>1 ED</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>1 I+Eto+V+A</td>
<td>1 ED</td>
</tr>
<tr>
<td>Rhinopharynx cancer</td>
<td>1</td>
<td>1 Carbo+Eto+V</td>
<td>1 NED</td>
</tr>
<tr>
<td>Myxoidt</td>
<td>1</td>
<td>1 I+M</td>
<td>1 ED</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>1 Cap+T</td>
<td>1 ED</td>
</tr>
<tr>
<td>Oral cancer</td>
<td>1</td>
<td>1 Cap+T</td>
<td>1 ED</td>
</tr>
<tr>
<td><strong>Haematological</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>4</td>
<td>4 ABVD</td>
<td>3 ED</td>
</tr>
<tr>
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<td>1 CHOEtoP</td>
<td>1 NED</td>
</tr>
<tr>
<td>ALL³</td>
<td>1</td>
<td>1 Purinethol+M</td>
<td>2 ED</td>
</tr>
<tr>
<td>AML³</td>
<td>1</td>
<td>1 M-AMSA+Eto+Ara-C</td>
<td>1 NED</td>
</tr>
<tr>
<td>Myelomatosis</td>
<td>1</td>
<td>1 VAD</td>
<td>1 ED</td>
</tr>
<tr>
<td>Myelobrosis</td>
<td>1</td>
<td>1 Ara-C+Hy</td>
<td>1 ED</td>
</tr>
<tr>
<td><strong>Status¹</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 NED, 26 ED</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*¹Status: ED = Evidence of disease; NED = No evidence of disease.
²Diagnosis: SCLC = small-cell lung cancer; NSCLC = non-small-cell lung cancer; NHL = Non-Hodgkin’s lymphoma; ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia.

*³Treatment: A = doxorubucin, ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine; Arac-C = Cytosinarabinosid, C = Cyklofosfamid, Cap = capecatebine, Carbo = carboplatin; CEF = cyclophosphamide, epirubicin, 5-fluorouracil; CHOETO = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; CMF = cyclophosphamide, methotrexate, 5-fluorouracil; E = epirubicin; ETO = etoposide; 5-FU = 5-fluorouracil; G = gemcitabine; HY = Hydrea; I = ifosfamide; Lv = leucovorin; M = methotrexate, P = cisplatin; PETO8 = cisplatin, etoposide, bleomycin; T = taxanes; ToP = topotecan; V = vincristine VAD = vincristine, doxorubicin, dexamethasone; Vin = Vinorelbine.
I was treated last Monday. I still feel pain in my muscles and joints but this time I didn’t need analgesics. I was interested in seeing whether exercise had any influence on the level of pain I was experiencing. The pain has been bearable, but, of course, it is difficult to know whether this is due to the exercise or just a different reaction to chemotherapy this time round.

(Female, ovarian cancer, ED, 39 years, Friday, week 3)
Fatigue

The sum of fatigue-related scores decreased during the intervention from 2.53 to 1.87 ($P = 0.069$) (Fig. 5).

The following citation describes a participant’s experience of fatigue:

It is difficult to describe the fatigue I feel in my body and my head. Of course, it’s probably a
combination of the disease and treatment and the psychological embarrassment that comes with it. This morning I was very tempted to go back to sleep—and then, after participating a couple of hours in the project "Body & Cancer", the whole situation turned around. I left the project feeling full of energy.

(Female, ovarian cancer, NED, 43 years, Monday, week 6)

**Constipation and diarrhoea**

The combined gastrointestinal symptoms/side-effects (constipation, diarrhoea) were reduced from 0.57 to 0.30 (P = 0.60) (Fig. 6).

The following citations describe two participants’ experience of constipation and diarrhoea:

I feel that my body is in restitution after the chock of training. I’ve had bowel movements after a period of constipation—maybe the exercise led to this positive effect.

(Male, Hodgkin’s disease, ED, 31 years, Wednesday, week 3)

Woke up with a headache and a feeling of having the flu. I feel pain in my joints, and had diarrhoea. I am mentally and physically tired. I cycled unenthusiastically to the “Body & Cancer” session. It is tough to exercise but I can feel that it helps my mood and my different symptoms for a while.

(Female, breast cancer, ED, 54 years, Friday, week 2)

**Lack of appetite, nausea and vomiting**

The combined score of these symptoms/side-effects related to food intake did not change (P = 0.083) over the 6 week multidimensional exercise programme (Fig. 7).

The following citation describes a participant’s experience of nausea:

I felt sick this morning, and I didn’t want to go—but I went anyway.

The first half-hour I didn’t feel well, I was dizzy and I felt nauseous. But then things changed—when I returned home after my massage, I was very happy that I participated. I felt well for a few hours today.

(Female, breast cancer, NED, 45 years, Friday, week 4)

**Discussion**

The results of this investigation indicate that cancer patients undergoing chemotherapy can reduce their symptoms and side-effects by participating in a 6 week multidimensional exercise intervention. A total of 67% of the patients experienced a reduction in the sum of their symptoms/side effects during the intervention. A change in the symptoms/side effects over time could be caused by a number of factors aside from treatment. This is contrary to the expected changes due to the antineoplastic treatment (i.e. increased fatigue, increased gastrointestinal problems, etc.). On the other hand, improvement in
the disease status of ED patients could lead to improvement of symptoms. This study identified a conceptualization of ways to reduce symptoms/side-effects of cancer and its treatment and could form the basis for a larger controlled and randomized study to conclude whether the observed changes in patients’ symptoms/side-effects result directly from this specific type of multidimensional exercise programme.

We used Common Toxicity Criteria—CTC because they are validated and internationally accepted methods for measuring symptoms/side-effects in cancer patients. Previous studies on the effect of physical activity on symptoms/side-effects typically focus on one or two selected symptoms/side-effects, and use questionnaires before and after the intervention (Schwartz, 1999; Winngham, 2001). These studies resulted in new knowledge to the field but did not lead to a detailed account of the patients’ total symptom/side-effects burden during the intervention. In the present study the patients experienced a reduction in 10 out of the 12 symptoms/side-effects and more particularly in the pain-related measures where the decrease reached statistical significance. Patients with ED had higher side-effect scores than NED-patients. Our results...
support the hypothesis that patients with advanced disease can also benefit from a rather strenuous multidimensional exercise intervention. This conclusion is in accordance with the findings of Dimeo et al. (1999), who studied patients undergoing high-dose chemotherapy followed by bone-marrow transplantation.

In many studies, patients rank nausea as the most troublesome side-effect of chemotherapy (Coates et al., 1990; Griffin et al., 1996; De Boer-Dennert et al., 1997; Ballatori and Roila, 2003). In contrast to the results of Winningham and MacVicar's (1988) study, we did not find any positive effect of the intervention on nausea. This could conceivably be due to the improvement of the antiemetic treatment, especially with the advent of 5 HT3 receptor antagonists in the 1990s. Some of our patients did in fact report temporary relief from nausea during the intervention—a relief not registered in the overall evaluation of daily symptoms/side effects and an effect which should be further investigated.

Nausea is still a significant problem. Different forms of fatigue can be reduced by physical exercise (Fig. 5). This finding is in accordance a study by Schwartz (1999), who found that women with breast cancer participating in an 8-week exercise programme (at home) experienced a reduction in fatigue using POMS (Profile of Mood States), fatigue inertia and the vigour activity subscale as well as the Schwarts cancer fatigue scale (SCFC). Dimeo et al. (1999) found, in a randomized study, that 30–50 min of daily exercise (cycling in bed) decreased fatigue in haematological patients who had been treated with high-dose chemotherapy followed by stem-cell transplantation.

The significant reduction in the pain scales found in the present study may be comparable with other studies that use a relaxation component, e.g. Sloman et al. (1994). Reduction in fatigue and pain found in the present study might be attributed to relaxation, exercise and/or a combination of both. Nevertheless, it is not possible to disentangle the effect of the diverse components of the programme.

The study sample has important section biases. The patients were attracted to the intervention by posters displayed only in the outpatient clinic or in the ward. Thus, not all eligible patients were informed about the project. The study population was self-selected and comprised cancer patients whose pre-illness motivated them to undertake physical training.

**Methodological considerations**

The use of diaries as a source of information over several weeks can give rise to some problems. Important information can be lost if the diary is not completed every day and there could be a tendency for the patient to use the same scoring during consecutive days—especially if he/she does not take sufficient time to make entries. We used a semi-structured version of the diary, that had a quantitative and a qualitative part, in order to reduce some of the drawbacks of the diary as a research tool. Among other factors, Richardson (1994) emphasizes that recording in a diary is very time-consuming for patients and that the results are dependent on the patient’s motivation, consequently leading to significant bias. An exclusion criterion could be if a patient refused or could not write. Collecting and analysing the data is difficult, complex and challenging. In our study, 14 patients did not complete 6 of their diaries. No patient was excluded from the study because he/she refused or was unable to write. A total of 87% of the patients used the qualitative part of the diary to write about experiences and sentiments related to their symptoms.

Focus on symptoms/side-effects could conceivably lead to an unrealistic assessment. In the present study we found the use of diaries valuable because the impact of daily variations is minimized when data are collected over several days and recorded while the patients still feel the side-effects—making recall unnecessary. The registration of symptoms/side-effects was structured into categories and gave a detailed picture of the reactions to the intervention at different points in time. The course of the individual symptoms/side-effects can be tracked and the course of events can be depicted for each patient, conceivably revealing more details than looking only at average scores.

As the diary is completed at home, a possibly negative or positive influence of the therapists is minimized and the free text is useful for revealing nuances and details.

It is a clear limitation in our categorization of symptoms/side-effects that their true status is not
depicted in detail. The categorization can only approximate the truth by using the five categories (0–4) in which the patient can place his or her score for a particular side-effect.

Another limitation not to be ignored is the possibility that the long period (6 weeks) of recording daily symptoms and side-effects could have led the patients to slacken their judgement in scoring, i.e. each patient continuously recording the same scores, and as such, this could negatively impact the overall results. A third limitation is the fact that data are missing for some of the patients at certain points in time. This could give rise to bias, as the patients could be in particularly bad shape on certain days when they did not make any diary entries.

A so-called total sum of symptoms/side-effects was constructed, with each symptom given equal weight in the total score. Thus, in this study we did not investigate whether or not some side-effects or symptoms experienced by the patient were perceived as more deleterious than others.

An important consideration in this paper is whether transforming answers in each category to a continuous variable is justifiable. If an answer in one category is interpreted as a continuous scale of the patients’ perception of symptoms/side-effects, this would imply that the difference between parallel categories would be the same for all categories. We think this is a reasonable assumption—and in the case where the category answer is not a precise reflection of the degree of symptoms/side-effects, we had no reason to suspect deviations to be the result of any bias. As all side effects and symptoms in the different “classes” (pain, fatigue, and gastrointestinal effects) are presumed to be equally troublesome for the patients, we took the liberty to stack the score in each of these classes.

The registration of symptoms/side-effects over time in diaries has been used in several clinically controlled trials with cancer patients. Often this technique has been used as a supplement to the objective recording of symptoms/side-effects carried out by the researchers or research nurses in connection with e.g. testing of new antineoplastic drugs, antiemetics, surgical techniques, radiotherapy and treatment of pain (Dodd 1984a,b; Mystakidou et al., 1997; Wymenga et al. 1999; Radbruch et al., 2001; Caffo et al., 2003). The form, focus and content of the diaries have varied from being highly structured, to patient diary cards that assess nausea and vomiting, to more open books such as “Health diaries” (Keleher and Verrinder, 2003) where the patient more or less writes what is on his/her mind. The number of days using diaries also varies a great deal among studies.

The use of diaries as a research instrument in connection with a study of symptoms/side-effects can be time consuming for the patient, but at the same time it can be a helpful tool for the patient to focus on own resources. This contemplation is necessary to improve the quality of life of cancer patients with or without evidence of disease, who are undergoing antineoplastic treatment. We believe the use of diaries in this process can contribute significantly to describe and evaluate symptoms/side-effects and to support the individual cancer patient.

Conclusion

The results of our study indicate that 6 weeks of a multidimensional exercise intervention for cancer patients with or without disease and who are undergoing chemotherapy can lead to a reduction in symptoms and side-effects. As such, the total burden of pain, including myalgia, arthralgia, paraesthesia and other pain was reduced significantly ($P = 0.046$).

Patients with evidence of residual disease scored higher in some symptoms/side-effects compared with patients without evidence of disease. However, both groups did respond positively to the intervention as indicated from the sum of symptoms and side-effect scores.

The commitment of the cancer patients in this investigation was positive. The patients completed the semi-structured diaries while undertaking 6 weeks of a multidimensional exercise intervention and simultaneously receiving chemotherapy in the oncological and haematological departments.

The study design adopted in this empirical study is non-experimental. The next step in this research development would be to undertake a randomized clinical trial to specifically evaluate possible effects of the multidimensional exercise programme described herein.

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The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue

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Abstract

Purpose: Cancer related fatigue (CRF) is a common problem for cancer patients across diagnoses during chemotherapy and is associated with physical inactivity, lower functional level and lack of energy. Few RCT exercise intervention studies have included cancer patients undergoing chemotherapy. The objective of this study is to evaluate whether a six-week supervised multimodal exercise intervention, adjunct to chemotherapy and standard care, can reduce the patient’s CRF level.

Methods: Data is based on analyses of a prospective randomised controlled trial ‘The Body & Cancer Trial’. 213 cancer patients with different diagnoses were randomised into an intervention group or wait-list control group. The primary outcome, Fatigue score (CRF), was evaluated by the Functional Assessment of Cancer Therapy-Anaemia Questionnaire (FACT-An) questionnaire.

Intervention: Supervised exercise, comprising high-intensity cardiovascular and heavy resistance training, relaxation- and body awareness training and massage, 9 h weekly for 6 weeks.

Results: CRF was significantly reduced in the intervention group, corresponding to a Fatigue score reduction of 3.04 (effect size of 0.44, 95% CI 0.17–0.72) (P = 0.002), the FACT-An score by 5.40 (P = 0.015), the FACT-An Tui score by 5.22 (P = 0.009) and the Anaemia-ANS by 3.76 (P = 0.002). There was no statistically significant effect on the General Quality of Life score (FACT-G) or on any of the individual wellbeing scores; Physical (P = 0.13), Emotional (P = 0.87), Social (P = 0.83) and Functional (P = 0.26).

Conclusion: In summary, this six-week supervised multimodal exercise intervention can lead to significant reduction in self-reported CRF in cancer patients undergoing chemotherapy.

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Keywords:
Cancer
Chemotherapy
Intensive exercise intervention
Cancer related fatigue
FACT-An questionnaire

Introduction

Cancer Related Fatigue (CRF) is a common complaint of cancer patients undergoing chemotherapy and is associated with the disease itself and with the antineoplastic treatment (Morrow et al., 2002; Hofman et al., 2007; Henry et al., 2008). The term CRF refers to a consistent burdensome feeling of physical, psychological and/or cognitive tiredness that affects the patient’s functional level and is not relieved by rest or sleep (Mock et al., 2003; Lucia et al., 2000). CRF is associated with physical inactivity, a lower functional level and lack of energy (Ahlberg et al., 2003; Lucia et al., 2000). The prevalence of CRF in patients undergoing chemotherapy has been reported as being as high as 90% in the weeks following treatment (Morrow et al., 2002; Stasi et al., 2003; Hartvig et al., 2006).

The focus of the present study is the cancer patient’s experience of fatigue while undergoing chemotherapy and participating in a multimodal exercise intervention. Attempts to prevent and treat CRF with drugs have not been successful (Minton et al., 2010; Campos et al., 2011). Inconsistent results are reported in systematic reviews and meta-analyses of randomized controlled trials (RCTs) of the physical exercise intervention effect on CRF in cancer patients during treatment (chemotherapy, radiation or hormonal therapy or a combination). Some meta – analyses (Cramp and Daniel, 2008; Kangas et al., 2008; Velthuis et al., 2010) have found significant positive effect on patients’ CRF while others (Markes et al., 2006; Jacobsen et al., 2007; Speck et al., 2010) have found no statistical significant effects on CRF during treatment. Cancer patients undergoing chemotherapy can benefit from exercise interventions as evidenced by increased physical capacity (VO₂
However, few exercise intervention studies in cancer patients undergoing high-dose chemotherapy (Dimeo et al., 1999; Chang et al., 2008; Battaglini et al., 2009; Jarden et al., 2009). The RCT exercise intervention studies have documented significant positive effects on CRF while undergoing chemotherapy (Dimeo et al., 1999; Coleman et al., 2003; Headley et al., 2004; Courneya et al., 2007, 2009; Chang et al., 2008) while other studies did not (Jarden et al., 2009; Dodd et al., 2010). Based on the results of a number of studies utilizing low intensity interventions, progressive muscle relaxation training, body-awareness training and massage have been recommended as a concomitant intervention to relieve side-effects and symptoms such as fatigue in patients undergoing chemotherapy (Berger et al., 2002; Post-White et al., 2003; Demiralp et al., 2010). A recent RCT study by Sawada et al. (2010) investigated 24 weekly relaxation sessions (visualization and acupuncture) in patients undergoing chemotherapy (n = 75) and found statistically significant effect on fatigue in favour of the intervention group.

In the ‘Body & Cancer’ trial, we included cancer patients undergoing chemotherapy during the study period with different diagnosis. By combining five components (cardiovascular and heavy resistance training, relaxation, body awareness training, massage) we aimed to maximize the benefits of each of the components. The patients were randomized into an intervention group and a wait-list control group. The intervention was a supervised, multimodal exercise programme with high and low intensity, heavy resistance and cardiovascular components in addition to relaxation and body-awareness training and massage (Adamsen et al., 2006; Quist et al., 2006). We found positive effects of the intervention on depression (Midgaard et al., 2011), aerobic capacity, muscular strength, physical and functional activity, vitality, emotional wellbeing and fatigue (Adamsen et al., 2009b).

The previous report on the “Body & Cancer” trial included fatigue measurement results using the European Organization for Research and Treatment of Cancer’s Quality of Life Questionnaire (EORTC QLQ-C30) (3 items) and a small but clinically significant change was found (effect-size 0.13) (Adamsen et al., 2009b). The present report from the same trial concerns a more detailed, unpublished assessment of fatigue using the Danish version of the Functional Assessment of Cancer Therapy-Anemia (FACT-An) questionnaire (fatigue 13 items) (Cella and Webster, 1997; Cella et al., 2002) and highlighting several dimensions of CRF.

The objective of this study is to evaluate whether a six-week supervised multimodal exercise intervention, adjunct to chemotherapy and standard care, can lead to a reduction in the patient’s CRF level. Here we report the results when using the FACT-An questionnaire.

Methods

Participants

The study design of the ‘Body & Cancer’ trial has been reported elsewhere (Adamsen et al., 2009b). Cancer patients were eligible to enter the study if they had received at least one cycle of chemotherapy for advanced disease or as adjuvant chemotherapy and were undergoing chemotherapy during the 6 week study period, had a WHO performance status of 0 or 1 and were between 18 and 65 years of age. Patients with brain or bone metastases, thrombocytopenia (<50 × 10^9/L), myocardial infarction within the past three months or uncontrolled hypertension (diastolic pressure >95 mm Hg.) were excluded.

Randomisation and ethical considerations

After written informed consent and baseline measures were obtained, the patients were randomized by computer (Clinical Internet Trial Management System: CTMAS) to the intervention group or to the wait-list control group. The patients were stratified by gender, cancer diagnosis (breast, bowel, other solid tumours, haematological malignancies) and disease status (no evidence of disease or evidence of disease). Patients with No Evidence of Disease (NED) received adjuvant chemotherapy after radical local treatment for their cancer disease. Patients with Evidence of Disease (ED) had residual or advanced disease after the initial diagnosis of cancer was made by biopsy or local treatment. Participants assigned to the control group received conventional medical care and were allowed to undertake unrestricted physical activity and they completed outcome measures identical to those of the intervention group. The wait-list control group patients were invited to participate in the intervention programme after their participation in the six-week study. After the 6 weeks study period, 57% of the wait-list control group patients in this study subsequently elected to participate in the Body & Cancer intervention and as such it was not possible to report the follow-up data after the 6-week study period.

The study was approved by the Scientific Committees of the Copenhagen and Frederiksborg Municipalities (Lnr. 01–273/00) that evaluated both the ethical aspects and methodologies used in the research project. In addition, the study was approved by the Danish Data Protection Agency (Lnr. 2000–41–0–149).

The intervention: high- and low-intensity exercising

The intervention took place at a fitness facility located at the Copenhagen University Hospital and was carried out over a six-week period, 9 h weekly, in the morning (Monday, Tuesday, Wednesday, and Friday (Table 1). The patients trained in mixed groups (female and male) with seven to 10 participants per group. Each exercise session started with 30 min of warm-up exercises. The session ended with cool-down exercises consisting of dynamic exercises with the large muscle groups, stretching and coordination training.

The exercise intervention consisted of four high- and low-intensity activities: (1) High-intensity physical training (heavy resistance — and cardiovascular training). The fitness training involved 10-min. interval efforts on stationary bicycles, with an intensity of 85–95% of each patient’s maximum heart rate. Warm-up and cool-down exercises comprised dynamic stretching actions with the large muscle groups, and coordination training (Saltin and Gollnick, 1983; Ainsworth et al., 2011); (2) Relaxation training in groups. The patients were instructed in the use of relaxation techniques, using principles of progressive relaxation when tensing and

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Multimodal exercise intervention, weekly schedule (values: hours).</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Monday</td>
</tr>
<tr>
<td>High intensity training</td>
<td>1.5</td>
</tr>
<tr>
<td>Low intensity training</td>
<td></td>
</tr>
<tr>
<td>Body awareness</td>
<td>1.5</td>
</tr>
<tr>
<td>Relaxation</td>
<td>0.5</td>
</tr>
<tr>
<td>Massage</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* Comprising: warm-up exercises, heavy resistance and cardiovascular training.
relaxing major muscle groups. Audiotapes with recorded instructions and relaxing background music were used by the patients (Lyles et al., 1982; Lerman et al., 1990); (3) Body-awareness training. This part of the training focused on stretching, respiration, yoga and Pilates techniques (Bower et al., 2005; da Costa and Vieira, 2008); and (4) Massage. Massage, administered individually, could be either relaxing, facilitative or therapeutic (Ferrell-Torry and Glick, 1993; Adamsen et al., 2009b).

Physiotherapists and cancer nurse specialists supervised the programme and participated in the physical training components. During physical training, the participants’ heart rates were continuously monitored by means of a wireless heart rate transmitter.

Pre-exercise screening was performed before high-intensity physical training (Monday, Wednesday and Friday) and the participants were advised to respect their own physical limitations. If one of the following criteria were met, the participant was excluded from the physical training component of the programme on that specific day: (1) diastolic blood pressure <45 mmHg or >95 mmHg; (2) heart rate at rest >100 beats per minute; (3) temperature >38 °C; (4) respiration frequency >20 per minute; (5) infections requiring treatment with antibiotics; (6) ongoing bleeding; (7) fresh petechiae; (8) bruises; (9) Blood values B-thrombocytes <50 x 10^9/L; (10) B-lymphocytes <1.0 x 10^9/L (Adamsen et al., 2009b).

Outcome assessment

Demographic data and leisure time physical activity level (pre-illness and baseline) were collected through self-report questionnaires and medical data were drawn from patient records.

Functional Assessment of Cancer Therapy – Anemia Questionnaire (FACT-An)

The primary outcome, Fatigue score (CRF), was assessed using the Fact-An Anaemia Subscale. The participants completed the cancer-specific and well validated FACT-An questionnaire (Version 4) before randomization and after the 6 week study period (Cella and Webster, 1997; Cella, 1998). FACT-An is a 47 item, cancer-specific questionnaire consisting of 27 items (FACT-General (FACT-G score)) that measures the four general domains of Quality of Life, and an additional 20 items related to anemia (FACT-An Anemia subscale) that measures 13 items related to fatigue (Fatigue score) and seven items indirectly related to fatigue (Anaemia – ANS Score) (Yellen et al., 1997). The four general domains of Quality of Life measured in the FACT-G include: Physical wellbeing (PWB); meeting daily needs without physical symptoms (7 items), Social wellbeing (SWB); social or family support (7 items), Emotional wellbeing (EWB); sadness and degree of worry (6 items), Functional wellbeing (FWB); enjoyment and fulfillment (7 items). The sum of PWB, FWB and FACT-An Anemia subscales form the Trial Outcome Index Anaemia (FACT-An Toi) (34 items) score and is regarded as a useful summary index to measure physical and functional capacity.

All items on the FACT-An questionnaire range 7 days back. Scores were registered on a 5-point Likert Scale ranging from 0 to 4 (“not at all” – “very much”) (Cella and Webster, 1997; Yellen et al., 1997; Cella, 1998). The possible score ranges are as follows: Fatigue (0–52), FACT-An (0–188), FACT-G (0–108), FACT-An Toi (0–136), PWB (0–28), SWB (0–28), FWB (0–24) and FWB (0–28). Low scores indicate poor quality of life while high scores indicate good quality of life. Likewise, high fatigue scores indicate less fatigue, with a range from 0 to 52.

Statistical analysis

Baseline comparisons were performed using univariate analysis of variance for continuous variables and likelihood χ² analysis for categorical variables. Primary analysis was undertaken post hoc and we examined whether significant differences in outcome (mean differences) between baseline and six weeks existed between the intervention and control groups with respect to CRF measures (FACT-An questionnaire Fatigue scale).

According to Cella et al. (2002), the minimal clinically important difference on the Fact-An scales is estimated to be for the five targeted scores: Fatigue Score = 3.0, FACT-An score = 7.0, FACT-G score = 4.0 and the FACT-An Toi score = 6.0. We performed a forward stepwise regression analysis using differences in outcome between baseline and six weeks (in all outcome measures) as the dependent variable in a general linear model (GLM). The stepwise procedure was initiated by identifying the covariate that was most strongly related to the dependent variable. The next strongest related covariate was then selected after controlling for the first covariate, and so on. As such, only significant covariates were included in the model. The variable intervention/control was fixed and the following 13 covariates were tested: sex, age, cohabitation, educational level, baseline outcome score, relative change in B-haemoglobin, VO2max, one repetition maximum knee extension and the five disease related covariates—diagnosis, evidence of disease, relapse of disease, chemotherapy cycles before the study period and chemotherapy during the study period (Adamsen et al., 2009b). All analyses were tested with a significance level of p < 0.05 by using the "intention to treat" principle. Available data for participants with missing data, were included under the ‘missing at random’ assumption. Clinically important changes were estimated using Cohen’s guidelines, whereby a value of 0.2 denoted a small effect size, 0.5 a medium and 0.8 a large effect size (Cohen, 1988; Nakagawa and Cuthill, 2007). Effect size (ES) was calculated by the mean difference divided by the pooled standard deviation and the root mean square error was estimated using the general linear model (GLM) (Adamsen et al., 2009b).

Results

Participants

A total of 1956 cancer patients between 18 and 65 years of age were referred to chemotherapy at the oncological and haematological departments of Copenhagen University Hospital during the study period (March 2004–March 2007). 506 patients attended pre-screening and 269 of these met the inclusion criteria and agreed to participate in the study. Post-intervention data after six weeks were obtained from 106 intervention group participants (78.5%) and 107 in the control group (79.8%) (n = 213), using the FACT-An Questionnaire (Table 2). The intervention group’s adherence rate to the 6 week, 9 h weekly exercise training programme (resistance – and cardiovascular training, relaxation training, body-awareness training and massage) was 73% (mean: 18 out of 24 training days; range 5–24). The control and intervention groups were well-balanced at baseline for both demographic and medical characteristics. Participants had a mean age of 47.5 years (range 20–65, median = 48). The intervention group included 22 men and 84 women while 30 men and 77 women participated in the control group. The study included patients with 20 different cancer diagnoses, 16 solid tumors and four malignant haematological diseases. 8 participants in the intervention group and 7 in the control group had received blood transfusions (range 1–14 blood transfusion)
during the 6-week study period. There were no statistical differences in the disease variables: diagnoses, relapsed disease, number of blood transfusion, B-Hemoglobin, days after diagnosis, NED and ED were observed between the intervention and the control groups at baseline (Table 3). The participants received a total of 52 different chemotherapy regimens during the study period (Table 4). The intervention and control group participants had received a mean of 2.5 and 2.9 cycles of chemotherapy respectively prior to entering the study period and a mean of 1.9 and 1.8 cycles respectively during the 6-week study period. The number of chemotherapy cycles did not differ significantly between the two groups.

Reduction of cancer related fatigue on the FACT-An fatigue score questionnaire

Table 5 shows a significant improvement in the primary outcome, the Fatigue score, by 3.04 (effect size of 0.44, 95% CI 0.17–0.71) (P = .002) in the intervention group compared to the control group.

Furthermore, there was a significant effect from baseline to six weeks in favour of the intervention group, as measured on the “anaemia scale” (FACT-An Anemia subscale). Significant improvement of 5.40 was seen in the FACT-An score (effect size of 0.34, 95% CI 0.07–0.66) (P = .015), 5.22 in the FACT-An Toi score (effect size of 0.37, 95% CI 0.1–0.65) (P = .009) and 3.76 in the Anaemia-ANS score (effect size of 0.44, 95 CI 0.17 to 0.71) (P = .002) compared with the control group. In addition, there was no statistically significant effect on the FACT-G score (P = .21) or on each of the individual wellbeing scores; Physical wellbeing (PW) (P = .13), the Emotional-wellbeing (EWB) (P = .87), Social wellbeing (SWB (P = .83) and Functional wellbeing FWB (P = .26). The results were adjusted for 13 covariates; baseline outcome score, disease, relative change in B-hemoglobin maximal oxygen uptake (VO2max), one repetition maximum knee extension, diagnosis, NED/ED, relapse of disease, chemotherapy cycles before the study period and chemotherapy during the study period and demographic covariates (sex, age, cohabitation educational level).

Discussion

Improvement of the Fatigue score with an effect size of 0.44 was found in this exercise study, using the more detailed FACT-An questionnaire, suggesting a small clinically significant effect. The effect of the 3.04 point on the Fatigue score exceeds the 3.0 minimal clinically important difference for this scale. In the previous report on this patient population (Adamsen et al., 2009b), we found an effect based on results from the EORTC QLQ-C30 questionnaire and on the Fatigue score with an effect size of 0.33, suggesting a small, but clinically important improvement of the fatigue dimension. The findings from the present study indicate that fatigue decreases in patients with different cancer diagnosis as they progress through
their cycles of chemotherapy and simultaneously participate in the exercise intervention.

Few published exercise studies are available for relevant comparison. Our effect size of 0.44 on the Fatigue score is comparable to what McNeely et al. (2006) reports in a meta-analysis of 14 RCT exercise studies ($n = 717$) with breast cancer patients, during or post cancer treatment, with a benefit of 6.6 points on the FACT-Breast scale and an effect size of 0.46 on the fatigue score. Likewise, Cramp and Daniel found in a meta-analysis that included 22 RCTs exercise studies ($n = 1662$) during or post- cancer treatment by 56% breast cancer patients an effect size of 0.23 on fatigue, while the effect size on fatigue for the breast cancer group alone was 0.34.

In the present study we noted an effect of 5.22 points on the FACT-An Toi score and an effect of 5.40 points on the FACT-An score which is not a minimal clinically important difference for these scales (6.0 is the cut-off points for the FACT-An Toi score and 7.0 is the cut-off points for the FACT-An score) (Cella et al., 2002). A few RCTs have evaluated fatigue as measured by the FACT-An questionnaire (Courneya et al., 2007, 2009; Jarden et al., 2009). It is not valid to compare our population with that used by Jarden et al. (2009), as the latter population included Hematopoietic Stem cell transplanted patients who were in an intensive and burdensome treatment context. In an RCT study by Courneya et al. (2007), 17 weeks of supervised aerobic exercise (cycle ergo meter training three times per week) versus resistance training (nine different exercises three times per week) was compared against a control group in 242 breast cancer patients undergoing adjuvant taxane-based chemotherapy. Neither aerobic exercise nor resistance training showed significant positive effect on the FACT-An or the FACT-An Toi score. However, Courneya et al. (2009) reported in a study with lymphoma patients ($n = 122$), a minimally significant difference in the score of 4.6 points on the Fatigue score; 9.0 points on the FACT-An Toi; and 9.6 points on the FACT-an scores after 12 weeks of a three times weekly, supervised aerobic exercise training programme. We did not find a minimally significant difference in the FACT-An Toi score. This could be explained by the fact that the control group’s FACT-An Toi score results increased during the study period (93.81–97.11) and, despite multiple chemotherapy

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Demographic and clinical characteristics, and physical activity level.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control group ($n = 107$)</td>
</tr>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>Married, cohabiting, or in a relationship</strong></td>
<td>76 (71.0)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>30 (28.0)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>77 (72.0)</td>
</tr>
<tr>
<td><strong>Completed secondary school or higher</strong></td>
<td>87 (81.3)</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td>15 (14.0)</td>
</tr>
<tr>
<td><strong>Medical characteristics</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Median days since diagnosis</strong></td>
<td>86.5</td>
</tr>
<tr>
<td><strong>No evidence of disease (NED) baseline</strong></td>
<td>62 (57.9)</td>
</tr>
<tr>
<td><strong>Evidence of disease (ED) baseline</strong></td>
<td>45 (42.1)</td>
</tr>
<tr>
<td><strong>Relapsed disease</strong></td>
<td>20 (18.7)</td>
</tr>
<tr>
<td><strong>Mean (SD) β-haemoglobin, mmol/l</strong></td>
<td>7.91 (0.82)</td>
</tr>
<tr>
<td><strong>Pt. received blood transfusions (number of transfusions)</strong></td>
<td>7 (range 1–2)</td>
</tr>
<tr>
<td><strong>Cancer of breast (NED/ED)</strong></td>
<td>51 (43.8)</td>
</tr>
<tr>
<td><strong>Cancer of bowel (NED/ED)</strong></td>
<td>15 (9.6)</td>
</tr>
<tr>
<td><strong>Oncological malignancies (NED/ED)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Cancer of ovaries</strong></td>
<td>9 (4.5)</td>
</tr>
<tr>
<td><strong>Cancer of testes</strong></td>
<td>7 (0.7)</td>
</tr>
<tr>
<td><strong>Cancer of oesophagus</strong></td>
<td>1 (0.1)</td>
</tr>
<tr>
<td><strong>Cancer of brain</strong></td>
<td>2 (0.2)</td>
</tr>
<tr>
<td><strong>Cancer of cervix</strong></td>
<td>2 (0.2)</td>
</tr>
<tr>
<td><strong>Cancer of pharynx</strong></td>
<td>1 (0.1)</td>
</tr>
<tr>
<td><strong>Cancer of pancreas</strong></td>
<td>1 (0.1)</td>
</tr>
<tr>
<td><strong>Cancer of stomach</strong></td>
<td>6 (2.4)</td>
</tr>
<tr>
<td><strong>Other malignancies</strong></td>
<td>10 (4.6)</td>
</tr>
<tr>
<td><strong>Haematological malignancies (NED/ED)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Hodgkin</strong></td>
<td>2</td>
</tr>
<tr>
<td><strong>Non Hodgkin lymphoma</strong></td>
<td>4</td>
</tr>
<tr>
<td><strong>Acute leukaemia</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>Chronic leukaemia</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>Physical activity level</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Pre-illness</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sedentary</strong></td>
<td>3 (2.9)</td>
</tr>
<tr>
<td><strong>Walking or cycling for pleasure</strong></td>
<td>26 (25.0)</td>
</tr>
<tr>
<td><strong>Regular physical exercise, at least 3 h/week</strong></td>
<td>64 (61.5)</td>
</tr>
<tr>
<td><strong>Intense physical activity, more than 4 h/week</strong></td>
<td>11 (10.6)</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sedentary</strong></td>
<td>17 (16.3)</td>
</tr>
<tr>
<td><strong>Walking or cycling for pleasure</strong></td>
<td>41 (39.4)</td>
</tr>
<tr>
<td><strong>Regular physical exercise, at least 3 h/week</strong></td>
<td>40 (38.5)</td>
</tr>
<tr>
<td><strong>Intense physical activity, more than 4 h/week</strong></td>
<td>6 (5.8)</td>
</tr>
</tbody>
</table>
cycles, the patients experienced improved physical and functional capacity.

In agreement with other studies, we did not note any statistically significant effects of the intervention on general quality of life in the FACT-G score of their 12 week, supervised group exercise programme during chemotherapy for 203 women with early stage breast cancer. In the present study, the FACT-G 6 weeks mean score for both the control and the intervention group levels (control: 81.45, intervention: 84.41) was higher than the FACT-G mean score from a general US adult population (80.1) (Brucker et al., 2005). It should be noted that both the intervention and control groups had a high baseline score (mean 20, range 0–28) making it difficult to improve the score (the “ceiling effect”). It would otherwise be difficult to improve general quality of life in a patient who did not report any significant effects of the intervention on seven out of eight somatic symptoms scales measured on EORCT QLQ-C 30 questionnaire. In this study we found no significant effect on each of the individual wellbeing scores (PWB) (P = .13), (SWB) (P = .87), (SWB) (P = .83) and FWB (P = .26). This finding may be related to patients generally receiving sufficient symptom and side effect treatment during chemotherapy and our inclusion criteria indicate a good performance stage score (WHO 1) in order to participate in the study.

The current study has several strengths, including its randomized design, participation by patients with early and...
Abbreviations: CI, confidence interval; SD, standard deviation. Bold values represent values that are significant at \( P < 0.05 \).

\( ^{a} \) Based on general linear model adjusted for sex, age, cohabiting, educational level, baseline outcome score, relative change in B-haemoglobin, maximal oxygen uptake (VO\(_{2\text{max}}\)), one repetition maximum knee extension, diagnosis, NED (no evidence of disease), ED (evidence of disease), Relapse of disease, chemotherapy prior and during intervention.

\( ^{b} \) Effect size (ES) on significant outcomes: Fatigue ES = 0.44 (CI: 0.17–0.72).

\( ^{c} \) Effect size (ES) on significant outcomes: FACT-An ES = 0.34 (CI: 0.07–0.6).

\( ^{d} \) Effect size (ES) on significant outcomes: FACT-An Tsi score ES = 0.37 (CI: 0.1–0.65).

\( ^{e} \) Effect size (ES) on significant outcomes: Anaemia ANS score ES = 0.44 (CI: 0.17–0.71).

### Table 5
FACT-An outcome variables and intervention effect estimates.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean (SD) Baseline</th>
<th>Mean (SD) 6 Weeks</th>
<th>Test (reference: control) mean difference (95% CI)</th>
<th>( P ) value(^{a} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue score (0–52)(^{a} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>35.34 (9.88)</td>
<td>36.34 (9.27)</td>
<td>3.04 (1.17–4.91)</td>
<td>0.002</td>
</tr>
<tr>
<td>Intervention</td>
<td>36.86 (9.54)</td>
<td>40.24 (7.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-An score (0–188)(^{b} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>135.27 (25.07)</td>
<td>139.14 (24.08)</td>
<td>5.40 (1.09–9.73)</td>
<td>0.015</td>
</tr>
<tr>
<td>Intervention</td>
<td>140.43 (24.16)</td>
<td>147.60 (21.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-G score (0–108)(^{c} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>78.84 (13.97)</td>
<td>81.45 (13.33)</td>
<td>1.55 (–0.90–4.01)</td>
<td>0.21</td>
</tr>
<tr>
<td>Intervention</td>
<td>81.14 (14.51)</td>
<td>84.41 (12.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-An Tsi score (0–136)(^{d} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>93.81 (21.70)</td>
<td>97.11 (20.51)</td>
<td>5.22 (1.34–9.11)</td>
<td>0.009</td>
</tr>
<tr>
<td>Intervention</td>
<td>96.80 (20.31)</td>
<td>105.08 (17.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaemia – ANS score (0–80)(^{e} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>56.42 (12.76)</td>
<td>57.69 (12.28)</td>
<td>3.76 (1.42–6.10)</td>
<td>0.002</td>
</tr>
<tr>
<td>Intervention</td>
<td>59.07 (12.06)</td>
<td>63.02 (10.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWB score physical well-being (0–28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>19.77 (5.44)</td>
<td>20.59 (5.19)</td>
<td>0.91 (–0.27–2.10)</td>
<td>0.13</td>
</tr>
<tr>
<td>Intervention</td>
<td>20.64 (5.41)</td>
<td>21.92 (4.58)</td>
<td></td>
<td></td>
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<tr>
<td>EWB score emotional well-being (0–24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>17.69 (4.32)</td>
<td>18.91 (3.73)</td>
<td>0.66 (–0.67–0.80)</td>
<td>0.87</td>
</tr>
<tr>
<td>Intervention</td>
<td>18.14 (4.01)</td>
<td>19.25 (3.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWB score social well-being (0–28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23.53 (3.77)</td>
<td>23.27 (3.73)</td>
<td>0.08 (–0.63–0.78)</td>
<td>0.83</td>
</tr>
<tr>
<td>Intervention</td>
<td>23.38 (4.20)</td>
<td>23.25 (3.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWB score functional well-being (0–28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>17.85 (5.81)</td>
<td>18.67 (5.10)</td>
<td>0.57 (–0.42–1.56)</td>
<td>0.26</td>
</tr>
<tr>
<td>Intervention</td>
<td>18.93 (4.97)</td>
<td>19.92 (4.88)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Several considerations must be taken into account when determining the clinically meaningfulness/clinically significant differences in the resulting CRF changes. We used the criteria proposed by Cohen for calculating effect sizes, and as such the magnitude of the effect of the intervention on CRF may be described for the entire group as being small. Similarly, based on Celis guidelines for estimating clinically important differences in the Fact-An Fatigue scores, 3.04 corresponds with a minimal (Fatigue scale; 3.0) clinically significant difference (Cohen, 1988; Cella et al., 2002). This finding is supported by our previous qualitative findings in which patients described their experience of fatigue during the intervention as having changed due to efforts in transforming chemotherapy-induced fatigue (Adamsen et al., 2004, 2009a). Our results cannot demonstrate whether the intervention may have greater clinical relevance for some diagnostic groups than for others since our heterogeneous sample consisted of 20 different cancer diagnoses.

In summary, this six-week supervised multimodal exercise intervention with cancer patients undergoing chemotherapy can lead to significant benefits in patient self-reported perception of CRF.

advanced stage cancer, a large sample size, and a high adherence rate (73%). In addition, we used the ‘intention to treat’ analysis and a validated questionnaire. One limitation of the study is the heterogeneity of the patients both with respect to diagnosis and to cytotoxic treatment schedules. This excludes a meaningful comparison between different diagnoses and treatments with respect to the specific effects triggered by the exercise intervention. It never was the intention of the study, nor was it possible, to respect the specific comparisons between different diagnoses and treatments with respect to the specific effects triggered by the exercise intervention. It never was the intention of the study, nor was it possible, to differentiate or isolate the separate effect of each intervention component. It cannot be excluded that the intervention context (in addition to the high- and low physical training components) involving group peer support and encouragement from coaches may have influenced the patients’ increased activity level and thereby reduced the patients’ experience of fatigue during the intervention period (Midtgård et al., 2005). The complexity of cancer-related fatigue, i.e. the patient’s daily experience of fatigue and energy levels, is described in the results of our previous studies where the patients distinguished between three different types of fatigue, i.e. treatment-related, mental and physical fatigue (Andersen et al., 2006).

One of the weaknesses of the study is that there is a self-referral of participants who were overly motivated to participate in group-based physical activity. In addition, the participants were well-educated and younger and as such they do not reflect the background population of cancer patients receiving chemotherapy. The exercise intervention in this study shows a short-term effect of some sub-scale components on the FACT-An questionnaire. Apart from registering the number of blood transfusions, the study lacked valid data on patients’ use of pharmacology, e.g. antiemetica, pre-dnisolone, pain killers, etc., which could have helped to further explain CRF reduction in relation to the effect of the intervention. Several considerations must be taken into account when determining the clinically meaningfulness/clinically significant differences in the resulting CRF changes. We used the criteria proposed by Cohen for calculating effect sizes, and as such the magnitude of the effect of the intervention on CRF may be described for the entire group as being small. Similarly, based on Celis guidelines for estimating clinically important differences in the Fact-An Fatigue scores, 3.04 corresponds with a minimal (Fatigue scale; 3.0) clinically significant difference (Cohen, 1988; Cella et al., 2002). This finding is supported by our previous qualitative findings in which patients described their experience of fatigue during the intervention as having changed due to efforts in transforming chemotherapy-induced fatigue (Adamsen et al., 2004, 2009a). Our results cannot demonstrate whether the intervention may have greater clinical relevance for some diagnostic groups than for others since our heterogeneous sample consisted of 20 different cancer diagnoses.
There was no statistically significant effect on the patients’ General Quality of Life score. Exercise interventions for cancer patients, specifically during the course of chemotherapy, are needed to gain insight into the complexity of CRF within the chemotherapy context.

Conflict of interest statement
None declared.

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References


Title:

Exercise despite pain - Breast cancer patient experiences of muscle and joint pain during adjuvant chemotherapy and concurrent participation in an exercise intervention.

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Abstract

Introduction. Little is known about breast cancer patient experiences with chemotherapy related side-effects, including muscle and joint pain while exercising and concurrently receiving adjuvant chemotherapy.

Aim. To explore the perceptions and management of muscle and joint pain experienced by women with operable breast cancer receiving adjuvant chemotherapy with Epirubicin and Cyclophosphamide (EC) followed by Docetaxel (D) and factor support (G-CSF) and who concurrently are participating in a six-week multimodal exercise intervention.

Design. Qualitative descriptive.

Methods. The study used individual semi-structured interviews prior to entering the training programme (pre–interview) and on its completion (post-interview, after six weeks). 15 women (29-57 years old) were interviewed. Data were analysed using a phenomenological approach. The training programme comprised supervised, high-intensity cardiovascular exercise, heavy resistance training and relaxation, massage and body-awareness training (9 hours weekly, over six weeks).

Results. The analysis revealed five categories: Abrupt pain – a predominant side effect, cogitated pain management, the adapted training, non-immediate exacerbation of pain and summarized into an overall sentence describing the essence of chemotherapy related muscle and joint pain in exercise breast cancer patients; exercise despite pain.

Conclusion. The findings indicate that muscle and joint pain started 2-3 days after chemotherapy infusion of D with G-CSF, and continued for 6-14 days. Pain intensity peaked between 2 and 9 days after chemotherapy. The muscle and joint pain did not worsen during the exercise intervention. The patients continued the multimodal exercise intervention, but often reduced the high intensity component of their physical training.

Keywords. Breast cancer, adjuvant chemotherapy, multimodal exercise intervention, chemotherapy related muscle and joint pain, phenomenological analysis methodology.
Introduction

In January 2007, the Danish Breast Cancer Cooperative Group (DBCG) introduced taxanes as a new standard of adjuvant chemotherapy in patients with operable breast cancer. This decision was based on results of meta-analyses showing that adjuvant taxanes could reduce the absolute rate of relapse and death after five years by 3-5% in patients with operable breast cancer (Estevez et al. 2007; Ferguson et al. 2007). The standard adjuvant chemotherapy regimen now consists of 3 cycles of EC (Epirubicin 90 mg/m² plus Cyclophosphamide 600 mg/m² every 3 weeks), followed by 3 cycles of D (Docetaxel 100 mg/m² every 3 weeks). Since 2008, the DBCG has recommended administration of hematopoietic growth factor support (G-CSF) 24 hrs. after the infusion of (D) to reduce the risk of febrile neutropenia (Danish Breast Cancer Cooperative Group 2010; Danish Breast Cancer Cooperative Group 2011). Bone pain is a well known side-effect to treatment with G-CSF in patients in adjuvant chemotherapy (Pinto et al. 2007; Waller et al. 2010; Sveikata et al. 2011; Lee et al. 2013). Waller et al. found that 16.8% of breast cancer patients (n=95) in adjuvant chemotherapy with E and D experienced such bone pain (Waller et al. 2010). The most frequently observed non-haematological side-effects during treatment with D are fatigue, mucositis, neuropathy and pain (Eckhoff et al. 2011).

Nociceptive and neuropathic pain are among the most frequent and troublesome side-effects in patients undergoing chemotherapy (Yamagishi et al. 2009; Karabulut et al. 2010; Spichiger et al. 2011). In a survey by Henry et al. (2008) (n=814) it was found that 48% of patients in chemo- and/or radiotherapy reported significant pain symptoms as important side-effect of their treatment. Breast cancer patients with such side-effects experience reduced quality of life (Miaskowski & Dibble 1995; Green et al. 2011). The pathophysiological background for taxane-induced muscle and joint pain is unknown and effects of analgesics are sparsely described. Following the introduction of D with G-CSF in clinical practice, several reports on pain, predominantly in muscles and joints, were published, e.g. Jones et al. (2006) and Saibil et al. (2010) indicating an incidence of 33% and 79% incidence, respectively.

Exercise interventions can improve the health related quality of life (HR QoL) in patients in active treatment, as summarized in a recent Cochrane review including patients with breast-, prostate-, gynecological and hematological cancers (n=4826) (Mishra et al. 2012). We therefore found it of particular interest to explore the effects of a well established exercise intervention in breast cancer patients being treated with D with G-CSF in the light of the above mentioned side-effects. Could the patients participate in the programme or would the pain increase during exercise? Could these patients, like other patients, benefit from the intervention?

Exercise interventions for breast cancer patients in adjuvant chemotherapy have been introduced over the past 20 years to improve physical functioning, capacity (VO2 max); management of weight gain and HR QoL
Few exercise intervention studies in breast cancer patients undergoing chemotherapy have investigated intervention impact on specific symptoms and side-effects, with the exception of fatigue (Mock et al. 1994; Schwartz 1999; Schwartz et al. 2001; Dodd et al. 2010; Ingram et al. 2010; Yang et al. 2011; Galantino et al. 2012). In a meta-analysis by Speck et al. (2010), 83% of participants were breast cancer patients (n= 6838) during active or post cancer treatment and found no significant effect of moderate to vigorous aerobic or combined activity interventions on pain.

The rehabilitation programme ‘Body & Cancer’ was initiated in 2001. This is a multimodal, structured and supervised exercise intervention with a heterogeneous population of cancer patients in chemotherapy and, to date, 1280 patients have participated in it. The intervention consists of 4 components: heavy resistance and cardiovascular training, body-awareness, massage and relaxation training, 9 hours weekly for six weeks (Adamsen et al. 2003). It has been observed by the ‘Body & Cancer’ team that women undergoing the adjuvant chemotherapy regimen introduced in 2007 EC followed by D with G-CSF had a markedly different burden of symptoms and side-effects during the exercise sessions compared with those entering the study before the change of regimen. In a descriptive pilot study of ten breast cancer patients in the same treatment as above, we explored the prevalence of muscle and joint pain (Andersen et al. 2010). The patients filled in an adjusted, well-validated scheme for registration of pain, i.e. Brief Pain Inventory questionnaire (Cleeland 2009) daily for nine weeks. The patients experienced pronounced muscle and joint pain during daily training (Andersen et al. 2010).

The purpose of the present study was to explore the perceptions and management of muscle and joint pain experienced by participants in the ‘Body & Cancer’ programme who receive adjuvant EC followed by D with G-CSF following surgery for early breast cancer. In this paper, we use the term ‘muscle and joint pain’ to refer to chemotherapy-related toxicity. Muscle pain is defined as ‘pain and tenderness in muscles’ and joint pain is defined as ‘pain at the end positions; reduced mobility and instability of the joints’. Both types of pain are either constant during treatment or can be induced by motion or other specified activities (Andersen et al. 2006).

Methods / Methodology

Design

This study is based on individual, semi-structured interviews using a descriptive, phenomenological approach.
Participants and Sampling

Participants in this study were selected from a population of cancer patients undergoing chemotherapy and concurrently included in the ‘Body & Cancer’ programme, from August 2011 to February 2012 (n= 82). Patient medical records were screened in advance and a criterion sampling method was used for purposes of patient inclusion in the study.

Patients who met the following inclusion criteria were eligible to participate in this qualitative study:

- Operable breast cancer patients aged >18 years.
- WHO performance status of 0 or 1.
- Undergoing adjuvant D with G-CSF after receiving three cycles of EC.

Exclusion criteria included:

- Myocardial infarction within the past three months.
- Uncontrolled hypertension (diastolic pressure >100 mm Hg).
- Medically treated for muscle and joint pain prior to the adjuvant chemotherapy.

The study adhered to guidelines by the Scientific Committees of the Copenhagen and Frederiksberg Municipalities and by the Danish Data Protection Agency (J.nr. 2000-41-0-149). In addition, the study was carried out in accordance with the Helsinki Declaration.

Participants

The breast cancer patients were solicited to participate in the ‘Body & Cancer’ programme by means of posters and pamphlets made available to them in the oncology outpatient clinics at Rigshospitalet and Herlev Hospital, both of which are Copenhagen University hospitals. The study, which was carried out during the period from August 2011 to February 2012, solicited 82 patients as participants in the ‘Body & Cancer’ programme. Sixty-seven of the 82 patients did not meet the study inclusion criteria: 45 did not have breast cancer, 20 breast cancer patients were not undergoing adjuvant chemotherapy and 2 breast cancer patients were treated with analgesics for muscle and joint. Thus 15 patients could enter the study and they all agreed to participate.

Patients were recruited for interviewing purposes after being included in the ‘Body & Cancer’ intervention. The author’s (CA) ‘face to face’ contact with patients took place during the first day of their participation in the intervention and information regarding the study was presented to them at that time. The author (CA) did not participate in the daily training sessions with patients during the interviewing period (August 2011
to February 2012). All 15 surveyed breast cancer patients provided written and verbal consent prior to their participation in the study.

**The intervention: High- and low-intensity exercising**

The ‘Body & Cancer’ multimodal exercise intervention took place during morning hours in a fitness facility located at Rigshospitalet, a Copenhagen University Hospital, and had a duration of nine hours weekly over a six-week period (values: hours)(see Table 1). The patients trained in mixed gender groups, with 12 to 16 participants per group. Each exercise session started with 30 minutes of warm-up exercises consisting of dynamic exercises with the large muscle groups, stretching and coordination training and ended with cool-down exercises. The exercise intervention consisted of four high- and low-intensity activities: (1) high-intensity physical training (heavy resistance - and cardiovascular training (Saltin & Gollnick Pearcey et al. 1983; Ainsworth et al. 2011); (2) relaxation training in groups (Lyles et al. 1982; Lerman et al. 1990); (3) body-awareness training (Bower et al. 2005; da Costa & Vieira 2008); and (4) individual massage (Ferrell-Torry & Glick 1993; Adamsen et al. 2009b). The theoretical basis of the intervention is built on the concept of self-efficacy by Bandura (2001), who presumes that behaviour is learned from the immediate and that earlier successful experiences with behavioural change strengthens belief that success can be achieved in a new setting (Bandura 1997). Training sessions were supervised by a physiotherapist- and a nurse-coach. While the physiotherapist-coach was the instructor and responsible for implementing the group-based physical training, the nurse-coach’s key function was to pre-screen daily all participants for inclusion in the high intensity training in order to prevent adverse reactions (exclusion criteria; pulse at rest > 100/min, diastolic blood pressure < 45 or >95 mmHg, temperature >38°C, respiration frequency at rest >20/min, Infection requiring treatment with antibiotics, ongoing bleeding, fresh petechiae, bruises, B leukocytes value < 1,0x10^9/l / B thrombocytes value < 50x10^9/l) (Adamsen et al. 2003). The nurse-coach was also responsible for individual coaching that targeted the patient’s physical goals with respect to symptoms and side effects (e.g. fatigue, muscle pain, nausea) during the intervention period. Participants’ heart rates were continuously monitored by means of wireless heart rate transmitters during training. The intervention is described in more detail elsewhere (Adamsen et al. 2009b)(p. 2-3).

**Individual Semi–structured Interview**

The individual semi-structured interviews were conducted on two occasions: before entering the intervention (pre–interview) and on completion of the intervention (post-interview after six weeks) and were carried out from August 2011 to February 2012. The participants were interviewed individually by CA
in an office close to the fitness facilities. The themes covered in the two interviews were (pre-interview): the impact of cancer diagnosis/treatment, previous experiences and interpretation of pain symptoms and anticipation of pain intensity during the intervention; (post-interview): description and perception of muscle and joint pain in relation to the intervention (warming-up, strength, fitness, relaxation and massage), intensity, management and correlation between expectations and experiences (Table 2). The average duration of the interviews was 50 minutes (minimum: 35 minutes; maximum: 100 minutes) and all interviews were tape-recorded and transcribed verbatim using Microsoft Word (DSS Player Pro Transcription Module, version 5). Following transcription, the interview tapes were listened to again in order to compare words emphasized, symbols and pauses for possible error detection (Heacock et al. 1996). Data saturation was reached after 13 participants were interviewed but to ensure no further themes and categories could be derived from the interviews, two further interviews were included (n = 15) (Crabtree & Miller 1999).

Analysis
The analysis was inspired by Giorgi’s phenomenological method of analysis, based on de-contextualization and re-contextualization (Giorgi 1985). In an attempt to reach an understanding of each participant’s personal experiences and management of chemotherapy-induced pain and to gain an insight into the participant’s transformation from a ‘healthy life’ to ‘a life with pain’, the study’s analytical process was carried out in four steps (Giorgi 1985). The first step consisted of reading the transcriptions in order to gain a comprehensive overview of the material and to pinpoint possible themes. In actuality, each participant's interview was read several times (Table 3, Sequence and Focus areas). The next step involved reading the interview material again, this time with the aim of identifying and framing important allegations from which the themes could be extracted as general meaningful text headers (Table 3, Meaning units). This was done to identify distinct thought segments in the interview transcripts and to underscore any common accounts given by the women. These meaningful text segments were then sorted by group and/or patterns and were copied onto a separate piece of paper and reread to identify central themes for each thought unit (Giorgi 1985). The third step involved identifying specific meaningful text headers (theme) related to the study’s goals (Table 3, Categories). According to Giorgi, it is at this stage in the process that estimation should be made of the understanding of the phenomenon, in order to avoid misinterpretation of the women’s accounts or being unable to see the phenomenon in an objective manner. An important development in this part of the analytical process was therefore to minimize and ‘put aside’ earlier knowledge about the phenomenon (phenomenological reduction). The final step of the process involved summarizing the sense of each category into a general analysis and establishing a comprehensive identification of ‘universal’ and
‘unique’ themes across all of the interviews, summing up each theme area to form a header so that the essence of the phenomenon could be clearly identified (Table 3, Essence).

To optimize the credibility of the study, a description of the analytical process was documented in a table that aims to show that all interpretations were drawn from the collective data (original sources). The analysis was carried out by the principal author (CA) in continuous collaboration with the co-author (LA). Throughout the analytical process and particularly at the final phase of the analysis when working on the themes of the phenomenon’s essence, several discussions took place between the author and the co-author (LA).

Table 3. Description of the Analytical Process.

Findings

**Description of Participants**
Characteristics of the 15 participants are presented in Table 4. Demographic data, recreational physical activity levels (pre-illness and baseline) and the participants’ own assessment of pain thresholds were collected using self-reported questionnaires and medical data were drawn from patient records. The women had a median age of 44 years (range 29-57) and most of them were married or cohabitated (n=12), had a mid-range education level (n=9) and were on full sick-leave while undergoing chemotherapy (n=11). Most of the women had undergone mastectomies (n= 9), and had exercised regularly, i.e. at least 3 hours weekly pre-illness (n=10). A third of the women (n = 5) had received one cycle of (D) (100 mg/m²) at the intervention’s baseline. Five patients received 75% doses of D (75mg/m²) during the exercise intervention due to grade 3/4 toxicity in non-hematologic side-effects such as mucous membrane irritation of the mouth and throat, muscle and joint pain and diarrhoea. All 15 women received Prednisone (pre-medication 50 mg x 1 - post -medication 50 mg x 1 two days) and analgesics (Paracetamol, 1-4 g daily and Ibuprofen 400-1200 mg daily) as part of the standard supportive care for this particular chemotherapy regimen. The participant adherence rate in the exercise intervention was 77.0% (mean: 18.5 out of 24 training days; range 9-22). Thereof, an average of two days of absence due to their outpatient chemotherapy. The women’s own estimation of their general pre-illness pain thresholds on a scale from 1– 10 (1=minimum pain threshold & 10=maximum pain threshold) showed an average score of 7 (range 4-9). Table

4 - Demographic and Clinical Characteristics, and Physical Activity Level
The themes

The analysis described in Table 3 is presented as two sequences, i.e. pre- and post-interview. Based on the selected meaning units that describe the participants’ pain levels across the study period, four categories were identified: Abrupt pain – a predominant side-effect, Cogitated pain management, Adapted training, no immediate exacerbation of pain and exercise despite pain as a final expression of the phenomenon’s essence.

Abrupt pain - a predominant side-effect

The women in the study were asked to describe their feelings regarding the pain they experienced during the intervention. All of them felt joint and muscle pain during days following chemotherapy sessions D with G-CSF and were convinced that their pain was primarily caused by the chemotherapy infusion. ‘I am convinced that it is the treatment that is causing my pain’, expressed a 49-year-old woman. The women describe in detail exactly when the pain started (2-3 days after chemotherapy infusion), the duration of the pain and its intensity and spread. A 32-year-old woman informs: ‘I went for treatment on Monday; on Tuesday I had to inject myself with the growth factor stimulant (G-CSF) and that night I woke up with pain all over my body ...’. A 50-year-old woman confirmed that her pain started three days following treatment: ‘I had chemotherapy on Thursday and two days later, when I actually thought that I couldn’t feel anything, I was thrilled... But 24 hours later around 10.30pm, I started to feel uneasy and pain set in. Then, 30 minutes later the pain shot through me and I hurt everywhere’.

In the women’s descriptions of their pain, a variety of terms were used to describe the type of pain they experienced. Several of the women (n=6) described their pain to be like stabbing, nagging growing pains and a feeling of restlessness in the body. ‘The symptoms that I feel are more like growing pains. I can’t stand pain anywhere; it hurts and you can’t lie down, stand up or sit.... such discomfort, aggravation and pain in my whole body’, said a 48-year-old woman. Other women expressed their pain as being influenza-like in nature, ‘... it’s influenza-like pain as well as discomfort in the legs – my knees – so I lie down but toss around in the bed and can’t find a comfortable position and it hurts around my entire body’, expressed the 29-year-old woman.

A common factor shared by the women was that the pain primarily stemmed from muscle and joint aching that occurs in different parts of the body (thighs, lower leg, knee, foot joints, arms, elbows, shoulders, back, hips, buttocks, jaw and neck) and that shifted around in the body during the weeks that the pain persisted. A 49-year-old woman expressed it as follows: ‘My legs hurt two days after treatment; they felt as heavy as lead, and then it started in my back where it hurt so much that I had to call the hospital and ask for
painkillers. I vomited and felt nauseous from the pain – so I felt really sick’. A 44-year-old woman described her pain threshold in the following way: ‘I couldn’t do a thing; I hurt all over... my jaws, teeth, neck, shoulders, muscles and arms’. Several of the women reported that during those periods in the weeks when the pain was most intense, they had difficulty sleeping at night and that once in a while they found it difficult to walk due to leg pain. A 45-year-old woman expressed the following: ‘Wow, did it hurt...in the hips, buttocks and muscles; it was like I was lying down on a raised hump, it hurt so much. Once in a while there would be a shooting pain that radiated throughout my entire body. When I tried to walk I had to constantly lean on something’.

A 47-year-old woman said: ‘It was 10 days (after treatment) before I started to feel normal again and pain-free, which is expected when you are undertaking chemotherapy’. The pain experienced by the women had a one-week duration on average, with a variation of between 6-14 days during which the pain intensity peaked from 2 to 9 days after the women had undertaken a chemotherapy cycle.

Cogitated Pain Management

With respect to the women’s pre-illness pain management efforts, e.g. headaches, menstrual pain and lower back pain, two strategies for pain management became apparent. One group of women (n=10) who regularly exercised at least 3 hours weekly used physical activity (jogging or walking) as a means of reducing their pain. They had positive experiences with this strategy as well as a self-rated relatively high pain threshold (6-9).

A 36-year-old woman, who had used physical activity as a remedy for migraine headaches and menstrual pain explains: ‘I have done sports for 15 years and know my body fairly well, so if I hurt anywhere, I use physical activity, volleyball training, to feel better’.

The other group of women (n=5) reported inform that they take analgesics when they experience physical pain (e.g. Paracetamol, 1 gram) and lie down quietly with a heating pad or ice pack, depending on the cause and type of pain. This group had a self-rated relatively low pain threshold (4-6).

A 54-year-old woman expressed: ‘... relaxing, being alone and lying down is the best for me when it comes to managing my pain’.

During the ‘Body & Cancer’ intervention, the majority of the study participants (n=12) used the same physical activity strategy for managing their pain as they had done prior to their cancer diagnosis, in addition to taking the recommended painkillers (according to the standards of the chemotherapy regimen).

‘My strategy was that I would do exercise no matter what. It is a brief period of time and even though it was painful and I had just finished a chemotherapy session and I felt miserable, another part of that
strategy was that I didn’t want to give up and quit’, expressed a 50-year-old woman who, pre-illness, had used walking as a part of her pain management.

A few of the women (n=3) who had expected that they could manage their chemotherapy related pain in the same fashion as they had with previously experienced pain, i.e. by using physical activity as a remedy, stated that it was not possible to maintain their strategy. The women described experiencing, despite the recommended painkillers that they were unable to join the training sessions or to participate in other daily activities. A 47-year-old woman described it in the following way: ‘While I was under Docetaxel treatment, I had to lie in bed every now and then. I needed more pain relief... I was completely exhausted by the pain. I wasted an entire day in bed. I didn’t do anything but lie on the sofa and then I felt better...and then by Friday I was able to go to training again’.

Those women (n=5) who, prior to their participation in the ‘Body & Cancer’ intervention, usually managed their pain by relaxation and remaining in bed, informed that they had to miss training sessions on some of the days following chemotherapy because of the pain and other side effects. A 47-year-old woman in the intervention was forced to reduce her chemotherapy dosage due to grade 3 level pain. She shared: ‘It was horrific with all that pain...I couldn’t go outside; I was buried under my duvet, lying on the sofa. I felt like an invalid...I couldn’t do anything. No, on those days there were no way that I could exercise’.

Adapted training

A consequence of the women’s symptoms and side-effects of their treatment was that they had to diminish the intensity and frequency of training and needed to take several breaks during the exercise intervention. In relation to the programme’s strength training component, the majority of the women (n=13) informed that, despite having pain sensations they were able to carry out their respective strength exercise intervention.

‘Strength training went surprisingly well – I just lowered the weight intensity on the strength training machines’, said the 47-year-old. The women informed that even prior to training sessions, they had planned to lower the strength intensity by 10-20%. Similarly, the women described their fitness training efforts on stationary bicycles as occurring at a slower pace, with less pedalling frequency, less resistance and with longer pauses between training intervals. A 50-year-woman described her training effort on the fourth day following chemotherapy as follows: ‘I wasn’t able to adjust the resistance on my bike as high as I usually did and I couldn’t cycle at a high tempo; but I did try to do as much as I could’.

None of the women in the study described their chemotherapy related pain as being associated with their participation in the body awareness training and massage components of the intervention. Very few of the women (n=2) expressed that their chemotherapy related pain influenced their ability to participate in relaxation training. ‘I just couldn’t lie still. I could feel my knee and buttocks – they hurt – I usually like the
relaxation component but I just couldn’t do it...I could not relax enough to lie still. It felt like the pain was moving around (my body).’

Furthermore, the women deemed that being together in a group was an important reason for them to participate in the training from a psychological perspective, despite their pain sensations. Being in a group that trains together and where the other participants - both the patients and the supervisors – motivated their willpower to persevere with the training despite discomfort and pain. One 51-year-old woman describes training in the group as having an impact on her exercise efforts: ‘It is hard to get through chemotherapy, but the ‘Body & Cancer’ intervention is a boost in the opposite direction. Even when I said to myself that I’m not feeling well and hurt all over, I still made an effort to go (to the training session) because I could then just sit on the stationary bike and hang-out with the others. We laugh, share camaraderie and do fun things together – and you tend to forget the pain’.

No immediate exacerbation of pain

Throughout the six-week training period, the women showed willpower and persistence in their attempts to attend the exercise sessions even with pain and other symptoms during those weeks following their chemotherapy. ‘It was a real effort with all the pain in my leg but I showed up for training and I biked ... and kept it up the whole way through’, explained a 29-year-old woman.

A pattern became apparent with respect to the intensity of the women’s muscle and joint pain and their participation in the exercise intervention. More specifically, the women tended to dismiss themselves from training on the third day following chemotherapy infusion. A few of the women (n=3) actually attended all of the exercise interventions, even during those days when they experienced muscle and joint pain caused by chemotherapy. The rest of the women claimed that they had to cancel their daily workouts at least twice (range 2 - 7) as their muscle and joint pain was so intolerable that they did not feel able to participate. The women’s descriptions express that even when they did make an effort to attend the exercise interventions with muscle and joint pain, their pain was not worsened by the exercise. A 44-year-old woman describes: ‘The pain was worse than I had expected. But the exercise did not worsen it’, or as explained by a 45-year-old woman: ‘My muscle and joint pain did not worsen; perhaps you could say that it was status quo’. Furthermore, a small group of the women (n=4) expressed that their pain diminished during the exercise intervention. The women said that they were uncertain whether their pain sensation diminished because of the exercise only. A 36-year-old woman expressed the following, ‘One day last week, when I was feeling ill with pain and nausea, I went anyway (to the ‘Body & Cancer’ intervention) and actually it was fun as I felt less nausea and pain afterwards. It was as if I suddenly had more energy in my
body’. A 47-year-old woman, who had received the full chemotherapy dose, said: ‘I believe, as I have said before, that my pain sensations diminished. Whether this was due to my body just getting used to chemotherapy or because of the exercise, I just don’t know. But, it (my pain) has diminished dramatically over the last six weeks, and I have not reduced the dose of chemotherapy’.

Exercise despite pain

The majority of the participants in ‘Body & Cancer’ maintained their participation in the training despite the pain, they experienced in the days after chemotherapy, but often with reduced intensity. A characteristic shared by the women in the study was the awareness that their pain was not related to their breast cancer diagnosis but to the adjuvant chemotherapy. The women therefore aimed to maintain the goal of completing the ‘Body & Cancer’ intervention despite their pain, and did so by diminishing the intensity of their exercise during the first days following treatment cycles. Whatever the women’s prior strategies were for managing pain (physical activity/relaxation), their own willpower, persistence and mental strength drawn from the camaraderie of the group made them want to train even if that meant experiencing muscle and joint pain in their upper or lower extremities. During the training process, the women showed their awareness that active participation in physical exercise can shift focus away from pain negative sensations.

Discussion

We undertook this study to gain insight into how women with breast cancer, who participated in an exercise intervention while undergoing adjuvant chemotherapy with G-CSF, perceive and manage muscle and joint pain. The women in the study reported some degree of pain from treatment with G-CSF; however, they managed to attend the daily training sessions (on average 18.5 out of 24 days).

’Abrupt pain’ is an important finding in the present study. The women described this type of pain as a predominant side-effect and consequently, the women can be said to have experienced ‘life with pain’ during the days following their treatment with chemotherapy. Daily life is dominated by persistent muscle and joint pain that starts 2-3 days after each treatment and varies in intensity and duration (6-14 days), while the pain characteristics (i.e. stabbing, nagging growing pains and restlessness) appear unpredictably. Breast cancer patients undergoing chemotherapy suffer from different types of pain (Saibil et al. 2010). A retrospective Danish study by Echhoff et al. (2011) found that 53% of breast cancer patients (n = 1143) during adjuvant chemotherapy (EC followed by D with GCSF) experienced muscle and joint pain and that 7% of patients reported grade 3-4 toxicity muscle and joint pain. The absence of pain 2-3 days following their treatment with chemotherapy could conceivably be due to the standard anti-inflammatory treatment.
with Prednisolone. While the pain clearly was related to treatment with D and G-CSF, it is not possible to
distinguish between the effects of these two components on the pain.

The theme ‘Cogitated Pain Management’ describes how the women, pre-illness, used two types of pain
management strategies, i.e. physical activity versus relaxation. The women used pain management
strategies with which they were familiar pre-illness, despite the introduction of two new components in
their lives, i.e. chemotherapy and participation in the Body & Cancer intervention. This behaviour parallels
Bandura’s description of self-efficacy (i.e. ‘belief in one’s capabilities to organize and execute the courses of
action required to produce given attainments’ (Bandura 1997) (p. 3)) and which assumes that behaviour
leading to success is repeated. It should be noted that those women who pre-illness used ‘relaxation’ as a
pain management strategy and who had a low pain threshold (score 4-6) may have experienced a major
total side-effects burden which made their participation in the exercise intervention more difficult on the
second and third days following their chemotherapy D with GCSF (Guy & National Institute of Mental Health
1976). Our study findings support the results of the Pickett et al. 2002 RCT exercise intervention with breast
cancer patients (n=42) undergoing adjuvant treatment and which found that the women who were
physically active pre-illness were, to a large extent, more inclined to complete the training programme than
those women who pursued a sedentary lifestyle (Pickett et al. 2002).

The ‘adapted training’ theme describes the women in the study, who regardless of their pain management
strategies (physical activity versus relaxation), reduced their high-intensity physical training and frequency
and chose to hold several breaks during some training sessions during days 2-9 days following their
respective chemotherapy. In line with our study results, the Ingram et al. qualitative study of eight breast
cancer patients undergoing adjuvant chemotherapy (doxorubicin, cyclophosphamide and paclitaxel or CEF)
and who concurrently participated in a home-based exercise training programme (aerobic exercise and
resistance exercise ), found that the women on the days following chemotherapy trained at a lower
intensity level (Ingram et al. 2010).

Consistent with our findings from of the ‘Body & Cancer’ Study (Midtgaard et al. 2005; Adamsen et al.
2009a), the women’s descriptions confirmed that group training, i.e. support from the training team and
the other patients was invaluable in lifting their spirits and motivating them to persevere with their exercise
despite discomfort and pain. Other exercise rehabilitation programmes for breast cancer patients during and
following treatment find comparative ‘patient to patient’ contact to be a supportive function in complying
with and completing training programmes (Pinto et al. 2005; Korstjens et al. 2006).

From the theme ‘No immediate exacerbation of pain’, it appears that the women in this study had to cancel
participation at least twice (range 2-7) during their 6-week exercise intervention because of unbearable
muscle and joint pain. Our findings are in line with result of an RCT exercise intervention by Courneya et al.
of breast cancer patients undergoing adjuvant taxane-based and non-taxane, which showed that disease/treatment related barriers accounted for 53% of all missed exercise sessions, of this 4% were related to pain (Courneya et al. 2008). During the 6 weeks of training the patients did not experience any worsening of the muscle and joint pain, and some did even indicate that the intervention reduced the pain. The patients were motivated for and did in full length participate in the low-intensity components; relaxation-, body awareness training and massage. It is possible, that these components could have a certain alleviating effect on the pain. Thus therapeutic massage has been shown to have a certain analgesic effect in cancer patients (Smith et al. 2002; Listing et al. 2009; Sturgeon et al. 2009), Yoga (Galantino et al. 2012) and relaxation (Kwekkeboom et al. 2010; Kwekkeboom et al. 2012).

The essence of the theme ‘exercise despite pain’ is that participants have the drive and willpower to maintain their participation in the six-week intervention even while experiencing muscle and joint pain during the days following their chemotherapy and this applies to all of the women whether they had used management strategies or relaxation for pain management pre-illness. These patients represent a selected group as they took the initiative to sign up to the Body & Cancer exercise intervention convinced that they would complete the six-week programme. This should of course be kept in mind when discussing the general application of our findings. Thus, the findings of Milne et al. (2007) suggest that in addition to side-effects, lack of commitment and motivation have a decisive influence on patients abstaining from physical training. The ability of the women to continue training while experiencing muscle and joint pain may be due to both psychological and physical factors. A possible explanation of why the women were able to implement the training programme despite intense pain, may be due to the fact that they do not associate their pain with their cancer disease but rather with the adjuvant treatment. Furthermore, the group-feeling, and the setting with high music etc made it possible for the women to better neglect their feeling of pain. The majority of the women had exercised regularly i.e. at least 3 hours weekly pre-illness and could conceivably have used the present exercise context as a motivating factor for recalling physical well-being and for achieving pain control. An intervention study by Steihaug comprising exercise and group-discussions with eight women found that the intervention motivated the women who were experiencing chronic pain, to increase their physical activity level (Steihaug 2007).

A PRO-Self Pain Control programme that in several RCTs (West et al. 2003; Kim et al. 2004; Miaskowski 2004) have shown to be a support to cancer patients in assessing and managing own pain, comprises education and skills building components as well as coaching by a nurse to improve cancer pain management. A more recent RCT (n=179) by Rustøen et al. (2012) that tested the effect of the PRO-Self Pain Control programme during a six-week intervention with patients experiencing bone metastases pain, showed that the patients obtained a considerable level of knowledge about pain management and control (including pain
medication), that then allowed them to improve management of their own pain. These results are promising but do not directly correlate with our study population, since the patient group had a poorer performance status, greater disease complexity with advanced disease and bone metastases. The nurse-coach function in the present study focuses on individual coaching in relation to the women’s collective symptoms and side-effects and not specific coaching related to the women’s pain during the intervention. The essence of the theme ‘exercise despite pain’ may indicate that the women in our study could benefit from a targeted pain management and control intervention.

Methodological reflections and study limitations
Several important factors may have influenced the women’s experience of pain during the exercise intervention. One-third of the women reduced their chemotherapy (D) dosage to 75% due to toxicity (grade 3/4 toxicity in relation to non-hematologic side effects such as mucous membrane irritation of the mouth and throat, muscle and joint pain and diarrhoea) and this could have caused a reduction in the burden of pain as a side effect ((Danish Breast Cancer Cooperative Group 2010; Danish Breast Cancer Cooperative Group 2011). Similarly, the women’s daily use of analgesics (Paracetamol and Ibuprofen) during the training period was not investigated.

The average attendance rate for the breast cancer patients in this study was 77% which is comparable with an earlier reported attendance rate for the entire group of cancer patients and for other population groups in exercise studies that included breast cancer patients undergoing adjuvant chemotherapy (Courneya et al. 2007b; Mutrie et al. 2007).

The small sample size made it impossible to draw any general conclusions from the qualitative data (Malterud 2001). As such, the study was unable to estimate the extent to which women's perceptions and management of pain differ from other descriptions of muscle and joint pain in breast cancer patients who did not participate in exercise interventions or who did exercise during adjuvant chemotherapy (D with G-CSF). Regarding the external validity of the study, the transferability of this study’s findings is relevant only to younger breast cancer patients undergoing adjuvant chemotherapy (EC followed by D with G-CSF). Our study population comprised a select group of breast cancer patients with a median age of 44 years compared with a median age of 64 in the total population of breast cancer patients in Denmark. In addition, 66% of our patients exercised regularly before being diagnosed with breast cancer (> 3 hours weekly) compared with only 18% of the total Danish age-related female population (Illemann Christensen et al. 2012). Only 40% of our patients received breast preserving surgery compared to 74% in the total population of breast cancer patients in Denmark (Danish Breast Cancer Cooperation Group 2012). The high frequency of mastectomy is only in part explained by the age at diagnose, and may otherwise in part be
explained by a higher motivation for participation in patients with locally more advanced disease. This study focused on the women’s recall of their pain experiences and management throughout the six-week intervention and this could have given rise to recall bias. Another limitation is that the women in the study specifically were asked to focus on their chemotherapy related muscle and joint pain during the intervention. This may have had both positive and effects on their perception of the symptoms. Other side-effects such as fatigue, neuropathic pain and bone pain could likewise have had positive or negative effects on the women’s perceptions and management of muscle and joint pain.

The semi-structured interview methodology proved useful in investigating participant perceptions of pain and in focusing on the nuanced descriptions of their experiences in relation to pain management (Denzin & Lincoln 2000).

The interviewer (first author) held the position of cancer nurse specialist in the ‘Body & Cancer’ exercise intervention for several years and as such had both an interest in and experience with exercise and was well acquainted with the research field (phenomenon). The interviewer’s prior knowledge could have overlooked important nuances throughout the interview process; however, she remained focused on her own responsibilities and attempted to be open to new perspectives. Efforts were made to minimize this bias by means of triangulation analysis conducted by two researchers (CA) (LA) (Malterud 2001). None of the patients were known to or had met the author (CA) prior to inclusion in the exercise intervention and the author (CA) did not participate in the daily training sessions with patients during the interviewing period (August 2011 to February 2012). Administration of G-CSF was standard procedure in the Department and in which the author was not involved.

Conclusion

In conclusion, analysis of a group of 15 younger breast cancer patients participating in a multimodal exercise intervention indicate that the patients’ perception of sudden onset of chemotherapy-related muscle and joint pain was not aggravated by training. The women described the pain as to be like stabbing pain and with a feeling of restlessness in the body restricting everyday life. Pain intensity peaked between 2 and 9 days after chemotherapy. The patients demonstrated a high adherence rate to the exercise intervention caused by their own willpower and camaraderie of the group. The breast cancer patients did not relate the pain to their cancer diagnosis but to their chemotherapy. Consequently, they maintained physical activity expressed in the phenomena ‘exercise despite pain’

Clinical implications and future research

It is recommended that further research focus on the continuous registration and analysis of breast cancer patient pain thresholds, pain prevalence, incidence and intensity during adjuvant chemotherapy (EC
followed by D with G-CSF) while participating in an exercise programme. This should be done using a well-
validated questionnaire and registration diaries, which are necessary to gain insight into the complexity of
pain and pain management. Our preliminary findings support the contention that these patients should not
abstain from participating in structured physical activities such as ‘Body and Cancer’.
REFERENCES


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http://www.dbcg.dk/PDF%20Filer/Retningslinjer%202011%20Kap%2006%200200111.pdf


Spichiger E., Muller-Frohlich C., Denhaerynck K., Stoll H., Hantikainen V., & Dodd M. (2011) Prevalence of symptoms, with a focus on fatigue, and changes of symptoms over three months in outpatients receiving cancer chemotherapy. *Swiss Medical Weekly* 141, w13303.


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<th>Wednesday</th>
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<td>Low intensity training</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Body awareness</td>
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*Comprising: warm-up exercises, heavy resistance and cardiovascular training
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<th>Focus areas</th>
<th>Sample Questions</th>
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<tr>
<td><strong>Pre interview - Baseline of Body &amp; Cancer</strong>&lt;br&gt;Impact of illness (cancer diagnosis) and treatment (chemotherapy EC followed by D with G-CSF).&lt;br&gt;Prior experience with and interpretation of pain symptoms&lt;br&gt;Expectations of the training program on pain</td>
<td>What do you attribute pain to when you experience it?&lt;br&gt;What has your doctor/nurse informed you regarding what symptoms and side effects to expect in relation to chemotherapy?&lt;br&gt;Do you relate chemotherapy to pain?&lt;br&gt;Have you experienced pain with, for example, headaches, menstruation cramps or backache? Do you speak about your pain with others?&lt;br&gt;What have you done to manage your pain?&lt;br&gt;What are your expectations of chemotherapy and pain? Do you think that your participation in the training program will reduce pain, worsen it or that there will be no difference in pain level?</td>
</tr>
<tr>
<td><strong>Post interview - Completion of Body &amp; Cancer</strong>&lt;br&gt;Descriptions of the pain: Intensity, management, compliance and correlation between expectations and experiences&lt;br&gt;Pain perception: Intensity and management with supervised high- and low physical training (warming-up, resistance – and cardiovascular training, relaxation-, massage- and body-awareness training)</td>
<td>Have you had any chemotherapy related muscle or joint pain in connection with your chemotherapy?&lt;br&gt;Did you experience any physical changes as a result of training after you were administered Docetaxel and G-CSF?&lt;br&gt;How has pain influenced your physical and emotional abilities?&lt;br&gt;Did you take any measures to control your pain?&lt;br&gt;What treatments did you take or adjustments [e.g. in medication] did you make in physical training?&lt;br&gt;Did you have muscle and joint pain during the exercise intervention?&lt;br&gt;Did you quit training because of pain?&lt;br&gt;Did you lower the intensity of your training?&lt;br&gt;Did you have breaks?&lt;br&gt;Did you train as usual?&lt;br&gt;Did you have a personal strategy to gain control over you pain during exercise?</td>
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Table 3: Description of the Analytical Process

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<tr>
<th>Sequence and focus Area</th>
<th>Selected Meaning Units</th>
<th>Categories</th>
<th>Essence</th>
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</thead>
<tbody>
<tr>
<td>Pre interview - Baseline of Body &amp; Cancer</td>
<td>Impact of illness (cancer diagnosis), treatment (chemotherapy [EC followed by D + G-CSF]). Prior experience with and interpretation of pain symptoms</td>
<td></td>
<td></td>
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<tr>
<td>Post interview - Completion of Body &amp; Cancer</td>
<td>Pain perception: Intensity and management with supervised high- and low physical training (warming-up, resistance- and cardiovascular training, relaxation-, massage- and body-awareness training) Descriptions of the muscle and joint pain: Intensity, management, compliance and correlation between expectations and experiences</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| | I'm not so afraid of pain | Pain is not a negative thing | Chemotherapy makes me nauseous – no pain | I take pain reducing medicine | I keep active | I get some fresh air | I go for a walk | I focus on doing something | I lie down and rest | I drink water | I relax | I feel restless and feel pain all over my body | My legs feel heavy like lead | The pain makes me feel really sick | The painkillers did not help at all | It was horrific with all that pain | I couldn't do a thing | Everything hurts | I used lower weight on the machines | I lowered the resistance level on the bike | I forgot the pain | It was great to do something physical I had to persist despite the pain I shifted my focus away from the pain | I felt some physical improvement | I had surplus energy to resist [the pain] | I informed that I would miss that session | The pain did not get worse, perhaps it stayed the same | The physical goal is to build strength despite muscle pain | Body and Cancer training did not worsen it | I think it helped with the pain |
| | Cogitated Pain Management | Abrupt pain - predominant side-effect | The adapted training | No immediate exacerbation of pain | Exercise despite pain |
Table 4: Demographic and Clinical Characteristics, and Physical Activity Level

<table>
<thead>
<tr>
<th>Patients (n=15)</th>
<th>Median</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
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<td>29-57</td>
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<tr>
<td><strong>Marital status</strong></td>
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</tr>
<tr>
<td>Married</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Cohabitating</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Single/Divorced</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Education level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (no education following grade school)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Short (under 3 years, high school certificate)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mid-range training (3-5 years- 4 year college degree)</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Long (over 6 years university graduate/post-graduate degree)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Employment status during chemotherapy</strong></td>
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<td></td>
</tr>
<tr>
<td>Full-time employment</td>
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<tr>
<td>Partial sick leave</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Sick leave</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Early retirement pension (not due to cancer diagnosis)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastectomy</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Lumpectomy</td>
<td>6</td>
<td></td>
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<tr>
<td><strong>Docetaxel before baseline exercise intervention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One cycle</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Two cycle</td>
<td>8</td>
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</tr>
<tr>
<td><strong>Docetaxel Dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel 100 mg/m2 (100%)</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Docetaxel 75 mg/m2 (75%)</td>
<td>5</td>
<td></td>
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<tr>
<td><strong>Physical Activity Level</strong></td>
<td></td>
<td></td>
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<tr>
<td>Pre-illness</td>
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<tr>
<td>Sedentary</td>
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<tr>
<td>Walking or cycling for pleasure</td>
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<tr>
<td>Regular physical exercise, at least 3 h/week</td>
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<td>Baseline</td>
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<tr>
<td>Regular physical exercise, at least 3 h/week</td>
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<td>Intense physical activity, more than 4 h/week</td>
<td>0</td>
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<tr>
<td><strong>Own assessment of pain threshold</strong></td>
<td>Median</td>
<td>Range</td>
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<tr>
<td>(Scale of 1 – 10)</td>
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<td>4-9</td>
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DECLARATION OF CO-AUTHORSHIP
This form must be filled in on the screen, printed, signed and sent to the Graduate School
- You can use the TAB-button to jump between the grey boxes.

Information on PhD student:

<table>
<thead>
<tr>
<th>Name of PhD student</th>
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<tbody>
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<td>University Hospitals Center for Health Research (UCSF )</td>
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<tr>
<td>Principal supervisor</td>
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Title of PhD thesis:

Body & Cancer – The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

This declaration concerns the following article:

The effect of a multidimensional exercise programme on symptoms and side-effects in cancer patients undergoing chemotherapy - the use of semi-structured diaries

The PhD student’s contribution to the article:

(please use the scale (A,B,C) below as benchmark*)

1. Formulation/identification of the scientific problem that from theoretical questions need to be clarified. This includes a condensation of the problem to specific scientific questions that is judged to be answerable by experiments  
   C
2. Planning of the experiments and methodology design, including selection of methods and method development  
   C
3. Involvement in the experimental work  
   C
4. Presentation, interpretation and discussion in a journal article format of obtained data  
   C

*Benchmark scale of the PhD student’s contribution to the article

A. refers to: Has contributed to the co-operation 0-33 %
B. refers to: Has contributed considerably to the co-operation 34-66 %
C. refers to: Has predominantly executed the work independently 67-100 %

Signature of the co-authors:

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<th>Name</th>
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<tr>
<td>16.01.13</td>
<td>Lis Adamsen</td>
<td>Professor, MSc Soc</td>
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<td>16.01.13</td>
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Signature of the PhD student and the principal supervisor:

<table>
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<tr>
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<th>Principal supervisor: Lis Adamsen</th>
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Principal supervisor: Lis Adansaen

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Name: Anders Tvetøås
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Date: 16.01.13
PhD student: Christina Andersen
Signature: [Signature]

Date: 16.01.13
Principal supervisor: Lis Adansaen
Signature: [Signature]
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</table>

Title of PhD thesis:

Body & Cancer -- The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

This declaration concerns the following article:

The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue

The PhD student's contribution to the article:

<table>
<thead>
<tr>
<th>Contribution Description</th>
<th>(A,B,C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Formulation/identification of the scientific problem that from theoretical questions need to be clarified. This includes a condensation of the problem to specific scientific questions that is judged to be answerable by experiments</td>
<td>C</td>
</tr>
<tr>
<td>2. Planning of the experiments and methodology design, including selection of methods and method development</td>
<td>C</td>
</tr>
<tr>
<td>3. Involvement in the experimental work</td>
<td>C</td>
</tr>
<tr>
<td>4. Presentation, interpretation and discussion in a journal article format of obtained data</td>
<td>C</td>
</tr>
</tbody>
</table>

*Benchmark scale of the PhD student's contribution to the article

<table>
<thead>
<tr>
<th>Reference</th>
<th>Contribution</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. refers to:</td>
<td>Has contributed to the co-operation</td>
<td>0-33 %</td>
</tr>
<tr>
<td>B. refers to:</td>
<td>Has contributed considerably to the co-operation</td>
<td>34-66 %</td>
</tr>
<tr>
<td>C. refers to:</td>
<td>Has predominantly executed the work independently</td>
<td>67-100 %</td>
</tr>
</tbody>
</table>

Signature of the co-authors:

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Title</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.01.13</td>
<td>Maria Singe</td>
<td>MSc pub health</td>
<td>Maria Singe</td>
</tr>
<tr>
<td>16.01.13</td>
<td>Tom Møller</td>
<td>Postdoc, ph.d.</td>
<td>Tom Møller</td>
</tr>
<tr>
<td>16.01.13</td>
<td>Julie Midtgaard</td>
<td>Assistant Professor, cand. psych</td>
<td>Julie Midtgaard</td>
</tr>
</tbody>
</table>

Signature of the PhD student and the principal supervisor:

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.01.13</td>
<td>Christina Andersen</td>
<td></td>
</tr>
<tr>
<td>16.01.13</td>
<td>Lis Adamsen</td>
<td></td>
</tr>
</tbody>
</table>
DECLARATION OF CO-AUTHORSHIP

This form must be filled in on the screen, printed, signed and sent to the Graduate School.
You can use the TAB-button to jump between the grey boxes.

<table>
<thead>
<tr>
<th>Information on PhD student:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of PhD student</td>
</tr>
<tr>
<td>E-mail</td>
</tr>
<tr>
<td>Date of birth</td>
</tr>
<tr>
<td>Work place</td>
</tr>
<tr>
<td>Principal supervisor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Title of PhD thesis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body &amp; Cancer – The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy</td>
</tr>
</tbody>
</table>

This declaration concerns the following article:

| The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue |

<table>
<thead>
<tr>
<th>The PhD student’s contribution to the article:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(please use the scale (A,B,C) below as benchmark*)</td>
</tr>
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<tr>
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</tbody>
</table>

*Benchmark scale of the PhD student’s contribution to the article

<table>
<thead>
<tr>
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</tr>
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<td>34-66 %</td>
</tr>
<tr>
<td>C. refers to:</td>
<td>Has predominantly executed the work independently</td>
<td>67-100 %</td>
</tr>
</tbody>
</table>

Signature of the co-authors:

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Title: Ph.d.-student, MSc Health Science</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.01.13</td>
<td>Morten Quist</td>
<td></td>
</tr>
<tr>
<td>16.01.13</td>
<td>Kira Bloomquist</td>
<td>MSc Health Sciences</td>
</tr>
<tr>
<td>16.01.13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Signature of the PhD student and the principal supervisor:

| Date: 16.01.13 | PhD student: Christina Andersen | Date: 16.01.13 | Principal supervisor: Lis Adamsen |
DECLARATION OF CO-AUTHORSHIP
This form must be filled in on the screen, printed, signed and sent to the Graduate School
- You can use the TAB-button to jump between the grey boxes.

Information on PhD student:

Name of PhD student: Christina Lageborg Andersen
E-mail: cla@rh.dk
Date of birth: 220569
Work place: University Hospitals Center for Health Research (UCSF)
Principal supervisor: Lis Adamsen

Title of PhD thesis:
Body & Cancer – The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

This declaration concerns the following article:
The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue

The PhD student's contribution to the article:

(please use the scale (A,B,C) below as benchmark*)
1. Formulation/identification of the scientific problem that from theoretical questions need to be clarified. This includes a condensation of the problem to specific scientific questions that is judged to be answerable by experiments
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3. Involvement in the experimental work
4. Presentation, interpretation and discussion in a journal article format of obtained data

(A,B,C)
C
C
C

*Benchmark scale of the PhD student's contribution to the article
A. refers to: Has contributed to the co-operation 0-33 %
B. refers to: Has contributed considerably to the co-operation 34-66 %
C. refers to: Has predominantly executed the work independently 67-100 %

Signature of the co-authors:

Date: 16.01.13
Name: Mikael Nørth
Title: Professor, dr. med.
Signature: Mikael Nørth

Date: 16.01.13
Name: Bent Ejlersen
Title: Professor, dr. med
Signature: Bent Ejlersen

Date: 16.01.13
Name: Lis Adamsen
Title: Professor, MSc.
Signature: Lis Adamsen

Signature of the PhD student and the principal supervisor:

Date: 16.01.13
PhD student: Christina Andersen
Principal supervisor: Lis Adamsen
DECLARATION OF CO-AUTHORSHIP
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<table>
<thead>
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<tbody>
<tr>
<td>Name of PhD student</td>
<td>Christina Ingeborg Andersen</td>
</tr>
<tr>
<td>E-mail</td>
<td><a href="mailto:cia@rh.dk">cia@rh.dk</a></td>
</tr>
<tr>
<td>Date of birth</td>
<td>220559</td>
</tr>
<tr>
<td>Work place</td>
<td>University Hospitals Center for Health Research (UCSF)</td>
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<tr>
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<td>Lis Adamsen</td>
</tr>
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</table>

**Title of PhD thesis:**

Body & Cancer – The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

**This declaration concerns the following article:**

"Pain is sidetracked" - Breast cancer patients' experience of muscle and joint pain during adjuvant chemotherapy and currently participating in an exercise intervention

**The PhD student's contribution to the article: (please use the scale (A,B,C) below as benchmark*)**

<table>
<thead>
<tr>
<th>Number</th>
<th>Contribution</th>
<th>(A,B,C)</th>
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   C. refers to: Has predominantly executed the work independently

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>C</td>
<td>0-33 %</td>
</tr>
<tr>
<td>34-66 %</td>
<td></td>
</tr>
<tr>
<td>67-100 %</td>
<td></td>
</tr>
</tbody>
</table>

**Signature of the co-authors:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Title</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.01.13</td>
<td>Mikael Rorth</td>
<td>Professor, dr. med.</td>
<td></td>
</tr>
<tr>
<td>16.01.13</td>
<td>Bent Ejlersen</td>
<td>Professor, dr. med</td>
<td></td>
</tr>
<tr>
<td>16.01.13</td>
<td>Lis Adamsen</td>
<td>Professor, MSc. Soc.</td>
<td></td>
</tr>
</tbody>
</table>

**Signature of the PhD student and the principal supervisor:**

| Date: 16.01.13 | PhD student: Christina Andersen | Date: 16.01.13 | Principal supervisor: Lis Adamsen |
APPENDIX 1

a. Search strategy
b. Description of the Analytical Process (Paper III)
c. Patient characteristics: demographic and physical activity level at baseline (Paper I)
d. Patient characteristics: diagnosis, treatment and status at baseline (Paper I)
e. Demographic and clinical characteristics and physical activity level (Paper II)
f. Chemotherapy treatment regimens at baseline by group assignment (Paper II)
g. Demographic and clinical characteristics, and physical activity level (Paper III)
a. Search strategy

The databases PubMed were searched through April, 2012 and October, 2012- following search strategy was used:


The databases CINAHL were searched through October, 2012- following search strategy was used:

((TI "Cancer") OR (MH "Neoplasm")) AND ((TX "Symptom") OR (TX "Sideeffect") OR (TX "Adverse effect") OR (TX "Fatigue") OR (TX "Pain") OR (TX "Nausea") OR (MH "Nausea and Vomiting") OR (TX "Vomiting") OR (TX "Paresthesia") OR (TX "Constipation") OR (TX "Myalgia") OR (TX "Arthralgia") OR (TX "Diarrhea") OR (TX "Diarrhoea") OR (TX "Nausea and Vomiting") AND ((TX "Aerobic exercise") OR (TX "Aerobic fitness") OR (TX "Aerobic training") OR (TX "Cardiopulmonary exercise") OR (TX "Cardiopulmonary fitness") OR (TX "Cardiopulmonary training") OR (TX "Cardiorespiratory exercise") OR (TX "Cardiorespiratory fitness") OR (TX "Cardiorespiratory training") OR (TX "Cardiovascular exercise") OR (TX "Cardiovascular fitness") OR (TX "Cardiovascular training") OR (MH "Exercise Test, Cardiopulmonary") AND ((TX "Resistance exercise") OR (TX "Resistance training") OR (TX "Strength training") OR (TX "Weight bearing") OR (TX "Weight lifting") AND (TX "Relaxation") AND (TX "Massage") AND ((TX "Body awareness") OR (TX "Physical awareness")) AND ((MH "Chemotherapy, Adjuvant") OR (MH "Chemotherapy, Cancer") OR (TX "Adjuvant treatment") OR (TX "During treatment") OR (TX "Undergoing treatment"))

Limiters - Exclude MEDLINE records; Human; Language: English

Following supplementary strategy were searched through April, 2012 and October, 2012:

## b. Description of the Analytical Process

<table>
<thead>
<tr>
<th>Sequence and focus Area</th>
<th>Selected Meaning Units</th>
<th>Categories</th>
<th>Essence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre interview - Baseline of Body &amp; Cancer</strong></td>
<td>I’m not so afraid of pain</td>
<td>Cogitated Pain Management</td>
<td>Exercise despite pain</td>
</tr>
<tr>
<td>Impact of illness (cancer diagnosis), treatment (chemotherapy (EC followed by D+ G-CSF)).</td>
<td>Pain is not a negative thing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemotherapy makes me nauseous – no pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I take pain reducing medicine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I keep active</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I get some fresh air</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I go for a walk</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I focus on doing something</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I lie down and rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I drink water</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I relax</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I feel restless and feel pain all over my body</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>My legs feel heavy like lead</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The pain makes me feel really sick</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The painkillers did not help at all</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It was horrific with all that pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I couldn’t do a thing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Everything hurts</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I used lower weight on the machines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I lowered the resistance level on the bike</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I forgot the pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It was great to do something physical I had to persist despite the pain I shifted my focus away from the pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I felt some physical improvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I had surplus energy to resist [the pain]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I informed that I would miss that session</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The pain did not get worse, perhaps it stayed the same</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The physical goal is to build strength despite muscle pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Body and Cancer training did not worsen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I think it helped with the pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Post interview - Completion of Body &amp; Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain perception:</td>
<td></td>
<td></td>
<td>Abrupt pain - predominant side-effect</td>
</tr>
<tr>
<td>Intensity and management with supervised high- and low physical training (warming-up, resistance - and cardiovascular training, relaxation-, massage- and body-awareness training)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Descriptions of the muscle and joint pain:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensity, management, compliance and correlation between expectations and experiences</td>
<td></td>
<td></td>
<td>The adapted training</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I lowered weight on the machines</td>
<td></td>
<td>No immediate exacerbation of pain</td>
</tr>
<tr>
<td></td>
<td>I lowered the resistance level on the bike</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I forgot the pain</td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
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<td>I informed that I would miss that session</td>
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<td></td>
</tr>
<tr>
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<td>Body and Cancer training did not worsen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I think it helped with the pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
c. Patient characteristics: demographic data \((n=54)\)

<table>
<thead>
<tr>
<th><strong>Age (years)</strong></th>
<th><strong>Mean (SD)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>18-34 years</td>
<td>43.9 (10.42)</td>
</tr>
<tr>
<td>35-50 years</td>
<td>14 (26%)</td>
</tr>
<tr>
<td>50-65 years</td>
<td>23 (43%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Gender</strong></th>
<th><strong>Count (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>14 (26%)</td>
</tr>
<tr>
<td>Female</td>
<td>40 (74%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Marital status/cohabiting</strong></th>
<th><strong>Count (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Married/Permanent Relationship (Living together with partner)</td>
<td>33 (61%)</td>
</tr>
<tr>
<td>Single/Divorced/Widowed (Living alone without partner)</td>
<td>21 (39%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Educational Level</strong></th>
<th><strong>Count (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>No education or lower level of education</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>High school (students included)</td>
<td>16 (30%)</td>
</tr>
<tr>
<td>Some college or technical school</td>
<td>20 (37%)</td>
</tr>
<tr>
<td>University degree</td>
<td>16 (30%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Level of physical activity pre-illness</strong></th>
<th><strong>Count (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Sedentary)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>II (Walking or cycling for pleasure)</td>
<td>15 (28%)</td>
</tr>
<tr>
<td>III (Regular physical exercise – at least 3h/week)</td>
<td>21 (39%)</td>
</tr>
<tr>
<td>IV (Intense physical activity – more than 4h/week, ‘Athletic’)</td>
<td>15 (28%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Level of physical activity baseline</strong></th>
<th><strong>Count (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Sedentary)</td>
<td>13 (24%)</td>
</tr>
<tr>
<td>II (Walking or cycling for pleasure)</td>
<td>35 (65%)</td>
</tr>
<tr>
<td>III (Regular physical exercise – at least 3h/week)</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>IV (Intense physical activity – more than 4h/week, ‘Athletic’)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

(Saltin & Gollnick 1983)
### d. Patient characteristics: Diagnosis, treatment and status (n=54)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Treatment **</th>
<th>Status***</th>
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<tbody>
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<td>5 Carbo + T (adjuvant)</td>
<td>5 NED</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 Carbo + T</td>
<td>6 ED</td>
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<tr>
<td></td>
<td></td>
<td>1 Carbo + Topo + T</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1 Carbo + V + Eto</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1 T</td>
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<td>3 5FU + Lv (adjuvant)</td>
<td>3 NED</td>
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</tr>
<tr>
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<td>1 P Eto B</td>
<td>1 ED</td>
</tr>
<tr>
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<td>1 ED</td>
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<tr>
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<tr>
<td>NSCLC*</td>
<td>1</td>
<td>P+ Vi</td>
<td>1 ED</td>
</tr>
<tr>
<td>Unknown primary tumour</td>
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<td>1 G + P + T</td>
<td>1 ED</td>
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<tr>
<td>Oesophagus cancer</td>
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<td>1 Cap+ T + Carbo</td>
<td>2 ED</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 SFU + P</td>
<td></td>
</tr>
<tr>
<td>Ewings Sarcoma</td>
<td>1</td>
<td>1 I + Eto + V + A</td>
<td>1 ED</td>
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<tr>
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<td>1</td>
<td>1 Carbo + Eto + V</td>
<td>1 NED</td>
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<tr>
<td>Myxoid Sarcoma</td>
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<td>1 I+M</td>
<td>1 ED</td>
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<td>Oral Cancer</td>
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<td>1 Cap+T</td>
<td>1 ED</td>
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<td>Hodgkin’s disease</td>
<td>4</td>
<td>4 ABVD</td>
<td>3 ED</td>
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<td>1 CHOEtoP</td>
<td>1 ED</td>
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<td>ALL*</td>
<td>1</td>
<td>1 Purinethol + M</td>
<td>2 ED</td>
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<td>AML*</td>
<td>1</td>
<td>1 M-AMSA + Eto + Ara-C</td>
<td>1 NED</td>
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<td>1 ED</td>
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<td>Myelofibrosis</td>
<td>1</td>
<td>1 Ara-C + Hy</td>
<td>1 ED</td>
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<tr>
<td><strong>Status</strong>*</td>
<td></td>
<td>28 NED, 26 ED</td>
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</table>

* Diagnosis: SCLC = small-cell lung cancer; NSCLC = non small-cell lung cancer; NHL = Non-Hodgkin’s lymphoma; ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia.

**Treatment:**
- A= doxorubicin, ABVD = doxorubicin, bleomycin, vinblastic, dacarbazine; Arac-C=Cytosinarabinosid, C=Cykelosfamid, Cap=capecatebine, Carbo = carboplatin; CEF = cyclophosphamide, epirubicin, 5-fluorouracil; CHOetoP = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; CMF = cyclophosphamide, methotrexate, 5-fluorouracil; E = epirubicin; Eto = etopside; 5-FU = 5-fluorouracil; G = gemcitabine; HY = Hydrea; I = ifosfamide; Lv = leucovorin; M = methotrexate, P = cisplatin; PEtoB= cisplatin, etoposid, bleomycin; T = taxanes; Topo = topotecan; V= vincristine VAD = vincristine, doxorubicin, dexamethasone; Vin = Vinorelbine.

***Status: ED = Evidence of disease; NED = No evidence of disease
### e. Demographic and Clinical Characteristics, and Physical Activity Level

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Control Group (n=107)</th>
<th>Intervention Group (n=106)</th>
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<tbody>
<tr>
<td><strong>Age, years</strong></td>
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<tr>
<td>Mean (SD)</td>
<td>47.8 (10.4)</td>
<td>47.1 (10.8)</td>
</tr>
<tr>
<td>Range</td>
<td>20-65</td>
<td>21-65</td>
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<tr>
<td>Married, cohabiting, or in a relationship</td>
<td>76 (71.0)</td>
<td>75 (70.8)</td>
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<tr>
<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
<td>30 (28.0)</td>
<td>22 (20.8)</td>
</tr>
<tr>
<td>Female</td>
<td>77 (72.0)</td>
<td>84 (79.2)</td>
</tr>
<tr>
<td><strong>Completed secondary school or higher</strong></td>
<td>87 (81.3)</td>
<td>83 (78.3)</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td>15 (14.0)</td>
<td>16 (15.1)</td>
</tr>
</tbody>
</table>

| Medical characteristics           |                       |                             |
| Median days since diagnosis       | 86.5                  | 82                          |
| No evidence of disease (NED) baseline   | 62 (57.9)            | 56 (52.8)                   |
| Evidence of disease (ED) baseline   | 45 (42.1)             | 50 (47.2)                   |
| Relapsed disease                  | 20 (18.7)             | 10 (9.4)                    |
| Mean (SD) β-haemoglobin, mmol/l    | 7.91 (0.82)           | 7.92 (0.78)                 |
| Pt. received blood transfusions (number of transfusions) | 7 (range 1-2) | 8 (range 2-14) |
| Cancer of breast (NED/ED)         | 51 (43/8)             | 52 (44/8)                   |
| Cancer of bowel (NED/ED)          | 15 (9/6)              | 14 (10/4)                   |
| Oncological malignancies (NED/ED)  |                       |                             |
| Cancer of ovaries                 | 9 (4/5)               | 11 (2/7)                    |
| Cancer of testes                  | 7 (0/7)               | 7 (0/7)                     |
| Cancer of oesophagus              | 1 (0/1)               | 1 (0/1)                     |
| Cancer of brain                   | 2 (0/2)               | 1 (0/1)                     |
| Cancer of cervix                  | 2 (0/2)               | 2 (0/2)                     |
| Cancer of pharynx                 | 1 (0/1)               | 2 (0/2)                     |
| Cancer of pancreas                | 2 (0/2)               | 1 (0/1)                     |
| Cancer of stomach                 | 1 (0/1)               | 1 (0/1)                     |
| Other diagnoses                   | 6 (2/4)               | 3 (0/5)                     |
| Haematological malignancies (NED/ED) | 10 (4/6)             | 11 (0/11)                   |
| Hodgkin                           | 2                     | 6                            |
| Non Hodgkin lymphoma              | 4                     | 5                            |
| Acute leukaemia                   | 3                     | 0                            |
| Chronic leukaemia                 | 1                     | 0                            |

| Physical Activity Level           |                       |                             |
| **Pre-illness**                   |                       |                             |
| Sedentary                         | 3 (2.9)               | 6 (5.7)                     |
| Walking or cycling for pleasure   | 28 (25.0)             | 33 (31.1)                   |
| Regular physical exercise, at least 3 h/week | 64 (61.5)          | 60 (56.6)                   |
| Intense physical activity, more than 4 h/week | 11 (10.6)          | 7 (6.6)                     |
| **Baseline**                      |                       |                             |
| Sedentary                         | 17 (16.3)             | 18 (17.3)                   |
| Walking or cycling for pleasure   | 41 (39.4)             | 59 (56.7)                   |
| Regular physical exercise, at least 3 h/week | 40 (38.5)          | 24 (23.1)                   |
| Intense physical activity, more than 4 h/week | 6 (5.8)              | 3 (2.9)                     |
### f. Chemotherapy Treatment Regimens at Baseline by Group Assignment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control Group (n=107)</th>
<th>Intervention Group (n=106)</th>
<th>Abbreviations</th>
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<tbody>
<tr>
<td><strong>Cancer of breast</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>CEF</td>
<td>42</td>
<td>45</td>
<td>A, doxorubicin; C, xeloda; Ca, caelyx;</td>
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<tr>
<td>CE</td>
<td>2</td>
<td>3 (1=chemo)</td>
<td>FOLFOX, 5-flourouracil, oxaliplatin; Carbo, carboplatin;</td>
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<tr>
<td>T</td>
<td>3</td>
<td>2</td>
<td>CE, cyclophosphamide, epirubicin; CEF, cisplatin, etoposide, epirubicin; 5-fluorouracil; E, epirubicin; Eto, etoposide; Erb, eribitux; 5-FU, 5-flourouracil; G, gemcitabine; I, irinotecan;</td>
</tr>
<tr>
<td>T + Herceptin</td>
<td>2</td>
<td>0</td>
<td>Lv, leucovorin; P, cisplatin; PEToB, cisplatin, etoposide, bleomycin; T, taxanes; TEGALOX, oxaliplatin, leucovorin, tegafur, uracil; Temo, temodal; Topo, topotecan;</td>
</tr>
<tr>
<td>T+C</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>T+G</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Vin + Herceptin</td>
<td>0</td>
<td>2</td>
<td></td>
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<tr>
<td><strong>Cancer of bowel</strong></td>
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<tr>
<td>FOLFOX</td>
<td>5</td>
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<td><strong>Cancer of ovaries</strong></td>
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<td>7</td>
<td>9</td>
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<tr>
<td>Ca</td>
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<td>1</td>
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<tr>
<td>Carbo+T+G</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Cancer of testes</strong></td>
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<tr>
<td>PEToB</td>
<td>6</td>
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<td>P+G+T+Eto (7 days)</td>
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<td>A</td>
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<tr>
<td>E+XeOX</td>
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<td>C</td>
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<td>G</td>
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<td>Neoadj, Temo+</td>
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<tr>
<td>ADE 3+8+5</td>
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Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; ADE (3+8+5), cytorabine, daunomycin, etoposide; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CHOEP (14-21), cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; CODOX-MI/VAC, cyclophosphamide, doxorubicin, high-dose methotrexate/ifosfamide, etoposide, high-dose cytarabine; COPP, cyclophosphamide, vincristine, procarbazine, prednisone; CVP-FC, cyclophosphamide, vincristine, prednisone–fludarabine, cyclophosphamide; DA3+8, daunorubicin, cytorabine; DHAP, dexamethasone, cytorabine, cisplatin; Hyper CVAD/Ara-C, cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytorabine; R-CHOP, retuximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-CVP retuximab, cyclophosphamide, vincristine, prednisone.
### g. Demographic and Clinical Characteristics, and Physical Activity Level

| Patients (n=15) |  
|-----------------|---  
| **Age** | Median  
| | 44 (range 29-57)  
| **Marital status** | Frequency  
| Married | 8  
| Cohabitating | 4  
| Single /Divorced | 3  
| **Education level** |  
| None (no education following grade school) | 1  
| Short (under 3 years, high school certificate) | 3  
| Middle-range training (3-5 years- 4 year college degree) | 9  
| Long (over 6 years university graduate/post-graduate degree) | 2  
| **Employment status during chemotherapy** |  
| Full-time employment | 0  
| Partial sick leave | 4  
| Sick leave | 11  
| Early retirement pension (not due to cancer diagnosis) | 0  
| **Surgery** |  
| Mastectomy | 9  
| Lumpectomy | 6  
| **Docetaxel before baseline exercise intervention** | 5  
| **Cycles of docetaxel during exercise intervention** |  
| One cycle | 7  
| Two cycle | 8  
| **Docetaxel Dose** |  
| Docetaxel 100 mg/m² (100%) | 10  
| Docetaxel 75 mg/m² (75%) | 5  
| **Physical Activity Level** |  
| Pre-illness |  
| Sedentary | 2  
| Walking or cycling for pleasure | 3  
| Regular physical exercise, at least 3 h/week | 10  
| Intense physical activity, more than 4 h/week | 0  
| Baseline |  
| Sedentary | 2  
| Walking or cycling for pleasure | 7  
| Regular physical exercise, at least 3 h/week | 6  
| Intense physical activity, more than 4 h/week | 0  
| **Own assessment of pain threshold** (Scale of 1 – 10)  
| (1= minimum level & 10= maximum threshold) | Median  
| | 7 (range 4-9)  


APPENDIX 2

a. Patients screening criteria
b. Patient information
c. Body & Cancer pre-post questionnaires
d. Semi-structured diaries
e. FACT-An questionnaires
f. Selected themes and questions from the semi-structured interview-guide
g. Approval from the scientific Committees of the Copenhagen and Frederiksberg Municipalities and by the Danish Data Protection Agency
**Krop og Kræft**

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<tr>
<th><strong>Patientdata</strong></th>
<th><strong>Køn:</strong></th>
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<td>Adresse</td>
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<tr>
<td>Tlf. nr.</td>
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<tr>
<td>Mobil nr.</td>
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<tr>
<td><strong>Diagnose:</strong></td>
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<tr>
<td><strong>Sygdomsstatus:</strong></td>
<td>(NED = No Evidence of Disease, ED Evidence of disease)</td>
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### Inklusionskriterier

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<tr>
<th>Kriterium</th>
<th>JA</th>
<th>Nej</th>
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<tbody>
<tr>
<td>1. Er patientens performancestadi 0 eller 1 *</td>
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<tr>
<td>2. Har patienten været diagnosticeret i mindst 4 uger</td>
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<tr>
<td>3. Er patienten i cytostatisk el. anden medicinsk kæftbehandling *</td>
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<tr>
<td>4. Har patienten modtaget første serie kemoterapi *</td>
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<tr>
<td>5. Er patienten mindst 18 år</td>
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<td>6. Er patientens diastolisk blodtryk i hvile &gt; 45 og &lt; 100</td>
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<tr>
<td>7. Er patientens puls regelmæssig med hvilepuls &lt; 110</td>
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</tr>
<tr>
<td>8. Forstår og læser patienten dansk</td>
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</tr>
<tr>
<td>9. Har patienten modtaget skriftlig patientinformation + underskrevet samtykke</td>
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</table>

### Eksklusionskriterier

<table>
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<th>Kriterium</th>
<th>Ja</th>
<th>Nej</th>
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<tbody>
<tr>
<td>1. Er der i journalen anført kontraindikationer for kropsig aktivitet *</td>
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<tr>
<td>2. Har patienten dokumenteret primær hjernetumor, metastaser/involvering i CNS *</td>
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</tr>
<tr>
<td>3. Har patienten dokumenteret knoglemetastaser eller myelomatose *</td>
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<tr>
<td>4. Har patienten trombocytter &lt; 40 mia/l *</td>
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<td>5. Har patienten leukocytter &lt;1 *</td>
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<td>6. Har patienten klinisk symptomgivende hjertesygdom *</td>
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<td>7. Har patienten haft diagnosticeret myokardieinfakt indenfor de sidste 3 mdr. *</td>
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<td>8. Er patienten senilment</td>
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</tr>
<tr>
<td>9. Er patienten psykotisk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Er patienten i terminal behandling *</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Jeg har vurderet og checket inklusions- og eksklusionskriterierne.

Patienten kan inkluderes i Krop og Kræft.

**Dato og Signatur:**

________________________________________________________________________

**Kommentarer:**

________________________________________________________________________

________________________________________________________________________

04-07-2013/Tom Møller og Christina Andersen Krop og Kræft Rigshospitalet
Inklusionskriterier

Ad 1) * Performancestatus 0 - 1: WHO rekommandation

<table>
<thead>
<tr>
<th>Performance Status</th>
<th>0</th>
<th>Normal, ingen tegn på sygdom</th>
<th>Symptomer, men fuldt mobiliseret</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>&gt; 50 % sengelligende</td>
<td>Delvist oppegående &lt; 50 % sengelligende</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Sengebunden, kræver hjælp</td>
<td></td>
</tr>
</tbody>
</table>

Ad 3) * Antineoplastisk behandling (IV. - P.O. - S.C - I.M) bortset fra hormon og antihormonbehandling alene (eks. Tamoxifen).

Ad 4) * Patienten skal have modtaget mindst 1 serie kemoterapi eller være i anden antineoplastisk behandling.

Eksklusionskriterier

Ad1) * Kontraindikation for kropslig aktivitet skal fremgå af journalnotat. OBS: Patienter, som er opereret abdominalt, gynækologisk, thoraxkirurgisk, ortopædkirurgisk indenfor de seneste 6 - 8 uger før træningsstart, skal drøftes med ansvarlig læge og eventuel kirurgisk vurdering.

Ad 2) * Patienter med dokumenteret primær hjernetumor, metastaser/involvering i central nervesystem CNS kan ikke medvirke.


Ad 4) * Vedvarende trombocytopeni < 40 mia/l som følge af sygdom eller aplastisk marvfunktion.

Ad 5) * Vedvarende leukopeni < 1 mia/l som følge af sygdom eller aplastisk marvfunktion.

Ad 6) * Patienter med klinisk symptomgivende hjertesygdom/hjerteinsufficiens og patologisk EKG, kan ikke medvirke.

Ad 7) * Patienter med diagnosticeret myokardieinfakt indenfor de sidste 3 måneder kan ikke medvirke.

Ad 10) * Terminal behandling defineres som forventet overlevelse i mindre end 3 måneder.
Patientinformation
Til videnskabeligt projekt "Krop og Kræft"


Hvad er projektets formål?
I projekt Krop og Kræft ønsker vi at undersøge, om du kan forøge din muskelstyrke, kondition og generelle velbefindende ved at deltage i et 6 ugers træningsprogram (intervention). Desuden vil vi gerne undersøge, om eventuelle bivirkninger og symptomer fra kræftsygdom og behandling kan reduceres.

For at vi kan vurdere effekten af træningsprogrammet, skal der foretages en sammenligning af to grupper kræftpatienter, der er i kemoterapi. En sådan sammenligning lader sig kun gøre i et randomiseret design (tilfældighedsprincipe), hvor den ene gruppe patienter deltager i træningsprogrammet (interventionsgruppe), og den anden gruppe patienter ikke deltager i træningsprogrammet (kontrolgruppe). Patienterne i de to grupper skal ligne hinanden så meget som muligt (diagnose, alder). En computer afgør ved lodtæknik, hvilken af de to grupper du tilbydes.

Denne fremgangsmåde er nødvendig for at få et videnskabeligt grundlag for at vurdere en eventuel forskel mellem patienterne i de to grupper. Projektet afsluttes når der er indgået i alt 125 personer i hver gruppe. Forventet afslutning primo 2007. Hensigten er at afprøve og udvikle et supplement til den behandling, du modtager og dermed medvirke til at forbedre tilbudene for nuværende og kommende kræftpatienter.

Hvad indebærer din deltagelse?
Du vil kunne deltage i projektet, hvad enten du er indlagt eller modtager kemoterapi ambulant. Hvad enten du indgår i kontrol- eller interventions gruppen, vil vi bede dig om at medvirke i følgende forskningsprogram, der indeholder undersøgelser af såvel din fysiske kapacitet som din livskvalitet.

• Din fysisk kapacitet (styrke, kondition, vægt, fedtprocent) vil blive testet tre gange (over en 4½ måneders periode.)
• Du vil få udleveret fem mindre spørgeskemaer (over en 4½ måneders periode), der omhandler din almene sundhedstillstand.
• Du vil blive bedt om - i en dagbog - at registrere evt. bivirkninger (kvalme, træthed etc.) over en 6 ugers periode.
• Du kan blive bedt om at medvirke i interview. Disse interview har en varighed på ca. 30 min og kan foregå pr. telefon.
• Du vil få målt din blodprocent ved en blodprøve tre gange (over en 4½ måneders periode.)
**Interventionsgruppe**

<table>
<thead>
<tr>
<th>Mandag</th>
<th>Tirsdag</th>
<th>Onsdag</th>
<th>Torsdag</th>
<th>Fredag</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.45 – 12.00</td>
<td>8.45-10.30</td>
<td>8.45-11.30</td>
<td></td>
<td>8.45-12.00</td>
</tr>
<tr>
<td>Styrke- og konditionstræning</td>
<td>Kropsbevidsthedstræning</td>
<td>Styrke- og konditionstræning</td>
<td>Styrke- og konditionstræning</td>
<td></td>
</tr>
<tr>
<td>Afspænding</td>
<td>Afspænding</td>
<td>Afspænding</td>
<td>Afspænding</td>
<td></td>
</tr>
<tr>
<td>Massage</td>
<td></td>
<td></td>
<td>Massage</td>
<td></td>
</tr>
</tbody>
</table>

**Kontrolgruppe**
Hvis du kommer i kontrolgruppen vil du indgå i nævnte forskningsprogram. Efter en 6-ugers periode (hvor du ikke indgår i træningsprogrammet) får du mulighed for at deltage på det efterfølgende træningshold med træning 4 gange om ugen i 6 uger (se ovennævnte skema). Efter afslutningen af træningsprogrammet (6 uger) har du mulighed for at deltage på et træningshold én gang ugentligt á 1,5 times varighed (opvarmning, styrke- og konditionstræning, udstrækning).

**Hvem har ansvaret for udførelsen af aktiviteterne?**

**Er der risici forbundet med din deltagelse?**
I dag findes der begrænset viden om de muligheder og forbehold, der bør tages når kræftpatienter i kemoterapi træner. Der kan forekomme uforudsigelige risici ved deltagelse i programmet. Programmet har siden 2001 været afprøvet på 101 kræftpatienter i kemoterapi, der er indtil videre ikke registreret alvorlige bivirkninger, ubehag eller andre risici i forbindelse med gennemforsel af de forskellige aktiviteter i programmet. Men som ved enhver form for fysisk aktivitet, kan det ikke udelukkes at sportsskader (fibersprængninger, etc.) kan forekomme. Ligeledes må du forvente at kunne opleve ømhed i musklerne. Din deltagelse i programmet vil ikke afholde dig fra sædvanlige gøremål. Du er velkommen til at fortsætte dine fritidsinteresser, havearbejde etc. som hidtil.
Frivillighed og sikkerhed
Din deltagelse i projektet er frivillig. Du kan til enhver tid ophøre med at deltage i projektet og trække dit samtykke tilbage, uden at det får betydning for din pleje og behandling eller tilknytning til afdelingen.
Der er ikke tale om, at du gennem din deltagelse i projektet er udelukket fra i øvrigt at modtage den på tidspunktet bedste behandling.

Fortrolighed

Med venlig hilsen

......................................................................
Klinikchef, professor, dr.med. Mikael Rørth

......................................................................
Klinikchef, professor, dr.med. Niels Borregaard

......................................................................
Overlæge, dr.med. Jørn Herrstedt

......................................................................
Forskningsleder, ph.d., sociolog, sygeplejerske Lis Adamsen

Kontaktpersoner
Har du spørgsmål vedrørende projektet, er du naturligvis velkommen til at kontakte:

Forskningsleder                  Projektfysioterapeut                  Sygeplejersker
Lis Adamsen                     Morten Quist                         Birgit Nielsen/Christina Andersen
UCSF                            Krop & Kræft                        Krop & Kræft
3545 7336                       3545 8531                           3545 7309
Samtykkeerklæring

"Jeg bekræfter hermed, at jeg efter at have modtaget ovenstående information, såvel mundtlig som skriftlig, indvilger i at deltage i projekt Krop & kræft. Jeg er informeret om, at det er frivilligt at deltage, og at jeg når som helst og uden begrundelse kan trække mit tilsagn om deltagelse tilbage, uden at dette vil påvirke den nuværende eller fremtidige behandling at mig".

........................................................
Patientens navn og CPR

........................................................
Patientens underskrift Dato

........................................................
Projektansvarliges navn

........................................................
Projektansvarliges underskrift Dato
PATIENT KOPI

Samtykkeerklæring

Jeg bekræfter hermed at jeg efter at have modtaget ovenstående information, såvel mundtlig som skriftlig, indviler i at deltage i projekt Krop & kræft. Jeg er informeret om, at det er frivilligt at deltage, og at jeg når som helst og uden begrundelse kan trække mit tilsagn om deltagelse tilbage, uden at dette vil påvirke den nuværende eller fremtidige behandling at mig”.

.................................................................
Patientens navn og CPR

.................................................................  ...................
Patientens underskrift  Dato

.................................................................
Projektansvarliges navn

.................................................................  ...................
Projektansvarliges underskrift  Dato
PROJEKT KROP
OG KRÆFT

SPØRGESKEMA
(Baseline)

Patient ID: ____________________________________

Indtastet: □

OPLYSNINGER OM DIG SELV

Skriv venligst dit navn og din alder her

Navn ___________________________________________   Alder _________

Mand  ☐
Kvinde  ☐

hvad er din ægteskabelige status?

Samboende  ☐
Lever i parforhold  ☐
Gift  ☐
Single  ☐
Enkemand/enke  ☐
Separeret/fraskilt  ☐

Har du børn?

☐ Ja  ☐ Nej

Hvis ja, angiv venligst

Antal __________   Alder ______________

Ryger du?

Ja, dagligt  ☐
Ja, men der er dage hvor jeg ikke ryger  ☐
Nej, jeg er holdt op inden for det sidste halve år  ☐
Nej, jeg er holdt op for længe siden  ☐
Nej, jeg har aldrig roget  ☐

Hvilken erhvervsuddannelse har du? (Sæt kun et kryds)

Under uddannelse  ☐
Ingen uddannelse  ☐
Kort uddannelse (under 3 år)  ☐
Mellemlang uddannelse (3-4 år)  ☐
Langvarig uddannelse (5 år og derover)  ☐

Hvad er din nuværende beskæftigelses situation? (Du må gerne sætte mere end et kryds)

Studerende  ☐
Arbejdsløs  ☐
Pensioneret  ☐
I arbejde på deltid  ☐
I arbejde på fuld tid  ☐

Hvis du har et arbejde, skriv da venligst din stillingsbetegnelse

Hvis du har et arbejde, er du da sygemeldt?

☐ Ja  ☐ Nej

Hvis ja, angiv venligst om sygemeldingen er ☐ hel (fuldtid) ☐ delvis (deltid)

Hvordan vil du kategorisere dit arbejde mht. fysisk belastning? (sæt kun et kryds)

Ikke fysisk belastende – overvejende stillesiddende (fx skole, kontor, chauffør etc.) ☐

Moderat fysisk belastende – involverer nogen fysisk aktivitet (fx går, løFTER, berer let, etc.) ☐

Meget fysisk belastende – overvejende tungt arbejde (arbejde fx jord og beton, gartner etc.) ☐

BEHANDLING OG TERAPI (Tag venligst stilling til samtlige tre punkter!)

Modtager du aktuelt behandling med kemoterapi? ☐ Ja ☐ Nej ☐ Ved ikke

Modtager du aktuelt behandling med stråleterapi? ☐ Ja ☐ Nej ☐ Ved ikke

Går du aktuelt i individuel terapi (psykolog/psykiater)? ☐ Ja ☐ Nej

Går du aktuelt i alternativ behandle (akupunktør, zoneterapeut, homøopath, healer, etc.) ☐ Ja ☐ Nej

FYSISK AKTIVITET

Inden du fik din kræftdiagnose.

Cyklen de du da dagligt (fx til og fra arbejde)? ☐ Ja ☐ Nej

Hvis ja, angiv antal minutter (dagligt) ……………

Dyrkedes du da let anstrengende sport? ☐ Ja ☐ Nej

(fx svømming, gymnastik, golf, sejlads, yoga, etc.)

Hvis ja, angiv hvor mange timer om ugen ……………

Dyrkedes du da meget anstrengende sport? ☐ Ja ☐ Nej

(fx løb, fodbold, håndbold, aerobic, etc.)

Hvis ja, angiv hvor mange timer om ugen ……………
Nedenfor er angivet nogle kategorier til beskrivelse af fysisk aktivitetsniveau.

Hvilket fysisk aktivitetsniveau passede bedst på dig inden du fik din kræftdiagnose?

I  Stillesiddende
   (Læser, ser fjernsyn eller anden stillesiddende beskæftigelse) □

II Gå- og/eller cykelture under 3 timer om ugen □

III Regelmæssig fysisk aktiv mindst 3 timer om ugen □

IV Hård fysisk træning mere end 4 timer om ugen □

Hvilket fysisk aktivitetsniveau passer bedst på dig i dag?

I  Stillesiddende
   (Læser, ser fjernsyn eller anden stillesiddende beskæftigelse) □

II Gå- og/eller cykelture under 3 timer om ugen □

III Regelmæssig fysisk aktiv mindst 3 timer om ugen □

IV Hård fysisk træning mere end 4 timer om ugen □

FYSISK KAPACITET OG KROPSLIGT VELBEFINDENDE

Hvor tryg føler du dig ved at skulle afprøve din kondition?

1 □ Slet ikke (tryg)  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget (tryg)

Hvor tryg føler du dig ved at skulle afprøve din fysiske styrke?

1 □ Slet ikke (tryg)  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget (tryg)

Hvordan var din fysiske styrke inden du fik din kræftdiagnose?

1 □ Meget dårlig  2 □ Dårlig  3 □ Moderat  4 □ God  5 □ Meget god

Hvordan er din fysiske styrke i dag?

1 □ Meget dårlig  2 □ Dårlig  3 □ Moderat  4 □ God  5 □ Meget god
Hvordan var din **kondition** inden du fik din kræftdiagnose?

| 1 | ☐ Meget dårlig | 2 | ☐ Dårlig | 3 | ☐ Moderat | 4 | ☐ God | 5 | ☐ Meget god |

Hvordan er din **kondition i dag**?

| 1 | ☐ Meget dårlig | 2 | ☐ Dårlig | 3 | ☐ Moderat | 4 | ☐ God | 5 | ☐ Meget god |

Hvordan var dit **fysiske velbefindende** inden du fik din kræftdiagnose?

| 1 | ☐ Meget dårligt | 2 | ☐ Dårligt | 3 | ☐ Moderat | 4 | ☐ Godt | 5 | ☐ Meget godt |

Hvordan er dit **fysiske velbefindende i dag**?

| 1 | ☐ Meget dårligt | 2 | ☐ Dårligt | 3 | ☐ Moderat | 4 | ☐ Godt | 5 | ☐ Meget godt |

Hvordan var dit **energiniveau** inden du fik din kræftdiagnose?

| 1 | ☐ Meget lavt | 2 | ☐ Lavt | 3 | ☐ Moderat | 4 | ☐ Højt | 5 | ☐ Meget højt |

Hvordan er dit **energiniveau i dag**?

| 1 | ☐ Meget lavt | 2 | ☐ Lavt | 3 | ☐ Moderat | 4 | ☐ Højt | 5 | ☐ Meget højt |

Hvordan var **din accept af din krop** inden du fik din kræftdiagnose?

| 1 | ☐ Meget lav | 2 | ☐ Lav | 3 | ☐ Moderat | 4 | ☐ Høj | 5 | ☐ Meget høj |

Hvordan er **din accept af din krop i dag**?

| 1 | ☐ Meget lav | 2 | ☐ Lav | 3 | ☐ Moderat | 4 | ☐ Høj | 5 | ☐ Meget høj |

I hvilken grad oplever du, at **dit udseende** (brug af protese/paryk, operationsar o.l.) hindrer dig i at deltage i idræts- og motionstilbud (fx svømmehal, idrætsklubber, fitnesscenter).

| 1 | ☐ Slet ikke  | 2 | ☐ En lille smule  | 3 | ☐ I nogen grad | 4 | ☐ En hel del | 5 | ☐ Meget |

I hvilken grad oplever du, at **din fysiske formåen** (kondition, styrke) hindrer dig i at deltage i idræts- og motionstilbud (fx svømmehal, idrætsklubber, fitnesscenter).

| 1 | ☐ Slet ikke | 2 | ☐ En lille smule | 3 | ☐ I nogen grad | 4 | ☐ En hel del | 5 | ☐ Meget |
SOCALE RELATIONER / NETVÆRK

Hvor meget har du brug for at tale med andre, der er i samme situation som dig?
I større udstrækning end det sker nu  □
Det er tilstrækkeligt som det sker nu  □

Har du inden for den sidste måned deltaget i støttegruppe (samtalegruppe, selvhjælpsgruppe) for kæftpatienter?
Ja  □
Nej  □
Ved ikke  □

HANDLEKOMPETENCE

Tag venligst stilling til rigtigheden af følgende udsagn.

“Jeg har tillid til, at jeg vil være i stand til at motionere regelmæssigt, sålænge jeg er i kemoterapi”
1  □ Slet ikke  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget

“Jeg har tillid til, at jeg generelt vil være er i stand til at motionere regelmæssigt”
1  □ Slet ikke  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget

“Jeg mener, at motion er nyttigt for kæftpatienter i kemoterapi”
1  □ Slet ikke  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget

“Jeg dyrker motion selv på dage, hvor jeg er dårligt tilpas”
1  □ Slet ikke  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget

”Træthed forhinder mig at motionere regelmæssigt”
1  □ Slet ikke  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget

Får du i øjeblikket motioneret så ofte som du gerne vil/ønsker?  □ Ja  □ Nej

Hvis nej (såfremt du ikke motionerer så ofte, som du gerne ville), skyldes det da:
(Du må gerne sætte flere krydser)

Utilpashed
□
Manglende fysisk overskud
□
Mangler motionstilbud som passer til mig
□
Økonomisk hensyn
□
Mangler en træningspartner/træningspartnere
□
Usikkerhed på, hvad jeg kan
□
Usikkerhed på, hvad jeg må
□
Travlhed i hverdagen
□

TAK FOR DIN MEDVIRKEN!

c.

PROJEKT KROP OG KRÆFT

SPØRGESKEMA

6 UGER: □
18 UGER: □

ID nummr: ___________
Dato: ___________
Indtastet: □
BESKÆFTIGELSE

_Hvad er din aktuelle beskæftigelsessituation? (Du må gerne sætte mere end et kryds)_

Studerende □
Arbejdsløs □
Pensioneret □
I arbejde på deltid □
I arbejde på fuld tid □
Sygemeldt □

Hvis du er _sygemeldt_, angiv da venligst om sygemeldingen er
□ hel (fuldtid) □ delvis (deltid)

BEHANDLING OG TERAPI (Tag venligst stilling til samtlige tre punkter!)

Modtager du aktuelt behandling med kemoterapi? □ Ja □ Nej □ Ved ikke
Modtager du aktuelt behandling med stråleterapi? □ Ja □ Nej □ Ved ikke
Går du aktuelt i individuel terapi (psykolog/psykiater)? □ Ja □ Nej
Går du aktuelt til alternativ behandler (akupunktør, zoneterapeut, homöopat, healer, etc.) □ Ja □ Nej

FYSISK AKTIVITETSNIVEAU

_Hvilket fysisk aktivitetsniveau passer bedst på dig i dag?_

_I Stillesiddende_  (Læser, ser fjernsyn eller anden stillesiddende beskæftigelse) □

_II Gå- og/eller cykelture under 3 timer om ugen_ □

_III Regelmæssig fysisk aktiv mindst 3 timer om ugen_ □

_IV Hård fysisk træning mere end 4 timer om ugen_ □

FYSISK KAPACITET OG KROPSLIGT VELBEFINDEnde

_Hvor tryg føler du dig ved at skulle afprøve din kondition?_

1 □ Slet ikke (tryg)  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget (tryg)

_Hvor tryg føler du dig ved at skulle afprøve din fysiske styrke?_

1 □ Slet ikke (tryg)  2 □ En lille smule  3 □ I nogen grad  4 □ En hel del  5 □ Meget (tryg)
Hvordan vurderer du din **fysiske styrke** i dag?

<table>
<thead>
<tr>
<th>Skala</th>
<th>Beskrivelse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meget dårlig</td>
</tr>
<tr>
<td>2</td>
<td>Dårlig</td>
</tr>
<tr>
<td>3</td>
<td>Moderat</td>
</tr>
<tr>
<td>4</td>
<td>God</td>
</tr>
<tr>
<td>5</td>
<td>Meget god</td>
</tr>
</tbody>
</table>

Hvordan vurderer du din **kondition** i dag?

<table>
<thead>
<tr>
<th>Skala</th>
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<tbody>
<tr>
<td>1</td>
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</tr>
<tr>
<td>4</td>
<td>God</td>
</tr>
<tr>
<td>5</td>
<td>Meget god</td>
</tr>
</tbody>
</table>

Hvordan vurderer du dit **fysiske velbefindende** i dag?

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>1</td>
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</tr>
<tr>
<td>4</td>
<td>Godt</td>
</tr>
<tr>
<td>5</td>
<td>Meget godt</td>
</tr>
</tbody>
</table>

Hvordan vurderer du dit **energiniveau** i dag?

<table>
<thead>
<tr>
<th>Skala</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>2</td>
<td>Lavt</td>
</tr>
<tr>
<td>3</td>
<td>Moderat</td>
</tr>
<tr>
<td>4</td>
<td>Højt</td>
</tr>
<tr>
<td>5</td>
<td>Meget højt</td>
</tr>
</tbody>
</table>

Hvordan vurderer du din **accept af din krop** i dag?

<table>
<thead>
<tr>
<th>Skala</th>
<th>Beskrivelse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meget lav</td>
</tr>
<tr>
<td>2</td>
<td>Lav</td>
</tr>
<tr>
<td>3</td>
<td>Moderat</td>
</tr>
<tr>
<td>4</td>
<td>Høj</td>
</tr>
<tr>
<td>5</td>
<td>Meget høj</td>
</tr>
</tbody>
</table>

I hvilken grad oplever du, at **dit udseende** (brug af protese/paryk, operationsar o.l.) hindrer dig i at (offentlige) deltage i idræts- og motionstilbud (fx svømmehal, idrætsklubber, fitnesscenter).

<table>
<thead>
<tr>
<th>Skala</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Slet ikke</td>
</tr>
<tr>
<td>2</td>
<td>En lille smule</td>
</tr>
<tr>
<td>3</td>
<td>I nogen grad</td>
</tr>
<tr>
<td>4</td>
<td>En hel del</td>
</tr>
<tr>
<td>5</td>
<td>Meget</td>
</tr>
</tbody>
</table>

I hvilken grad oplever du, at **din fysiske formåen** (kondition, styrke) hindrer dig i at deltage i (offentlige) idræts- og motionstilbud (fx svømmehal, idrætsklubber, fitnesscenter).

<table>
<thead>
<tr>
<th>Skala</th>
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</thead>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>4</td>
<td>En hel del</td>
</tr>
<tr>
<td>5</td>
<td>Meget</td>
</tr>
</tbody>
</table>

**SOCIALE RELATIONER / NETVÆRK**

Hvor meget har du brug for at **tale med andre, der er i samme situation som dig**?

I større udstrækning end det sker nu

Det er tilstrækkeligt som det sker nu

Har du inden for den sidste måned **deltaget i en støttegruppe** (samtalegruppe, selvhjælpsgruppe) for kræftpatienter?

Ja

Nej

Ved ikke

---

HANDLEKOMPETENCE

Tag venligst stilling til rigtigheden af følgende udsagn.

“Jeg har tillid til, at jeg vil være i stand til at motionere regelmæssigt, sålænge jeg er i kemoterapi”

1 □ Slet ikke 2 □ En lille smule 3 □ I nogen grad 4 □ En hel del 5 □ Meget

“Jeg har tillid til, at jeg generelt vil være i stand til at motionere regelmæssigt”

1 □ Slet ikke 2 □ En lille smule 3 □ I nogen grad 4 □ En hel del 5 □ Meget

“Jeg mener, at motion er nyttigt for krebspatienter i kemoterapi”

1 □ Slet ikke 2 □ En lille smule 3 □ I nogen grad 4 □ En hel del 5 □ Meget

"Jeg dyrker motion selv på dage, hvor jeg føler mig dårligt tilpas”

1 □ Slet ikke 2 □ En lille smule 3 □ I nogen grad 4 □ En hel del 5 □ Meget

"Træthed forhinder mig i at motionere regelmæssigt”

1 □ Slet ikke 2 □ En lille smule 3 □ I nogen grad 4 □ En hel del 5 □ Meget

Får du i øjeblikket motioneret så ofte som du gerne vil/ønsker?  □ Ja □ Nej

Hvis nej (såfremt du ikke motionerer så ofte, som du gerne ville), skyldes det da:

□ Utpashed
□ Manglende fysisk overskud
□ Manglende motionstilbud som passer til mig
□ Økonomisk hensyn
□ Mangler en træningspartner/træningspartnere
□ Usikkerhed på, hvad jeg kan
□ Usikkerhed på, hvad jeg må
□ Travlhed i hverdagen

(Du må gerne sætte flere krydser)

TAK FOR DIN MEDVIRKEN!

Krop og Kræft

En kropsorienteret indsats til kræftpatienter i kemoterapi – 
Et klinisk kontrolleret forsøg.

KROPSDAGBOG

Uge nr. _____ af 6

Patient ID: ________________________________

Indtastet: □
INTRODUKTION

Vi opfordrer til, at Dagbogen føres **hver dag** og så vidt muligt udfyldes sidst på dagen, således at din besvarelse bliver et **tilbageblik på dagen**, der er gået. Vi vil bede dig udfylde dagbøgerne i seks uger (en for hver uge) og aflevere dem til projektteamet, når du møder op til din afsluttende fysiske tests.

Dagbogen indeholder to dele:

1. **Et registreringsskema** i to dele, hvor du dagligt registrerer eventuelle bivirkninger, smerter og træthed. Desuden vil vi gerne have oplyst, om du har modtaget kemoterapi og/eller blodtransfusion, samt hvorvidt og hvor meget, du har motioneret den pågældende dag. Skemaet finder du på næste side sammen med en vejledning, der forklarer, hvordan det skal udfyldes. Desuden har vi vedlagt en beskrivelse af, hvad der menes med de forskellige ord i skemaet (se sidste side).


Har du spørgsmål vedrørende udfyldelsen af Kropsdagbogen, er du meget velkommen til at kontakte projektteamet.

Med venlig hilsen

**Projektteamet**

Forskningssygeplejerske Christina Andersen tlf. 35457309,  
Projektfysioterapeut Morten Quist tlf. 35458531,  
Forskningsleder Lis Adamsen tlf. 35457345  
Cand. psych., Ph.d. Studerende Julie Midtgaard tlf. 35457355.
Registreringsskema

På de følgende to sider skal du dagligt vurdere og registrere dine bivirkninger, smerter og træthed. Du bedes endvidere oplyse, hvorvidt du den pågældende dag har modtaget kemoterapi og/eller blodtransfusion, samt hvorvidt og hvor meget du eventuelt har motioneret. Din vurdering sker ved, at du ud for hver enkelt punkt angiver et tal fra 0-4 afhængig af "sværhedsgrad".

Den første del (nedenstående) vedrører **appetit, kvalme, opkast, diarré og føleforstyrrelser** og for disse punkter gælder følgende retningslinier for, hvilket tal du vælger at angive:

<table>
<thead>
<tr>
<th>Skala:</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appetit</strong></td>
<td>Øget</td>
<td>Uændret. Spiser som tidligere (100%).</td>
<td>Let nedsat apparit. Spiser 75% i forhold til tidligere.</td>
<td>Moderat nedsat apparit. Spiser 50-75% i forhold til tidligere.</td>
<td>Svær nedsat apparit. Spiser &lt;50% i forhold til tidligere.</td>
</tr>
<tr>
<td><strong>Kvalme</strong></td>
<td>Ingen</td>
<td>I stand til at spise, men mindre end vanligt.</td>
<td>Svært ved at spise (evt. er kosten overvejende flydende).</td>
<td>Ingen mad indtagelse.</td>
<td>Over 10 gange i døgnet.</td>
</tr>
<tr>
<td><strong>Opkast</strong></td>
<td>Ingen</td>
<td>Kaster op en gang i døgnet.</td>
<td>2-5 gange i døgnet.</td>
<td>6-10 gange i døgnet.</td>
<td>Over 10 gange i døgnet.</td>
</tr>
<tr>
<td><strong>Føleforstyrrelser</strong></td>
<td>Ingen</td>
<td>Let / lidt føleforstyrrelser</td>
<td>Moderat føleforstyrrelser, let eller moderat følelsesløshed</td>
<td>Svær / meget føleforstyrrelser svær følelsesløshed som påvirker funktionen.</td>
<td></td>
</tr>
</tbody>
</table>

---

**Bivirkninger:**

<table>
<thead>
<tr>
<th>Mandag</th>
<th>Tirsdag</th>
<th>Onsdag</th>
<th>Torsdag</th>
<th>Fredag</th>
<th>Lørdag</th>
<th>Søndag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetit</td>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kvalme</td>
<td>0-1-2-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opkastning</td>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarré</td>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Føleforstyrrelser</td>
<td>0-1-2-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Angiv hvor:
Den anden del af skemaet vedrører bl.a. **forstoppelse, smerner og træthed** og her gælder følgende:

0: Ingen
1: Let / lidt
2: Moderat
3: Svær / meget
4: Intolerabelt / uudholdeligt

**Motion, kemoterapi og blodtransfusion** angives ved hjælp af et X med evt. tilføjelse af **varighed** og/eller **mængde**.

<table>
<thead>
<tr>
<th>Bivirkninger:</th>
<th>Mandag</th>
<th>Tirsdag</th>
<th>Onsdag</th>
<th>Torsdag</th>
<th>Fredag</th>
<th>Lørdag</th>
<th>Søndag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forstoppelse</td>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smerter:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledsmerter</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muskelsmerter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andre smerner</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1-2-3-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiv hvor:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Træthed: (Se evt. ordforklaring på sidste side)**

<table>
<thead>
<tr>
<th>Fysisk træthed</th>
<th>0-1-2-3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental træthed</td>
<td>0-1-2-3-4</td>
</tr>
<tr>
<td>Behandlingsrelateret træthed</td>
<td>0-1-2-3-4</td>
</tr>
</tbody>
</table>

**Motion:**

| Hør du i dag cyklet (fx til og fra arbejdet eller rindkøb)?
Hvis ja, sæt X og angiv minutter |
|------------------------|
| Hør du i dag dyrket let anstrengende motion (fx svømning, gymnastik o.lign.)?
Hvis ja, sæt X og angiv minutter |
| Hør du i dag dyrket meget anstrengende motion (fx aerobic, løb, fodbold o.lign.)?
Hvis ja, sæt X og angiv minutter |
| Hør du i dag fået kemoterapi?
Hvis ja, sæt X |
| Hør du i dag fået blodtransfusion?
Hvis ja, sæt X og angiv evt. angiv antal poser. |
**Uge nr. ____ af 6**

<table>
<thead>
<tr>
<th>Ugedag</th>
<th>Her kan du vælge at fortælle om evt. forandringer i dine symptomer og bivirkninger samt dit hverdagsliv (gøremål, aktivier, tanker).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MANDAG</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TIRSDAG</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Uge nr. ____ af 6

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>ONSDAG</td>
<td></td>
</tr>
<tr>
<td>TORSDAG</td>
<td></td>
</tr>
<tr>
<td>Ugedag</td>
<td>Her kan du vælge at fortælle om evt. forandringer i dine symptomer og bivirkninger samt dit hverdagsliv (gøremål, aktivier, tanker).</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>FREDAG</td>
<td></td>
</tr>
<tr>
<td>LØRDAG</td>
<td></td>
</tr>
<tr>
<td>SØNDAG</td>
<td></td>
</tr>
</tbody>
</table>
Ordforklaring

- **Føleforstyrrelser:** Eksempler på føleforstyrrelser kan være snurren og prikken i fingre eller tæer, smerter under fødderne eller i fingerspidserne eller andre former for følelsesløshed. Ved besvarelse af dette punkt i skemaet bedes du angive hvor i kroppen du oplever føleforstyrrelser.

- **Andre smarter:** Andre smerter (ud over ledsmarter og muskelsmaerter) kunne være hovedpine, ondt i ryggen eller smerter i operationsar. Du bedes angive hvilke typer smerter der er tale om.

- **Fysisk træthed:** Med fysisk træthed mener vi den følelse af træthed, som kan være en følge af fysisk træning og andre kropsligt relaterede aktiviteter i hverdagen. Kan være kendetegnet ved fx afslappethed, at have energi samt følelsen af ro og varme i kroppen.

- **Mental træthed:** Med mental træthed tænker vi på følelsen af at være "træt i hovedet" og mangle energi til at udføre ønskede aktiviteter.

- **Behandlingsrelateret træthed:** Denne type træthed kan være forårsaget af den kemoterapi (og eventuelt strålebehandling) du modtager og kan være kendetegnet af fx influenzasymptomer, svimmelhed og – selv om man sover eller ligger stille opnår man ikke følelsen af at være udhvilet.

- **Motion:** Med motion, tænker vi på aktiviteter, som du udfører for at bevæge og træne kroppen. Ved besvarelse af disse punkter i skemaet bedes du angive hvorvidt og hvor længe du eventuelt har cyklet, dyrket let og/eller anstrengende motion.
### FACT-An (Version 4)

Nedenfor er anført en række udsagn, som andre mennesker med din sygdom har sagt, er vigtige. **Ved at sætte en ring omkring et af tallene i hver linie, bedes du angive, hvor sandt hvert enkelt udsagn har været for dit vedkommende i løbet af de sidste 7 dage.**

<table>
<thead>
<tr>
<th><strong>FYSISK VELBEFINDENDE</strong></th>
<th>Slet ikke</th>
<th>En lille smule</th>
<th>I nogen grad</th>
<th>En halvdel</th>
<th>Meget</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP1</td>
<td>Jeg mangler energi..........................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP2</td>
<td>Jeg har kvalme ..................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP3</td>
<td>På grund af min fysiske tilstand har jeg svært ved at opfylde min families/mine nærmestes behov .................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP4</td>
<td>Jeg har smerter ..................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP5</td>
<td>Jeg er generet af bivirkninger af behandlingen ....................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP6</td>
<td>Jeg føler mig syg ................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GP7</td>
<td>Jeg er tvunget til at være sengeliggende noget af tiden ......</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>SOCIALT/FAMILIEMÆSSIGT VELBEFINDENDE</strong></th>
<th>Slet ikke</th>
<th>En lille smule</th>
<th>I nogen grad</th>
<th>En halvdel</th>
<th>Meget</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS1</td>
<td>Jeg føler, jeg har et tæt forhold til mine venner .............</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GS2</td>
<td>Jeg får følesemæssig støtte fra min familie/mine nærmeste ..............................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GS3</td>
<td>Jeg får støtte fra mine venner ........................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GS4</td>
<td>Min familie/mine nærmeste har accepteret min sygdom ...</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GS5</td>
<td>Jeg er tilfreds med den måde vi taler om sygdommen på i familien/blandt mine nærmeste .........................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>GS6</td>
<td>Jeg føler mig tæt knyttet til min partner (eller den person, der er min bedste støtte) .................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q1</td>
<td>Uanset om du er seksuelt aktiv eller ej, bedes du venligst besvare følgende spørgsmål - Hvis du ikke har lyst til at besvare spørgsmålet, bedes du sætte kryds i boksen og gå videre til næste udsagn.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GS7</td>
<td>Jeg er tilfreds med mit sexliv ..............................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
FACT-An (Version 4)

Ved at sætte en ring omkring et af tallene i hver linie, bedes du angive, hvor sandt hvert enkelt udsagn har været for dit vedkommende i løbet af de sidste 7 dage.

**FØLELSESMÆSSIGT VELBEFINDENDE**

<table>
<thead>
<tr>
<th>GE1</th>
<th>Jeg er ked af det......................................................................................................</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>GE2</td>
<td>Jeg er tilfreds med den måde, jeg klarer min sygdom på .........................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>GE3</td>
<td>Jeg er ved at give op i kampen mod min sygdom .......................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>GE4</td>
<td>Jeg føler mig nervøs ...............................................................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>GE5</td>
<td>Jeg er bekymret for at dø .......................................................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>GE6</td>
<td>Jeg er bekymret for, at min tilstand vil forværre ses ................................................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**FUNKTIONELT VELBEFINDENDE**

| GF1      | Jeg er i stand til at arbejde (inkluderer arbejde i hjemmet) .................................................. | 0 | 1 | 2 | 3 | 4 |
| GF2      | Mit arbejde (inkluderer arbejde i hjemmet) er tilfredsstillende ............................................... | 0 | 1 | 2 | 3 | 4 |
| GF3      | Jeg er i stand til at nyde livet ............................................................................................... | 0 | 1 | 2 | 3 | 4 |
| GF4      | Jeg har accepteret min sygdom ................................................................................................. | 0 | 1 | 2 | 3 | 4 |
| GF5      | Jeg sover godt ........................................................................................................................... | 0 | 1 | 2 | 3 | 4 |
| GF6      | Jeg nyder det, jeg plejer at lave i min fritid ......................................................................... | 0 | 1 | 2 | 3 | 4 |
| GF7      | Lige nu er jeg tilfreds med min livskvalitet ........................................................................... | 0 | 1 | 2 | 3 | 4 |
**FACT-An (Version 4)**

Ved at sætte en ring omkring et af tallene i hver linie, bedes du angive, hvor sandt hvert enkelt udsagn har været for dit vedkommende i løbet af de sidste 7 dage.

### ANDRE BEKYMRINGER

<table>
<thead>
<tr>
<th>#</th>
<th>Udsagn</th>
<th>Slet ikke</th>
<th>En lille smule</th>
<th>I nogen grad</th>
<th>En hel del</th>
<th>Meget</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3</td>
<td>Jeg føler mig udmattet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>H3</td>
<td>Jeg føler mig svag i hele kroppen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A1</td>
<td>Jeg har mistet livslysten</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A2</td>
<td>Jeg føler mig træt</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A3</td>
<td>Jeg har svært ved at komme i gang med noget, fordi jeg er træt</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A4</td>
<td>Jeg har svært ved at afslutte noget, fordi jeg er træt</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A5</td>
<td>Jeg har energi</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A6</td>
<td>Jeg har besvær med at gå</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A7</td>
<td>Jeg er i stand til at udføre mine normale aktiviteter</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A8</td>
<td>Jeg har brug for at sove i løbet af dagen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A9</td>
<td>Jeg føler mig svimmel</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A10</td>
<td>Jeg får hovedpine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>B1</td>
<td>Jeg bliver let forpustet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A11</td>
<td>Jeg har smerter i brystet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A12</td>
<td>Jeg er for træt til at spise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>B4</td>
<td>Jeg er interesseret i sex</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A13</td>
<td>Jeg er motiveret for at udføre mine normale aktiviteter</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A14</td>
<td>Jeg har brug for hjælp til at udføre mine normale aktiviteter</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A15</td>
<td>Jeg er frustreret over, at jeg er for træt til at gøre de ting, jeg gerne vil</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>A16</td>
<td>Jeg er nødt til at begrænse min selskabelige omgang med andre, fordi jeg er træt</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
‘Exercise despite pain - Breast cancer patient experiences of muscle and joint pain during adjuvant chemotherapy and concurrent participation in an exercise intervention’ (Paper III)

Temaer og udvalgte spørgsmål i interview-guide før deltagelse i Krop & Kræft

Indledning
Demografisk oplysning: civilstatus, hjemmeboende børn, uddannelse, beskæftigelse?
Fortæl hvilket fysisk aktivitetsniveau der passer bedst på dig før du fik din kræft diagnose? Fortæl hvilket fysisk aktivitetsniveau der passer bedst på dig i dag?

Sygdoms- og behandlingshistorie
Fortæl kort om dit sygdoms og behandlingsforløb?
Forbandt du din kræft diagnose med smerter?
Hvilke forestillinger vedr. smerter havde du i forhold til din kræft diagnose? Fortæl hvilke forestillinger du gør dig om kemoterapi og smerter?

Smertesymptom erfaring og fortolkning
Beskriv om du tidligere har haft smerter (fx hovedpine, menstruationssmerter, operationssmerter)
Fortæl om du italesatte dine smerter over for andre?
Fortæl med dine egne ord, hvad du selv har gjort for at håndtere dine smerter? Hvilke forklaringer giver du dig selv, når du oplever, at du får ondt?

Forventninger til deltagelse i Krop og Kræft i forhold til smerter
Hvilke forventninger har du til din deltagelse i Krop & Kræft i forhold til dine symptomer – bivirkninger?
Muskel og led smerter? Reduceret, forværet, status quo?

Temaer og udvalgte spørgsmål i interview-guide efter Krop & Kræft

Smertefortælling

Erfaringer med kemoterapi relatedede smerter
Fortæl om du har oplevet at få muskel- og led smerter i forbindelse med din adj. kemoterapi? Fortæl hvor har du haft smerter og hvornår smerterne opstod og hvor længe de varede?

Fortolkning af smerter
Fortæl hvad smerterne har betydet for dig og om du har foretaget dig noget aktivt for at mindske dine smerter?
Fortæl om du har lagt en personlig strategi for at mindske dine smerter under træningen?
Er det en strategi du har anvendt tidligere i forhold smertekontrol?
Fortæl hvordan smerterne har haft indflydelse på din fysiske og emotionelle formåen?

Vedr. deltagelse i Krop og Kræft
Fortæl om din deltagelse i træningen (Krop & Kræft) og om smerterne har været anderledes end du forventede? Fortæl om du har meldt afbud til træning, trænet med nedsat intensitet, trænet som vanligt, holdt flere pauser?
'Exercise despite pain - Breast cancer patient experiences of muscle and joint pain during adjuvant chemotherapy and concurrent participation in an exercise intervention' (Paper III)

Temaer og udvalgte spørgsmål i interview-guide før deltagelse i Krop & Kræft

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Fortæl hvilket fysisk aktivitetsniveau der passer bedst på dig før du fik din kræftdiagnose? Fortæl hvilket fysiske aktivitetsniveau der passer bedst på dig i dag?

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Temaer og udvalgte spørgsmål i interview-guide efter Krop & Kræft
Smertefortælling

Erfaringer med kemoterapi relaterede smerter
Fortæl om du har oplevet at få muskel- og led smerter i forbindelse med din adj. kemoterapi? Fortæl hvor har du haft smerter og hvornår smerterne opstod og hvor længe de varede?

Fortolkning af smerter
Fortæl hvad smerterne har betydet for dig og om du har foretaget dig noget aktivt for at mindske dine smerter?
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Vedr. deltagelse i Krop og Kræft
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Vedrørende projekt (KF) 01-273/00: "Projekt Krop og Kræft. En kropsorienteret indsats til kræftpatienter i kemoterapi"


Efter nøje at have gennemgået projektet er det komitéens opfattelse, at der i det foreliggende tilfælde ikke er tale om en sådan biomedicinsk forskning, som falder indenfor komitéens område.

Komitéen har derfor ikke realitetsbehandlet projektet, som er henlagt uden videnskabeligt bedømme.

De Videnskabelige Komitéer for Københavns og Frederiksberg Kommuner har inden at indvene det gennemføres efter protokollen.
Komitéens afgørelse kan – via vor komité – indømkes for Den Centrale Videnskabelige Komité.

Med venlig hilsen

Rikard Vrogaard

[Signature]

[Signature]

Fælles sekretariat: Københavns Kommune, Sundhedsforvaltningen, Sjællandsvang 40, 2200 København N
Besøgsadresse: De Gamle By, Bygning V, Edith Rodes Vaj 2, 1. th., 2200 København N
Telefon: 35 30 34 02, 35 30 34 05, 35 30 34 07, 35 30 34 09
Telefax: 35 30 39 30
Vedrørende anmeldelse af projektet: Krop og Kræft - En kropsorientoert indsats til kræftpatienter i kemoterapi

Ovennævnte projekt er den 7. september 2000 anmeldt til Datatilsynet efter lov om behandling af personoplysninger § 48, stk. 1. Der er samtidigt søgt om Datatilsynets tilladelse.


Oplysningerne vil blive behandlet på følgende adresse: Universitetshospitalernes Center for Sygepleje- og Omsorgsforskning, Rigshospitalet, Afsnit 7331, Blegdamsvej 9, 2100 København Ø.

Tilladelse

Datatilsynet meddeler hermed tilladelse til projektets gennemførelse, jf. lov om behandling af personoplysninger, § 50, stk. 1, nr. 1. Datatilsynet fastsætter i den forbindelse nedenstående vilkår:

Generelle vilkår

1. Forkningsleder Ph.D, Lis Adamsen er ansvarlig for overholdelsen af de fastsatte vilkår.
2. Oplysningerne må kun anvendes til brug for projektets gennemførelse.
4. Enhver, der foretager behandling af projektets oplysninger, skal være bekendt med de fastsatte vilkår.
5. De fastsatte vilkår skal tillige igtages ved behandling, der foretages af databehandler.


8. Oplysninger må ikke opbevares på en måde, der giver mulighed for at identificere de registrerede i et længere tidsrum end det, der er nødvendigt af hensyn til projektets gennemførelse.

9. En eventuel offentliggørelse af undersøgelsens resultater må ikke ske på en sådan måde, at det er muligt at identificere enkeltpersoner.

10. Eventuelle vilkår, der fastsættes efter anden lovgivning, forudsættes overholdt.

**Elektroniske oplysninger**


14. Udtagelige lagringsmedier, sikkerhedskopier af data m.v. skal opbevares forsvarligt aflåst og således, at uvedkommende ikke kan få adgang til oplysningerne.

**Manuelle oplysninger**

15. Manuelt projektmateriale, udskrifter, fejl- og kontrollister, m.v., der direkte eller indirekte kan henføres til bestemte personer, skal opbevares forsvarligt aflåst og på en sådan måde, at uvedkommende ikke kan gøre sig bekendt med indholdet.
Oplysningspligtig for den registrerede

16. Hvis der skal indsamles oplysninger hos den registrerede (ved interview, spørgeskema, klinisk eller paraklinisk undersøgelse, behandling, observation m.v.) skal der uddelas/fermes sendes nærmere information om projektet. Den registrerede skal heri oplyses om den dataansvarlighedens navn, formulæt med projektet, at det er frivilligt at deltage, og at et samtykke til deltageren kan trækkes tidligere. Hvis oplysningerne skal videregives til brug i anden videnskabelig eller statistisk sammenhæng, skal der også oplyses om formulæt med videregivelsen samt modtagers identitet.

17. Den registrerede bør endvidere oplyses om, at projektet er anmeldt til Datatilsynet efter lov om behandling af personoplysninger, samt at Datatilsynet har fastsat nærmere vilkår for projektet til beskaffelse af den registreredes privatliv.

Indsigtsret

18. Den registrerede har ikke krav på indsigt i de oplysninger, der behandles om den pågældende.

Videregivelse

19. Videregivelse af personhenførbare oplysninger til tredjepart må kun ske til brug i andet statistisk eller videnskabeligt øjemed.


Ændringer i projektet


22. Ændring af udsigtspunktet for projektets afslutning skal altid anmeldes.

Ved projektets afslutning

23. Senest ved projektets afslutning skal oplysningerne slettes, anonymiseres eller tilintetgøres, således at det efterfølgende ikke er muligt at identificere enkeltpersoner, der indgår i undersøgelsen.

25. Den dataansvarlige skal meddele Datatilsynet, når projektet er afsluttet, og oplysningerne slettet, anonymiseret, tilintetgjort eller overført til Statens Arkiver.


Ovenstående vilkår er gældende indtil videre. Datatilsynet forbeholder sig senere at tage vilkårene op til revision, hvis der skulle vise sig behov for det.

Anmeldelsen vil snarest blive offentliggjort i fortegnelsen over anmeldte behandlinger på Datatilsynets hjemmeside www.datatilsynet.dk.

Med venlig hilsen

[Signature]

Peter Ahlesøn

Bilag: Lov om behandling af personoplysninger
PhD thesis
Christina Andersen

**Body & Cancer**
– The effects of a multimodal exercise intervention on symptoms and side-effects in cancer patients undergoing chemotherapy

The University Hospitals Centre for Health Research,
The Copenhagen University Hospital, Rigshospitalet, Denmark
November 2013