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PhD thesis

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EXHALE

Exercise as a strategy for rehabilitation in inoperable lung cancer patients undergoing chemotherapy

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List of Studies

I. Quist M, Rorth M, Zacho M, Andersen C, Moeller T, Midtgaard J, Adamsen L. High-intensity resistance and cardiovascular training improve physical capacity in cancer patients undergoing chemotherapy. Scand.J.Med.Sci.Sports 2006;16: 349-357.

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IV. Quist M, Langer SW, Rorth M, Christensen KB, Adamsen L. "EXHALE": exercise as a strategy for rehabilitation in advanced stage lung cancer patients: a randomized clinical trial comparing the effects of 12 weeks supervised exercise intervention versus usual care for advanced stage lung cancer patients. BMC Cancer 2013;13: 477.

Abbreviations

NSCLC	Non-Small Cell Lung Cancer
SCLC	Small Cell Lung Cancer
LD-SCLC	Limited Disease Small Cell Lung Cancer
ED-SCLC	Extensive Disease Small Cell Lung Cancer
HRQOL	Health-Related Quality Of Life
FACT-L	The Functional Assessment of Cancer Therapy – Lung
1RM	One Repetition Maximum
W	Watt
MPO	Maximum Power Output
RER	Respiratory Exchange Ratio
6MWD	6 Minute Walking Distance
ATS	American Thoracic Society
FEV1	Forced Expiratory Volume in one second
COPD	Chronic Obstructive Pulmonary Disease
PWB	Physical Wellbeing
FWB	Functional Wellbeing
EWB	Emotional Wellbeing
SWB	Social Wellbeing
LCS	Lung Cancer Subscale
HADs	Hospital Anxiety and Depression scale
HADs-A	Hospital Anxiety and Depression scale - Anxiety
HADs-D	Hospital Anxiety and Depression scale – Depression
MOS SF-36	The Medical Outcomes Study Short Form
EORTC-QLQ-C30 – LC13	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
PSQI	The Pittsburgh Sleep Quality Index
SD	Standard Deviation
CI	Confidence Intervals
SAE	Severe Adverse Events
AE	Adverse Events
VAS	Visual Analogue Scale

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DANSK RESUMÉ

Baggrund: Lungekræft er en af de hyppigste kræftformer i Danmark med ca. 4.300 nye tilfælde pr år. Patienter med lungekræft har en betydelig symptombyrde både fysisk og psykosocialt, specielt de patienter som har en inoperabel lungekræft (stadie IIIa-IV), som udgør ca. 70-80 % af alle nydiagnosticerede patienter med lungekræft.

Flere studier har påvist effekt af fysisk træning til patienter med kræft både under og efter behandlingen, langt størstedelen af disse studier er udført på kvinder med brystkræft. De studier, der har undersøgt effekten af fysisk træning til patienter med lungekræft, er hovedsageligt foretaget på patienter med lungekræft i et tidligt stadie (NSCLC I-III, SCLC LD) før og efter operation. Resultaterne indikerer øget fysisk kapacitet, funktionel kapacitet og muskel kapacitet, mens der ikke er fundet entydig signifikante forbedringer på livskvalitet (HRQoL) eller angst og depression. I alt har 8 studier - 6 feasibility og 2 randomiserede undersøgelser - undersøgt effekten af fysisk træning til patienter med inoperabel lungekræft. Der er forskel på varigheden af interventionerne, den intensitet der blev trænet med og hvilken type træning, der blev tilbudt.

Denne afhandling tager udgangspunkt i det kliniske og idrætsfysiologiske udviklingsarbejde, der er gennemført i forbindelse med udvikling af "Krop og Kræft" som beskrevet i studie I. Trænings-intervention og de anvendte fysiologiske test, er udviklet og afprøvet i "Krop og Kræft" projektet på en heterogen population af patienter med kræft, som dermed har dannet grundlag for videreudvikling af interventionen og målemetoder appliceret til patienterne med inoperabel lungekræft. Desuden er effekten af træning undersøgt på patienter med lungekræft i studie II-III. Endvidere er en randomiseret klinisk undersøgelse (RCT) igangsat. Denne afprøver effekten af træning til patienter med inoperabel lungekræft, og er skitseret i protokolartiklen (studie IV). Denne afhandling er et samarbejde mellem Universitetshospitalernes Center for Sundhedsfaglig Forskning og Onkologisk Klinik, Rigshospitalet. Projektet indgår i forskningsprogrammet relateret til Center for Integreret Rehabilitering af Kræftpatienter (CIRE).

Formål og Hypotese: Afhandlingens formål er at undersøge effekten af en 6 ugers fysisk og psykosocial intervention bestående af: superviseret, struktureret træning i grupper (kardiovaskulær og muskelstyrke træning, afspændingstræning) for patienter med inoperabel lungekræft, der modtager kemoterapi. Afhandlingen tester følgende hypotese: At en 6 ugers intervention er sikker og gennemførlig, vil øge fysisk kapacitet, funktionel kapacitet, muskelstyrke, livskvalitet og reducere angst og depressionsniveauet.

Metoder og population: Forskningen er gennemført som et hypotese-generende, prospektivt fase I studie, samt fase II og III studier med præ og post test. Der anvendes kvantitative forskningsmetoder. Patienterne (n=70) fik målt fysisk kapacitet og muskelstyrke (VO_2max, 1RM) i studie I og i studie II (n=29). I studie III (n=71) blev fysisk kapacitet (VO_2max), funktionel kapacitet (6MWD), muskelstyrke (1RM), livskvalitet (FACT-L), samt angst og depression (HADs) målt. I den randomiserede undersøgelse (studie IV) (n=216) bliver udover førnævnte metoder også brugt spørgeskemaer for livskvalitet (SF-36 og EORTC-LC13), spørgeskema for søvnkvalitet (PSQI) samt eget-udviklet skema for social support.

Resultater: Resultaterne i studie I viste, at en 6 ugers intervention forbedrede patienternes fysiske kapacitet og muskelstyrke signifikant, samt at den var sikker og gennemførbar.

I Studie II fandt, vi at patienter med inoperabel lungekræft kunne gennemføre en 6 ugers intervention. Studiet viste, at adherence til den superviserede intervention var 73 %, hvorimod hjemmetræningen viste 8,7 %. Patienterne opnåede signifikant fremgang i fysisk kapacitet, funktionel kapacitet og muskelstyrke. Desuden fandt vi en signifikant forbedring i "emotionel well-being". Der blev ikke rapporteret Severe Adverse Events (SAE) eller Adverse Events (AE).

I studie III opnåede patienterne signifikante fremgang i fysisk kapacitet, funktionel kapacitet, muskelstyrke, "emotionel well-being", samt en signifikant reduktion i "social well-being" og i angst niveau.

Studie IV er i gang og pr. 1. februar 2015 er 139 patienter med inoperabel lungekræft er inkluderet og randomiseret. Der er allokeret 70 patienter med ligelig kønsfordeling til interventionsgruppen og 68 patienter til kontrolgruppen, hvoraf 33 er kvinder og 35 mænd.

Konklusion: Som en konklusion på studie I og studie II i denne afhandling kan vi dokumentere, at patienter med inoperabel lungekræft kan gennemføre en 6 ugers trænings og afspænding intervention uden træning relaterede SAE. Desuden fandt vi, på baggrund af resultaterne fra feasibility studiet (studie II), at adherence til hjemme-trænings komponenten var lav, og derfor udgik denne komponent af interventionen.

Herudover kan vi konkludere, at patienter med inoperabel lungekræft kan øge VO_2max ($p=0.005$), den funktionelle kapacitet (6MWT), ($p<0.0001$)) og muskel styrke ($p<0.0001$) signifikant. Yderligere fandt vi, at interventionen reducerede patienternes angstniveau. Patienterne opnåede ikke signifikant fremgang på HRQoL, men vi observerede en signifikant fremgang på parameteren "emotional well-being".

Den endelige effekt af exercise intervention kombineret med relaxation afprøves i et randomiseret design (studie IV) for patienter med inoperabel lungekræft.

Perspektivering: Et fund fra denne afhandling er patienternes fremgang på væsentlige fysiske parametre, hvorved tab af vigtige fysiske funktioner kan forebygges eller reduceres. Med en fremgang i de fysiske parametre i kombination med reduktionen i angstniveau imødekommes patienternes eksplicitte ønske om at lykkes med at fastholde uafhængighed og dagligdags aktivitetsniveau uanset dårlig prognose og massive symptombyrde. I studie IV vil vi kunne afgøre, om de gavnlige effekter fundet i studie III er fremkommet på grund af patient selektion. Uanset om resultaterne forbliver positive eller ej, vil studie IV bidrage med ny viden til et ret uudforsket felt inden for exercise til patienter med inoperabel lungekræft.

ENGLISH SUMMARY

Background: Lung cancer is one of the most common cancers in Denmark, with roughly 4,300 new cases annually. Patients with lung cancer have a significant symptom burden, both physically and psychosocially, especially patients with inoperable lung cancer (stages IIIa-IV), who account for about 70-80% of all newly diagnosed patients with lung cancer.

Numerous studies have demonstrated the effect of physical training in patients with lung cancer both during and after treatment. The vast majority of these studies were on women with breast cancer. Studies examining the effect of physical training in patients with lung cancer have primarily been conducted in patients with early-stage lung cancer (NSCLC I-III, SCLC LD) pre- and post-surgery. The findings indicate increased physical capacity, functional capacity and muscular capacity, but no unambiguously significant improvements in HRQOL or anxiety and depression levels. Eight studies – six feasibility and two randomised – examine the effect of physical training in patients with advanced lung cancer. The studies differ with regard to duration of the interventions, the level of training intensity and the type of training that was offered.

This thesis is based on research on clinical and physiological work carried out during exercise in connection with the development of "Body and Cancer", as described in Study I. The exercise intervention and the physiological tests were developed and tested in the "Body and Cancer" project in a heterogeneous group of patients with a variety of cancer diagnoses and form the basis for the further development of the intervention and measuring methods applied to patients with inoperable lung cancer. The effect of training has also been studied in patients with lung cancer in Study II and III. A randomised clinical trial testing the effect of exercise in patients with inoperable lung cancer, outlined in the protocol article (Study IV), has been initiated.

This thesis was carried out in cooperation with the University Hospitals Centre for Health Research, Rigshospitalet, University of Copenhagen and the Department of Oncology, Rigshospitalet, University of Copenhagen. The project is part of a research programme involving the Centre for Integrated Rehabilitation of Cancer Patients (CIRE).

Aim and hypothesis: This thesis aims to investigate the effect of a six-week physical and psychosocial intervention comprising supervised structured training in groups (cardiovascular, strength and relaxation training) for patients with inoperable lung cancer undergoing chemotherapy. The thesis tests the following hypothesis: That a six-week intervention is feasible and safe, will increase physical capacity, functional capacity, muscle strength and quality of life, and reduce the degree of anxiety and depression.

Methods and population: The research was conducted as a hypothesis-generating prospective phase I study, as well as phase II and III studies with pre and post testing. Quantitative research methods were used. Patients (n=70) had their physical capacity and muscle strength measured (VO_2max, 1RM) in Study I, and in Study II (n=29) and Study III (n=71) physical capacity (VO_2max); functional capacity (6MWD); muscle strength (1RM), QOL (FACT-L); and anxiety and depression (HADS) were measured. In addition to the aforementioned methods, the randomised study (Study IV) (n=216) also used the health survey MOS SF-36, the QOL questionnaire EORTC QLQ-LC13, the sleep quality index PSQI, and a self-developed structured questionnaire on social support.
Results: The findings in Study I showed that a six-week intervention increased the physical capacity and muscle strength of patients significantly, and that it was feasible and safe.
Study II showed that patients with inoperable lung cancer are able to complete a six-week intervention. The adherence rate for the supervised intervention in the study was 73% compared to 8.7% for home-based training. Patients showed significant improvement in physical capacity, functional capacity and muscle strength. We also found a significant improvement in emotional well-being. No serious adverse events (SAE) or adverse events (AE) were reported.
In Study III patients also showed significant improvement in physical capacity, functional capacity, muscle strength and "emotional well-being", as well as a significant reduction in "social well-being" and the level of anxiety.
Study IV has been initiated and as of 1 February 2015 there were 139 patients with inoperable lung cancer enrolled and randomised. Seventy patients (35 women and 35 men) have been allocated to the intervention group and 68 patients (33 women and 35 men) have been allocated to the control group.
Conclusion: As a conclusion of Study I and Study II in this thesis, we can document that the patients with inoperable lung cancer are able to complete a six-week exercise and relaxation intervention without exercise-related SAE. Based on the results of the feasibility study (Study II), we also found that adherence to the home-based training component was low, which is why that component was taken out of the intervention. In addition we can conclude that patients with inoperable lung cancer can increase VO_2max ($p=0.005$), functional capacity (6MWD, $p<0.0001$) and muscle strength ($p<0.0001$) significantly. We also found that the intervention significantly reduced the patients' level of anxiety. The patients did not improve their HRQOL significantly, but we did observe a significant improvement in emotional well-being. The final effect of the combined

exercise and relaxation intervention is being tested in a randomised design (Study IV) in patients with inoperable lung cancer.

Perspectives: An important finding from this thesis is the improvement of essential physical parameters by which the loss of important physical functions can be prevented or reduced. With an improvement in the physical parameters combined with a reduction in the level of anxiety the patients' explicit desire to succeed in maintaining independence and their level of daily activity is met regardless of poor prognosis and full-blown symptom burden. Study IV will enable us to determine whether the beneficial effects found in Study III were obtained due to patient selection. Regardless of whether the results remain positive or not, Study IV will contribute with new knowledge to a relatively unexplored area within exercise for patients with inoperable lung cancer.

INTRODUCTION

Since the first intervention study on physical training in patients with cancer was conducted in 1986 [1] by Winningham and MacVicar, two pioneering oncology nurses, the professional attitude towards exercise has changed significantly from being viewed as harmful to patients to being beneficial. A number of meta-analyses has found effects on a variety of physiological, emotional and psychosocial parameters [2-4]. At present various countries are discussing whether the time is ripe to develop evidence-based guidelines on physical activity in cancer patients [5, 6]. Evidence pertaining to the beneficial effect of exercise on cancer patients is based on relatively few cancer diagnoses, mainly breast cancer and early-stage cancer (stages I-II) where the initial treatment has been completed (surgery, chemotherapy, radiation therapy).

Since 2000 I have been part of a research team involved in a study called Body and Cancer that has examined the effect of exercise on patients in chemotherapy [7-9]. With regard to diagnosis, the enrolled group of individuals comprises a heterogeneous sample of cancer patients covering 22 diagnoses both with and without residual disease. Patients with lung cancer comprise only 3% of the sample, despite the fact that lung cancer is one of the most common forms of cancer in Denmark, with roughly 4,300 new cases annually. Findings from Body and Cancer show that a six-week intervention (nine hours weekly) can improve fatigue, endurance and strength, as well as reduce various symptoms, such as depression [10, 11]. Patients with lung cancer have a significant symptom burden physically and psychosocially, especially patients with inoperable lung cancer (stage IIIa-IV), who account for about 70-80% of all newly diagnosed patients with lung cancer.

This thesis is based on research on clinical and physiological work carried out during exercise in connection with the development of Body and Cancer, as described in Study I. The exercise intervention and the physiological tests were developed and tested in the Body and Cancer project and form the basis for the further development of the intervention on patients with inoperable lung cancer. Studies II-III investigated the effect of exercise in patients with lung cancer, and a randomised clinical trial (RCT) testing the effect of exercise in patients with inoperable lung cancer, outlined in the protocol article (Study IV), was initiated 2012.

BACKGROUND

Lung cancer

Incidence and staging

Lung cancer is the leading cause of cancer deaths in the world, and with 1.6 million patients newly diagnosed with lung cancer annually, lung cancer represents an urgent health issue with significant personal and social costs. An estimated 2.2 million people are projected to get lung cancer in 2020 [12]. With an incidence of approximately 4,300 cases a year, lung cancer is the second most common form of cancer in Denmark and the leading cause of cancer death.

Lung cancer can be divided into two types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The most common type, NSCLC, comprises around 85% of all lung cancer cases, does not progress as quickly as SCLC and is generally associated with a better prognosis [13]. Symptoms in lung cancer patients often appear late in the progression of the disease and can be confused with symptoms of much more frequent ailments such as chronic obstructive pulmonary disease (COPD) or upper respiratory infections, which can delay diagnosis [14]. This can lead to patients debuting with metastases in the lymph nodes, brain and other organs [15].

SCLC is generally divided into two stages: limited disease (LD-SCLC) and extensive disease (ED-SCLC). In LD-SCLC the primary tumour and any lung and lymph node metastases can be covered by a tolerable radiation field. Tumour burden beyond this are described as ED-SCLC and comprise over 85% of all cases. NSCLC stages are categorised according to the TNM Classification of Malignant Tumours cancer staging system. Based on this classification NSCLC can be divided into four stages depending on the extent of the disease. Stage I: the cancer is limited to the lungs and has not spread to the lymph nodes; stage II: the cancer has spread to the lymph nodes, and the tumour is larger than 5 cm (Stage IIa) or 7cm (Stage IIb); stage III: the cancer has spread considerably in the thoracic cavity and has typically reached the mediastinal lymph nodes; and stage IV: the disease has spread to both lungs, the pleural space or outside the thoracic cavity [13].

Prognosis and treatment modalities

The prognosis for lung cancer patients as a whole is poor and depends on the stage, sites of disease and comorbidity (Table 1). The one-year relative survival rate for the entire group of patients with lung cancer is 35-40%, while the five-year survival rate is 10-12%, with the longest relative survival rate in women. For operable patients with NSCLC (stage I-IIIa) a five-year survival rate of

25-60% can be achieved. In patients with inoperable NSCLC (stage IIIb-IV) the survival rate is less than 1% and the median survival rate for treated patients is 8-14 months.

Table 1: TNM-classification and expected survival in NSCLC

TNM-Classification	Stage	Five year survival (%)	Estimated distribution (%)
T1a,bN0M0	IA	40-60	25
T2aN0M0	IB	30-40	
T2bN0M0;T1a,bN1M0; T2aN1M0	IIA	30	
T2bN1M0;T3N0M0	IIB	20-30	
T1a,b,T2a,bN2M0; T3N1,N2M0;T4N0,N1M0	IIIA	10-15	
T4N2M0;T1-4N3M0	IIIB	5	10
T1-4N1-2M1	IV	1	65

With ED-SCLC the median survival rate despite an initially high response rate is less than a year, and the long-term survival rate is only a few percent. Chemotherapy and radiation therapy are used to treat LD-SCLC and the median survival rate is approximately 20 months, with 20% of the patients alive after five years [16-18].

In stage I-III, NSCLC is potentially curable with radical surgery. This requires an adequate lung function and that there is no significant comorbidity. After radical surgery, patients with stage Ib (for tumours>4 cm) or worse are offered adjuvant platinum-based chemotherapy, which has been shown to increase the number of patients who achieve long-term survival. Inoperable patients with stage III/N2 disease can be treated with a combination of chemotherapy and intentionally curative radiation therapy, given concomitantly or sequentially.

Treatment of patients with stage IIIb and IV, which represents approximately 65% of patients, is undertaken with palliative and life-prolonging aims. The choice of treatment depends on the histology, presence of certain mutations, comorbidity and general condition. Patients in good general condition are offered treatment with 4-6 cycles of platinum-based chemotherapy (cisplatin or carboplatin) in combination with several other cytotoxic agents (pemetrexed, vinorelbine, paclitaxel, docetaxel, gemcitabine or irinotecan). The composition depends, for example on whether the histology is squamous or non-squamous. In some cases the antiangiogenic antibody bevacizumab is added. When activating mutations in the epidermal growth factor receptor have been detected, the patient is offered initial treatment with tyrosine kinase inhibitor (gefitinib or

erlotinib) instead of chemotherapy, and patients with anaplastic lymphoma kinase (ALK) translocation are offered targeted treatment with an ALK inhibitor, e.g. crizotinib.
The treatment of patients with LD-SCLC is conducted with curative intent and includes chemotherapy with cis-/carboplatin combined with etoposide given concomitantly with thoracic radiation. If remission is achieved, prophylactic cranial irradiation (PCI) is offered, which reduces the risk of developing brain metastases. Surgical removal of very limited disease SCLC is only possible exceedingly rarely. The treatment can then include surgery, chemotherapy and thoracic irradiation in addition to subsequent PCI.
About 85% of patients have ED-SCLC, often with considerable morbidity, which requires rapidly implementing palliative / life-prolonging treatment with cis-/carboplatin and etoposide. If the treatment response to chemotherapy is good, PCI follows subsequently.

Symptoms of lung cancer

Patients with lung cancer often experience severe physical and psychological symptoms, such as decreased exercise capacity, muscle weakness, compromised health-related quality of life (HRQOL) and increased anxiety and depression levels, as a direct consequence of the disease or the antineoplastic therapy [19, 20]. The distress associated with symptoms from lung cancer has been reported as the most intense compared to other types of cancer, especially in patients with metastatic, incurable tumours [21, 22]. A comparison of HRQOL in lung cancer patients with that of other cancer diagnoses indicated that patients with lung cancer suffer in particular from several physical and psychosocial problems [23-25]. This was confirmed in a Danish study that focused on physical, psychological and social problems among cancer patients with a broad spectrum of diagnoses. The study showed that lung cancer patients had more symptoms and side effects, increased anxiety and depression levels and impaired HRQOL compared to patients with ten other cancer diagnoses [26]. Respiratory symptoms like dyspnoea, cough and haemoptysis are highly predominant and the cause of profound distress at the time of diagnosis and as disease progresses [27]. Pain and dyspnoea affect patients with advanced lung cancer and have a profound effect on their emotional, social and spiritual well-being [20, 28-30]. The levels of psychological distress have been reported for clinical depression, clinical anxiety and for overall emotional distress [31-35]. Additionally it has been shown that patient anxiety increases when the symptom burden is high. Physical function is impaired in advanced lung cancer [36, 37].
Patients with inoperable lung cancer generally have a strong need for supportive care, poorer physical functioning, greater symptom burden, higher levels of distress and lower satisfaction with

healthcare combined with higher levels of intrusive thoughts about cancer [38]. Furthermore, studies have shown that high levels of anxiety and depression are associated with diminished Quality of life, decreased adherence to chemotherapy and increased intensive care burden at the end of life for lung cancer patients [39-41].

Physical activity and cancer

Exercise oncology

In the late 1980s Winningham and MacVicar initially introduced physical activity / training for patients with breast cancer to reduce their nausea during treatment [1]. Numerous studies examining the effects of physical training in patients with cancer before and after treatment have been carried out since the first article was published [2, 42, 43]. Besides improving physical capacity, a reduction has also been found in nausea, pain, fatigue, anxiety and depression, in addition to increased HRQOL [2, 42, 43]. In 2006 our research group found in a non-randomised trial that six hours of intervention (nine hours weekly) comprising cardiovascular training, strength training, relaxation, massage and body awareness training were beneficial for patients with various cancer diagnoses (both with and without residual disease) who were undergoing chemotherapy [7, 44]. The effect of the intervention was confirmed in a 2009 RCT, where we found, for example a significant reduction in fatigue, as well as significant improvement in physical capacity and muscular strength [8].

Physical activity and lung cancer

Operable patients

Studies examining the effect of physical training in patients with lung cancer have mainly been conducted in patients with early-stage lung cancer (NSCLC I-III, LD-SCLC) pre and post-surgery [45-48]. The interventions have primarily involved cardiovascular training because the patients' VO_2max has been shown to be associated with the risk of postoperative complications [49, 50]. The findings indicate increased physical capacity, functional capacity and muscular capacity [47, 48], but no unambiguously significant improvements in HRQOL. An overall feature of the studies is that they included relatively few patients and they used different types of interventions (hospital-based, home-based training [47, 48]). Jones et al. [45] and Granger et al. [46] point out in their reviews of literature on patients with lung cancer that there is a lack of studies that include patients with advanced / inoperable lung cancer.

Inoperable patients

Temel et al. were the first to do a study investigating whether patients with advanced lung cancer could profit from physical training [51]. A total of 25 patients were enrolled in an eight-week intervention (2 x weekly) and 14 patients completed the intervention, which comprised cardiovascular and strength training. Apart from showing a significant increase in muscle strength in a single muscle group, their study did not show any significant changes in physical or functional capacity. The study measured HRQOL with the Functional Assessment of Cancer Therapy – Lung (FACT-L) scale and did not find any significant improvement in HRQOL, but could show significant improvement in the Lung Cancer Subscale (LCS) FACT-L. Based on this, Temel et al. concluded that future studies on this patient population ought to include less comprehensive interventions. Since their study [51] seven studies (five feasibility [52-56], including Study II in this thesis, and two RCTs [57, 58]) have examined the effect of physical training in patients with advanced lung cancer. The studies differed with regard to duration of the interventions, intensity of the training and type of training offered. Overall the studies showed, however, significant improvements in physical capacity, functional capacity and muscular capacity, but no improvement in HRQOL, anxiety or depression. These findings must be assessed with caution as substantial methodological limitations may have influenced the results. Moreover, the number of patients enrolled (n=24-46) and the number of patients who completed the interventions was limited (n=11-31). In total, the number of enrolled patients across the studies with advanced lung cancer was 164, out of which 118 were assessed (Table 2) [51-59]. There are a few studies that have examined the impact functional capacity has on the prognosis in patients with advanced lung cancer [60, 61]. In a cross-sectional study Kansymjanova et al. found that a low functional level measured using the six-minute walk distance (6MWD) 400 metres in patients with advanced lung cancer before the first cycle of chemotherapy was associated with earlier disease progression and death [60]. This study also showed that treatment with two cycles of chemotherapy reduced the functional level significantly. A comparable study by Jones et al. confirms these findings [61].

Table 2: Literature review of exercise studies with inoperable lung cancer

Author - Study design - Sample	**Type of Intervention Frequency, duration**	**Outcome**	**Results**	
			Significant	**non-significant**
Temel et al 2009 [51] Feasibility study (NSCLC III-IV) n=25 Chemotherapy N=23 Completion Rate=44% Dropout = 11	Structured cardiovascular and strength training. 2 x weekly in 8 weeks	1RM, FACT-L, HAD, 6MWT	1RM p<0,03	FACT-L, HAD 6MWD
Cheville et al 2013 [52] RCT-study 66 patients with Stage IV 34 lung cancer, 32 colon rectal. Chemotherapy Lung cancer = 10 Completion Rate=85% Dropout Intervention=7 Control=3	Incremental walking and home-based strength training intervention vs usual care 8 weeks	AM-PAC CAT AM-PAC Mobility and Activities Short Forms. FACT-L	Mobility $p=0.002$, fatigue p<0,03, Sleep quality P=0,002	Activity short form General HRQOL (FACT-G), pain
Hummler et al 2014 [54] Feasibility / descriptive study 49 NSCLC Stage IV= 16, IIIb= 1, IIIa=1, IIa=2, Ib= 2. SCLC LD=6 ED=11 Chemotherapy=34 Completion Rate=87.7% Dropout= 6	Cardiovascular and strength rehabilitation programme 8 weeks	hand-held dynamometry, 6MWT, FEV1, FACT-L, PHQ9, MFI		hand-held dynamometry, 6MWT, FEV1, FACT-L, PHQ9, MFI
Hwang et al 2012 [58] RCT-study 24 NSCLC: 2=IIIa, IIIb=2, IV=20 Chemotherapy=24 Completion rate=71.2% Dropout Intervention =2 Control=4	Cardiovascular exercise intervention supervised “one on one” vs usual care 3 x weekly in 8 weeks	VO_2peak, muscle strength, endurance, EORTC- LC13	VO_2Peak (p<0.005)	HRQOL
Kuehr et al [55] Feasibility study 40 NSCLC stage IIa-IV, IIa 2, IIIa 3, IIIb, 8; IV 27 Chemotherapy=33 Completion rate=55% Dropout = 18	Combined intervention inpatient (first 5 days) and home-based (interval walking) 8 weeks	endurance and strength capacity, FACT-L, MFI, and PHQ9, 6MWT	6MWT FACT-L score	HRQOL
Glattki et al 2012 [53] Feasibility study 47 NSCLC stage I-IV (21 with stage I-II and 26 with stage III-IV) Chemotherapy = 0 Completion rate = not described	Pulmonary and cardiovascular rehabilitation Cardiovascular 3-5 x weekly and Breathing exercise 3-4 daily in 4 weeks	6 MWD BODE index, Modified Medical Research Council dyspnoea scale.	FEV1, FVC, 6 MWD	
Henke et al 2013 [57] RCT-study 46 NSCLC IIIA/IIIB/IV Chemotherapy=46 Completion rate=63% Dropout Intervention=6 Control=9	Physiotherapeutic training - strength and endurance training vs conventional physiotherapeutic care Endurance training and breathing techniques 5 days a week, strength training 3 x weekly 9 weeks	Barthel index; EORTC QLQ-C30/LC1, 6MWT	Barthel index; 6MWT (Physical functioning, p =.025;hemoptysis, p =.019; pain in arms or shoulder, p =.048;peripheral neuropathy	

Development and testing of the intervention in patients with advanced lung cancer

This thesis is based on an intervention used in a heterogeneous group of patients with a variety of cancer diagnoses [8]. The intervention consisted of components with high-intensity cardiovascular and strength training, in addition to a low-intensity part with relaxation, massage and body awareness training. The interventions were group based on the premise that interaction between the patients and the project team and interaction between the patients would be beneficial and create positive psychosocial interactions [62, 63]. The intervention involved four days spread out over six weeks (Table 3).

Table 3: Weekly schedule "Body and Cancer"

Monday	Tuesday	Wednesday	Thursday	Friday
Cardiovascular and strength	Body awareness	Cardiovascular and strength		Cardiovascular and strength
Relaxation	Relaxation	Relaxation		Relaxation
Massage				Massage

Study I [44] describes the composition of the components in the intervention. The 2009 RCT had 269 patients enrolled with various cancer diagnoses, only a small number of whom had lung cancer (n=10). Analyses showed that the patients with lung cancer achieved the same level of improvement as the other enrolled patients. The patients with lung cancer, however, had a significantly lower VO_2max at baseline compared to the other diagnostic groups (VO_2max at baseline = 1.15 l/min (lung) vs. 2.27 l/min (other diagnoses)). The patients with lung cancer also indicated that the frequency of the training (4 x weekly) and the duration of the training (nine hours weekly) was too strenuous.

The intervention in Study II was designed to meet the patients' desire to reduce the frequency of the weekly exercise and duration. The group-based training was maintained because the patients indicated that the interaction with the project team was motivational and created a sense of safety [64, 65]. They also described how their interaction with other patients provided rewarding experiences, was supportive and facilitated participation in the training [62, 63]. The intervention comprised two supervised sessions at the hospital (2 x weekly) combined with three home-based sessions (1.5 hours weekly) for six weeks. The body awareness and massage components were not continued to reduce the number of participation days (Table 4).

Table 4: Weekly schedule Study II

Monday	Tuesday	Wednesday	Thursday	Friday
Home-based training	Cardiovascular and strength	Home-based training	Cardiovascular and strength	Home-based training
Relaxation	Relaxation	Relaxation	Relaxation	Relaxation

The intervention consisted of cardiovascular and strength training but also relaxation therapy. The intervention, described in Study II [56], was assessed in our qualitative study [66], which showed, for example that the patients were not able to carry out the home-based training component on their own and that they only wanted to do the supervised component. Study III was designed based on what we learned from these experiences.

In Study III the intervention comprised weekly supervised training sessions (two hours per session) for six weeks consisting of cardiovascular and strength training, as well as relaxation training, which was continued from Study II (Table 5) [67]. Study III describes the intervention in detail.

Table 5: Weekly schedule Study III-IV

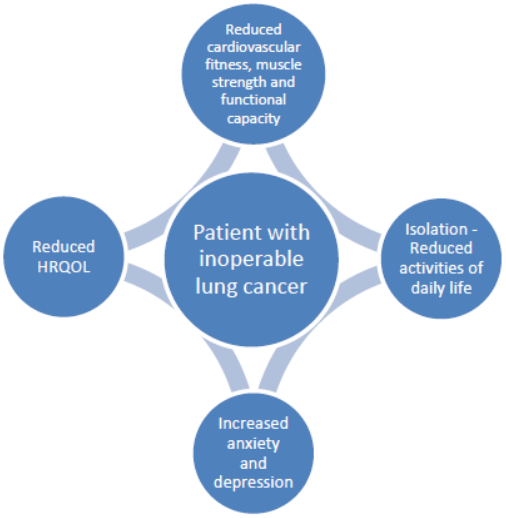
Monday	Tuesday	Wednesday	Thursday	Friday
	Cardiovascular and strength		Cardiovascular and strength	
	Relaxation		Relaxation	

The components of the intervention in Study III were maintained and have been continued in the RCT intervention in Study IV. The duration was changed from six to twelve weeks to maximise the effect of the intervention and also to make the deconditioning visible that is described as a consequence of treatment in patients with advanced lung cancer [60, 61]. The intervention is described in Study IV [68].

Theoretical inspiration and rationale

The theoretical framework of this thesis draws inspiration from exercise oncology [4]. Exercise oncology and the multiple-hit hypothesis is based on the typically inactive and unhealthy lifestyle of cancer patients, the symptoms of their disease and any side effects from treatment (chemotherapy, radiation therapy) [69]. This combination of lifestyle, symptoms and treatment reduces the patient's level of cardiovascular fitness, muscle strength and functional capacity, which

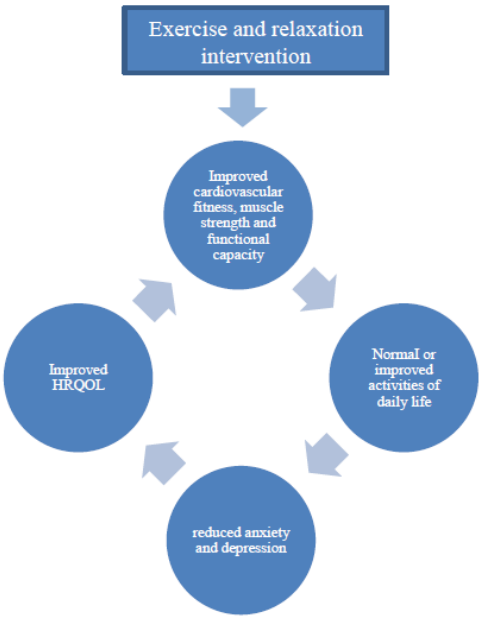
Figure 1: Model of negative spiral affecting a patient with inoperable lung cancer



affects HRQOL negatively. In addition when diagnosed with advanced lung cancer patients experience shock, increased anxiety, uncertainty and worry about the future. This contributes to patients isolating themselves and being less able to cope with daily life [69]. This negative spiral affects the patient physically and psychosocially [70] (figure 1).

A key factor in reversing this negative spiral is improving their physical capacity. Maintaining or enhancing the physical capacity can reverse the negative consequences, which means that the patient can still do what they have always been able to do, or perhaps even more. Fear and anxiety about the future can be reduced simultaneously with patients experiencing a change in their own situation. When testing physical activity, patients are taught to use fitness and relaxation as a tool to manage symptoms [71, 72] (figure 2).

Figure 2: Impact of exercise and relaxation.



AIM

The overall aim of this thesis was to investigate the effect of a physical and psychosocial intervention consisting of supervised, structured training in groups (cardiovascular and strength training, relaxation training) in patients with inoperable lung cancer undergoing chemotherapy. This thesis tests the hypothesis that a six-week exercise intervention in patients with inoperable lung cancer undergoing chemotherapy: Is feasible and safe, will increase physical capacity, functional capacity, muscle strength and HRQOL, and reduce the degree of anxiety and depression.

Specific aims

1. To investigate and evaluate the effect of a six-week physical and psychosocial programme for cancer patients with different diagnoses undergoing chemotherapy. (Study I)
2. To examine the feasibility and safety of a six-week supervised and home-based intervention for patients with advanced-stage lung cancer. (Study II)
3. To investigate the benefits of a six-week supervised and structured multimodal group exercise intervention in patients with advanced stage lung cancer undergoing chemotherapy and to outline the benefits on physical capacity, functional capacity and muscular strength. (Study III)
4. To investigate the benefits of a six-week supervised and structured multimodal group exercise intervention in patients with advanced-stage lung cancer undergoing chemotherapy and to outline the benefits on HRQOL, anxiety and depression. (Study III)
5. To develop a protocol for an RCT assessing the effects of a twelve-week, twice weekly programme consisting of supervised, structured training in a group of advanced lung cancer patients (cardiovascular and strength training, relaxation). (Study IV)

METHODS AND MATERIALS

Design

A combination of objective and subjective methods was applied in this thesis. The research in Studies I-III was based on a hypothesis-generated, prospective, clinical and explorative design, while the design in Study VI involved a RCT. Pre and post-tests were used in both designs.

Recruitment

All patients (Study I-IV) were recruited from the Department of Oncology, Rigshospitalet, University of Copenhagen. In Study I posters and leaflets at the department were used to advertise the study to patients, and upon showing an interest in participating the patients were screened by the project team [44]. To be included the patient had to be 18 to 65 years of age, have a cancer diagnosis and had to undergo chemotherapy. The patient was excluded if one of the following criteria were met: documented brain or bone metastases; anticoagulation treatment; symptomatic cardiac disease, including clinical congestive heart disease and treatment for arrhythmia or myocardial infarction within the last three months; dementia and psychotic conditions; terminal care; and the inability to read and write Danish.

In Study II-III a study nurse screened all patients for participation [56, 67]. Patients could only be enrolled if they were over 18 years of age, were diagnosed with advanced lung cancer (NSCLC IIIb-IV; ED-SCLC) and had to undergo chemotherapy. The patient was excluded if one of the following criteria were met: brain or bone metastases; prolonged bone marrow suppression; anti-coagulant treatment; symptomatic heart disease, including congestive heart failure and arrhythmia or myocardial infarction diagnosed within the last three months; and the inability to provide informed written consent. Patients were enrolled in Study IV based on the same inclusion and exclusion criteria used in Study II-III [68].

Sample

Study I

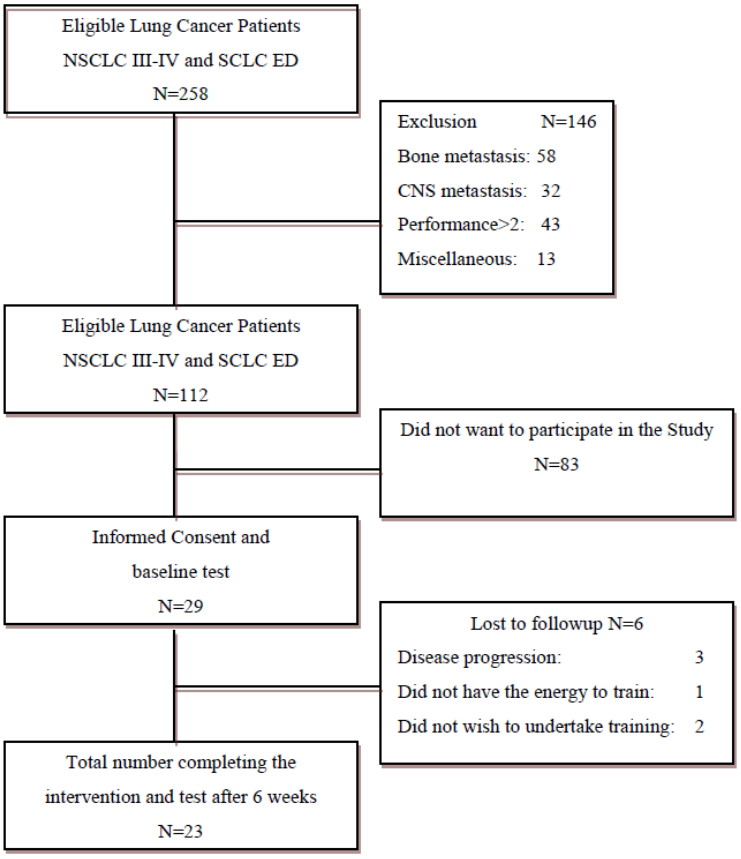
Ninety-three cancer patients were enrolled in the study from April 2001 to June 2003. Eight patients dropped out, six patients due to progressive acute illness and two because they lacked a sense of belonging to the group. Eighty-five patients completed the six-week intervention and three were excluded from the data set because their chemotherapy treatments had ended. A further 12 patients were dismissed because they did not perform test 2 (VO_2max or one repetition maximum (1RM)). A total of 70 patients (49 females, 21 males; median age 43 years) completed the programme for a completion rate of 76%. The adherence rate to the exercise sessions was 77.4%. Medical variables showed that 81% were oncological patients and 19% were haematological patients. Regarding status of the disease, 47% of the patients had evidence of remaining illness. No differences in age,

education, previous exercise history or type of treatment were observed between those who completed both tests and those who did not.

Study II

From October 2008 to December 2009, 258 patients with inoperable NSCLC were screened for eligibility (figure 3). Twenty-nine patients were included (16 females, 13 males; median age 63

Figure 3: Flow chart over eligible lung cancer patients in Study II



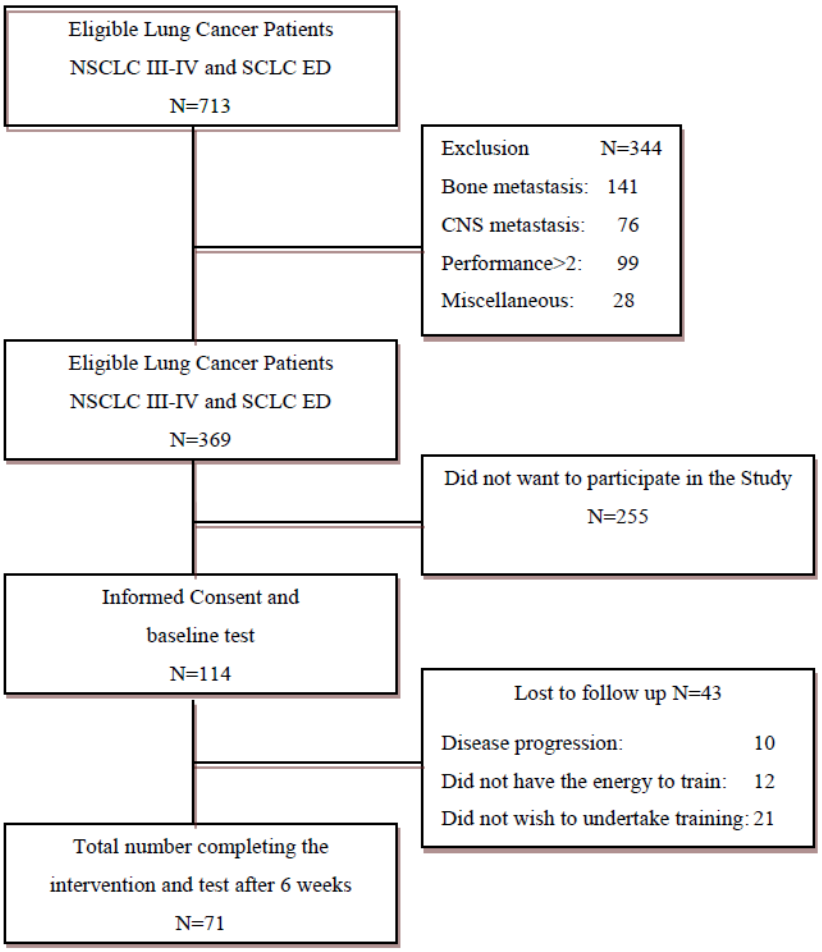
years) and all of them completed the baseline testing. Six patients (20.6%), however, did not perform the six-week test due to either a loss of motivation (n = 3) or to a decrease in performance status (n = 3). Hence, 23 patients undergoing concurrent systemic treatment were eligible for analysis.

Study III

From October 2008 to January 2012, 713 patients with inoperable NSCLC and SCLC were screened for eligibility (figure 4), 344 of whom were excluded, leaving 369 eligible patients.

With 114 patients included in the study (57 females, 57 males; median age 66), the recruitment rate was 30.8%. Patients (n=29) who were included in the feasibility study [56] were also included in this study. All 114 patients completed the baseline testing; however, 43 dropped out (37.7%) and did not perform the six-week test due to disease progression (n=10), lack of energy (n=12) or because they did not wish to participate in the training (n=21). They did not differ demographically or regarding treatment from the patients included in the analyses. Thus there were results available from 71 patients for most of the analyses. Seventy patients were available for analysis of anxiety, depression and the FACT variables.

Figure 4: Flow chart over eligible lung cancer patients in Study III



Study IV

Based on a power calculation from Study III with VO_2max as the primary outcome, 108 patients were enrolled in the intervention combined with relaxation training or in a control group that

received usual care. Because 40% of the enrolled patients in Study III dropped out from baseline to test 2 we chose to double the number of enrolled patients to 216. We also expanded the intervention from six to 12 weeks. Patients were enrolled in Study IV based on the same inclusion and exclusion criteria used in Study III. Patients with bone metastases in non-weight-bearing bones, however, were included.

Following baseline testing, patients were sequentially numbered, stratified by gender and lung cancer type (NSCLC, SCLC) and a computer programmed in the Copenhagen Trial Unit was used to randomise (equal weight 1:1) patients.

Data collection

The author of this thesis was responsible for the data collection and in charge of the exercise intervention (Study I-III). The oncology nurse specialist participated in the intervention to observe the patients, carry out the screening for exclusion and inclusion in the study and completed the pre-screening file for each exercise test and session. Any SAE and/or AE were monitored by the project team and recorded in the patient's training and screening file. Data entry and analysis were carried out by staff not involved in the intervention.

For the collection of data, a variety of assessment methods was used in accordance with each design. The data were intended to provide a broad and general view of the impact of physical training in patients with advanced lung cancer. Each of the methods was performed at baseline and repeated at the end of the intervention. In Study IV the baseline test is executed before randomisation. Table 6 provides an overview of the assessment methods.

Outcome measures

Physical capacity

A stationary ergometer (MONARK Ergomedic 839 Sweden) watt-max test was used to calculate physical capacity (VO_2max) in Study I-III. The test started with a 27-47 watt load, after which the load was increased by 5-10 watts. The test was complete when the patient could no longer maintain a momentum of rounds per minute or if the patient suddenly became pale, experienced dizziness, a cold sweat or had a sudden change in heart rhythm. The load achieved (maximal power output (MPO)) was used to calculate the estimated VO_2max = 0.16 + (0.00117×MPO) and was expressed in l/min [73].

In Study IV, VO_2max is assessed with a physical capacity incremental watt-max test on a cycle ergometer (MONARK, Ergomedic 839 Sweden). The watt-max test is carried out by a physiotherapist who is blinded to the patient's study group allocation. The test consists of a warm-up phase comprising 2-4 minutes of cycling at a sub-maximal load (10–50 watts). After the warm-up period the load increases after a short break (<2 minutes) by 5-10 watts every minute until exhaustion or a possible symptom limitation (e.g. dizziness, sudden pain, nausea). Expired gases are analysed continuously by a metabolic breath-by-breath analysis and calculated as an average over 15 seconds using the Oxycon Pro, Jaeger measurement system Germany. During the watt-max test, oxyhemoglobin saturation and heart rate (HR) are continuously monitored. After each test, maximum ventilation and the respiratory exchange ratio (RER) possibly plateau in the increase inVO_2max, self-perceived exertion perception in the final seconds of the watt-max test and maximal HR (Polar Team System 2, Polar, Finland) are recorded. Rating of perceived exertion is evaluated at the end of each work load using the modified Borg Scale. The primary outcome will be a comparison of VO_2 peak in the intervention and control arms at the conclusion of the intervention (i.e. at the 12-week assessment).

Muscular strength

Muscle strength is measured by the 1RM [74] test using a Technogym™ that includes a leg press (lower extremity), chest press (pectoral muscles), lateral machine (latissimus dorsi), leg extension (quadriceps femoris), abdominal crunch (rectus abdominis) and lower back press (erector spinae). Prior to each test patients have time to familiarise themselves with each machine. The 1RM test has been found to be a reliable assessment for measuring upper and lower extremity strength [74]. In Study IV the 1RM test is carried out by a physiotherapist who is blinded to the patient's study group allocation.

Functional capacity

Functional capacity is measured by a 6MWD test in study II-IV carried out over a pre-measured distance of 20 meters, in compliance with the American Thoracic Society (ATS) [75]. The 6MWD test has demonstrated good reliability and validity in Chronic Obstructive Pulmonary Disease (COPD) patients, who are similar to patients with lung cancer with regard to disease pathophysiology and symptomatology [76]. A physiotherapist blinded to the patient's study group carried out the 6MWD in Study IV.

Lung capacity

Forced expiratory volume in 1 second (FEV1) was measured using a Piko-meter (piko-6, Ferraris Respiratory) in Study II-III. In Study IV, the Oxycon Pro, Jaeger measurement system Germany is used. FEV1 is carried out by a physiotherapist blinded to the patients's group allocation.

The Functional Assessment of Cancer Therapy – Lung (FACT-L)

FACT version 4 was used to evaluate HRQOL and cancer-related symptoms in Study II-IV [77]. FACT-General (FACT-G), which measures multiple dimensions of HRQOL for the previous seven days, is a 26-item questionnaire in which patients rate their physical well-being (PWB),functional well-being (FWB), emotional well-being (EWB) and social well-being (SWB) on a five-point Likert scale ranging from zero to four. FACT-L consists of the FACT-G and a LCS FACT-L that addresses seven symptoms specific to lung cancer, including cough, shortness of breath and thoracic discomfort. The reliability and validity of FACT-L has been documented in patients with lung cancer [78].

The Hospital Anxiety and Depression Scale (HADS)

Used to measure anxiety and depression in Study II-IV, HADS is a 14-item questionnaire comprising two scales, one covering anxiety (HADS-A) and the other depression (HADS-D). HAD-A (seven items) measures generalised autonomic anxiety and indicates physiological and emotional states characterised by high muscle tension and strong feelings of subconscious, uncontrollable fear or anger. HADS-D (seven items) measures anhedonia, which is the complete inability to experience pleasure. Each item is scored on a four-point Likert scale [79].

Medical Outcomes Study: 36-Item Short Form Health Survey (MOS SF-36)

Used in Study IV to measure general well-being [80], MOS SF-36 contains eight scales measuring general health concepts: limitations in physical activities because of health problems; limitations in social activities because of physical or emotional problems; limitations in usual role activities because of physical health problems; bodily pain; general mental health; limitations in usual role activities because of emotional problems; vitality and general health perceptions.

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30 - LC13)

Used in Study IV to measure QOL in lung cancer patients, EORTC QLQ-C30 - LC13 is composed of both multi-item and single-item measures that include functional scales (physical role and

emotional, cognitive and social functioning); three symptom scales (fatigue, nausea and vomiting), a global health status / QOL scale; and six single items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties). The range of measurement for all of the scales and single-item measures is 0-100, with a high score representing a higher response level [81].

Pittsburgh Sleep Quality Index (PSQI)

Used in Study IV to measure self-reported sleep quality and disturbances during the previous four weeks, PSQI was developed and tested in subjects with good sleep (control group) and subjects with poor sleep and depressive symptoms [82]. PSQI contains 19 items and measures seven components of sleep: subjective sleep quality, sleep latency, sleep duration, sleep disturbances, use of sleeping medication, habitual sleep efficiency and daytime dysfunction. The component scores are combined for one global score, which distinguishes good sleep (PSQI ≤ 5) from poor sleep (PSQI > 5).

Demographic and clinical variables

Demographic data such as gender, age, employment, smoking and alcohol consumption and data on social support and network (multidimensional scale of perceived social support) were obtained using a structured self-developed questionnaire. Medical data (diagnosis, chemotherapy regime) were drawn from the patients' medical records. A self-developed patient exercise diary was used in Study II to register home-based training.

Table 6: Overview of the assessment methods in study I-IV

Variables	Assessments methods	Study I	Study II	Study III	Study IV	
					Baseline	Post-test
Physical capacity	VO_2max	X	X	X	X	X
	Patient exercise diary		X			
Functional capacity	6 MWD		X	X	X	X
	Patient exercise diary		X			
Muskular strength	1RM	X	X	X	X	X
	Patient exercise diary		X			
Lung Capacity	FEV1		X	X	X	X
HRQOL	FACT-L		X	X	X	X
	EORTC-QLQ-C30- LC13				X	X
	SF36				X	X
Anxiety and Depression	HADs		X	X	X	X
Sleep quality	PSQI				X	X
Social support	Questionnaire				X	X
Demographic and clinical	Medical records	X	X	X	X	X
	Questionnaire	X	X	X	X	X

Data analysis

All statistical analyses were carried out in collaboration with a statistician (Anders Tveteraas, University Hospitals Centre for Health Research in Study I, and Karl B. Christensen, associate professor, Department of Biostatistics, University of Copenhagen, in Study II-IV). Data were entered onto spreadsheets (Excel, Microsoft, USA) (Study I-III). Descriptive statistics and paired sample t-tests were computed using SPSS 11.0 for Windows and statistical analysis software. OpenClinica is being used in Study IV for data entry. The statistician prepared results without knowledge of the randomisation coding. The significance level was set at $p<0.05$.

In Study I and Study II paired t-tests were used to compare scores for physical capacity, muscular strength, functional capacity and FACT-L at baseline and after the intervention. The values are expressed as mean ± standard deviation (SD) [44, 56].

In Study III [67] baseline values of the study population were compared to baseline values in the subgroup (dropout) for whom measurements were not obtained at follow-up, for each of the following variables: aerobic capacity, muscle strength, functional capacity, lung capacity and for each subscale of FACT and HADS. Independent sample t-tests were used for this purpose.

The variables are reported as means and SD at baseline and at follow-up, respectively.

The effect of the intervention is reported as change scores with corresponding 95% confidence intervals (CI) and the groups (completer and dropout) were compared using independent samples t-tests. The effect of the intervention was examined using a linear mixed model taking into account the effect of gender, age, marital status, smoking and cancer stage.

Effect sizes were estimated using Cohen's guidelines, whereby a value of 0.2 denotes a small, 0.5 a medium, and 0.8 a large effect size [83]. Effect size was calculated as the mean difference divided by the pooled baseline SD and the root mean square error estimated from the general linear model.

In Study IV the sample size calculation for the primary outcome VO_2 peak is based on earlier data, where 55 patients who participated in six weeks of training achieved an increase of 0.85 ml/kg/min (SD=2.48) [56, 68]. It is assumed that patients in the control group of the current study will have a reduction of 0.5 ml/kg/min for VO_2 peak and thus a total of 108 patients (54 in each arm) will be sufficient to achieve a power of 80% (risk of type 2 error set at 0.20) using a significance level of 0.05 (risk of type 1 error set at 0.05). We expect a dropout rate of 50%, which is why another 108 patients must be included, yielding a sample size of 216 patients. The primary endpoint will be

reported as a two-sample t-test comparing change scores in the two randomisation groups. The patient-reported outcomes (PRO) will be reported as either means with corresponding 95% confidence limits or as medians interquartile range for continuous data. Categorical data will be reported as proportions and compared across randomisation groups using chi-squared tests.

ETHICAL CONSIDERATIONS

Physical training is not presently routinely offered to patients with inoperable lung cancer, which is why no patients will be hindered from receiving what is currently the best option. Participation in the intervention or the control group did not prevent the patients from participating in other physical activities. The stressful treatment regime and reduced QOL of lung cancer patients indicate that specific, broad-spectrum programmes need to be developed and tested that are aimed at meeting the specific needs of lung cancer patients. Our goal is to strengthen the physical capacity, well-being, energy and QOL of lung cancer patients throughout the trajectory of the disease and treatment. Overall the findings will contribute new knowledge that can be applied to lung cancer patients.
The study is registered with Clinicaltrials.gov, registration no. NCT01881906. Ethics approval has been obtained from the scientific Ethics Review Committee for the Capital Region of Denmark Study I (J.no.01–273/00), Study II-III-IV (file no. HA-2008-06). Study I was approved by the Danish Data Protection Agency (J.no.2000-41-0-149) and Study II-III-IV is approved under file no. 2008-41-2279. In addition the studies were carried out in accordance with the second Declaration of Helsinki II and patients provided informed oral and written consent in compliance with the requirements of the ethics committee.

RESULTS

High-intensity resistance and cardiovascular training improve physical capacity in cancer patients undergoing chemotherapy (Study I)

The aim of Study I was to investigate the impact of a six-week, nine-hour weekly intervention that included high-intensity cardiovascular and strength training. The hypothesis was that the intervention would increase physical capacity (VO_2max) and muscle strength (1RM) in cancer patients with various diagnoses and stages of the disease and who were concurrently undergoing chemotherapy [44]. We found significant increases in physical capacity (p<0.001) and muscular strength: chest press (p<0.001), leg press (p<0.001) and lateral machine (p<0.001) (Table 7).

Table 7: Physical capacity and Muscular strength in Study I

Variables (n=70)	Base Mean (SD)	Post Mean (SD)	*p* value
VO_2max (L/min)	2.27 (0.59)	2.56 (0.64)	< 0.001
Muscular strength			
Legpress (Kg)	100.8 (26.9)	142.9 (36.6)	< 0.001
Chestpress (Kg)	42.6 (17.1)	55.5 (18.6)	< 0.001
Lat machine (Kg)	46 (16.9)	59.3 (17.6)	< 0.001

Furthermore we found no serious adverse events (SAE); however, during daily screening procedures, seven patients were excluded at various times from the exercise training component (three patients: one on three occasions; three patients: three on eight occasions; and one patient on eight to 11 occasions) throughout the program because of fever, infection requiring treatment, and/or risk of bleeding. In accordance with the daily exclusion criteria, no patient who participated in the exercise training component suffered from marrow toxicity with thrombocytes <50 bn/l and/or leukocytes <1.0 bn/l. The patients did not show any signs of unintentional physical reaction, cardiac or respiratory arrest or hypotension. Two patients pulled their hamstrings and one patient had a scraped knee.

Safety and feasibility of a combined exercise intervention for inoperable lung cancer patients undergoing chemotherapy: A pilot study (Study II)

The aim of Study II was to investigate the impact on aerobic capacity (VO_2 max), muscle strength (1RM) and HRQOL) in patients with lung cancer (NSCLC stage III–IV and ED-SCLC) undergoing a six-week hospital-based, supervised and structured, muscle-cardiovascular-relaxation training programme and a home-based exercise programme while undergoing chemotherapy.

Home-based training

Implementation, safety and adherence

Two patients completed the training diaries used to monitor home-based training. Twenty-one patients did not do the home-based training programme, leading to a participation rate of 8.7%. No SAE or AE were reported.

Intervention

Physical capacity, functional capacity and muscular strength

Table 8 shows the results of physical capacity, functional capacity and muscular strength after the six-week programme. There was a significant increase in physical capacity (VO_2 peak (p=0.014))

and functional capacity (6MWD (p=0.006)). There was significant improvement in strength: leg press (p<0.001), chest press (p<0.001), lateral machine (p=0.049), abdominal crunch (p<0.001), lower back (p<0.001) and leg extension (p<0.001).

Table 8: Physical capacity, functional capacity and muscular strength in study II

Variable (n=23)	Base Mean (SD)	Post Mean (SD)	Change (95 % CI)	*P value*
BMI	25.1 (5.0)	25.3 (4.8)	0.2 (-0.3 to 0.5)	0.076
Lung Capacity				
FEV1	1.76 (0.70)	1.96 (0.63)	0.20 (-0.01 to 0.41)	0.061
Aerobic capacity				
VO_{2peak} (L/min)	1.48 (0.41)	1.57 (0,41)	0.09 (0.02 to 0.16)	0.014
Functional capacity				
6 MWD (m)	524.7 (88.5)	564.0 (88.6)	39.3 (12.5 to 66.1)	0.006
Muscular strength				
Leg press (Kg)	70.4 (26.9)	86.9 (28.8)	16.5 (11.5 to 21.7)	0.000
Chest press (Kg)	30.8 (13.2)	40.3 (16.3)	9.5 (6.4 to 12.7)	0.000
Lat machine (Kg)	35.8 (13.8)	39.2 (17.6)	3.4 (0.0 to 6.7)	0.049
Abdominal crunch (Kg)	24.9 (10.7)	29.5 (11.3)	4.6 (3.2 to 6.0)	0.000
Lower back (Kg)	35.3 (14.1)	43.1 (16.2)	7.8 (4.8 to 10.8)	0.000
Leg Extension (Kg)	38.6 (15.5)	45.1 (18.9)	6.5 (4.1 to 8.9)	0.000

Quality of life

HRQOL results are shown in Table 9. There was a significant change in the parameter for EWB (p=0.025) and a moderate effect size of 0.38 when comparing baseline to the six-week evaluation. However, there were no significant improvements in general HRQOL, or FACT-L subscales (i.e. PWB, EWB, FWB, SWB and LCS).

Table 9: Functional Assessment of Cancer Therapy (FACT-L) in Study II

Variable (N=23)	Baseline Mean (SD)	Follow-up Mean (SD)	change (95% CI)	P value
FACT-L Total score	91.7 (16.7)	94,3 (14.2)	2.6 (-4,2 to 9.4)	0.452
Physical Well-being	20.3 (5.0)	20.3 (4,0)	0.0 (-2.1 to 2.2)	0.973
Social Well-being	22.9 (3.6)	21.8 (5.4)	-1.1 (-2.8 to 0.6) 2,83	0.182
Functional well-being	15.9 (6.5)	16.0 (5.1)	0.1 (-2.3 to 2.4)	0.940
Emotional well-being	14.3 (4.7)	16.1 (4.3)	1.8 (0.3 to 3.4)	0.025
Lung cancer subscale	18.3 (4.6)	20.1 (2.9)	1.8 (0.4 to 4.0)	0.099
Trial outcome index	54.5 (11.8)	56.4 (9.8)	1.9 (-3.2 to 7.0)	0.442
FACT fatigue scale	73.4 (14.2)	74.2 (12.4)	0.8 (4.7 to 6.1)	0.780

Safety

During the pre-screening process before the supervised training, 2 patients were excluded from one physical training component, due to fever (38.3 ◦C) and dizziness (B-haemoglobin5.2×10^9/l). No patients showed spontaneous or unexpected reactions (e.g. heart or respiratory stop, hypotension, etc.) during the supervised training or AE.

The impact of a multidimensional exercise intervention on physical and functional capacity, anxiety and depression in patients with advanced-stage lung cancer undergoing chemotherapy (Study III)

The aim of study III was to investigate the benefits of a six-week supervised and structured multimodal group exercise intervention in patients with advanced-stage lung cancer undergoing chemotherapy and to outline the benefits on aerobic capacity, muscle strength, HRQOL, anxiety and depression.

Physical capacity and functional capacity

Table 10 shows the results of physical -, functional capacity and muscular strength after the six-week program. There was a significant increase in physical capacity, VO_2max (p<0.0001, effect size 0.22) and functional capacity, 6MWD (p<0.0001, effect size 0.27). There was a significant improvement in strength: Leg press (p<0.0001, effect size 0.46); chest press (p<0.0001, effect size 0.35); lateral machine (p=0.0063, effect size 0.13); leg extension (p<0.0001, effect size 0.31); abdominal crunch (p<0.0001, effect size 0.47); and lower back press (p<0.0001, effect size 0.36).

Table 10: Physical capacity, functional capacity and muscular strength in Study III

Variable (n=71)	Baseline	Post	Change score	
	Mean (SD)	Mean (SD)	(95 % CI)	*P value*
BMI	24.7 (3.8)	24.8 (3.8)	0.08 (-0.06 to 0.22)	0.2578
Lung Capacity				
FEV_1 (L/sec)	1.9 (0.7)	1.9 (0.7)	-0.08 (-0.08 to 0.16)	0.5080
Aerobic capacity				
VO_{2peak} (L/min)	1.3 (0.4)	1.4 (0.5)	0.08 (0.04 to 0.12)	0.0003
Functional capacity				
6 MWD (m)	527.4 (121.5)	561 (124.7)	33.6 (20.3 to 47.0)	<0.0001
Muscle strength				
Leg press (Kg)	71.5 (30.2)	86.1 (32.8)	14.5 (11.6 to 17.4)	<0.0001
Chest press (Kg)	29.3 (13.4)	34.5 (15.8)	5.2 (3.7 to 6.7)	<0.0001
Lat machine (Kg)	34.6 (13.3)	36.5 (15.0)	1.9 (0.6 to 3.3)	0.0063
Abdominal crunch	35.5 (13.5)	42.2 (15.7)	6.7 (5.3 to 8.2)	<0.0001
Lower back (Kg)	37.5 (14.7)	43.3 (16.7)	5.9 (4.4 to 7.3)	<0.0001
Leg Extension (Kg)	24.9 (9.9)	28.3 (11.5)	3.4 (2.5 to 4.3)	<0.0001

Anxiety and depression

There was a statistically significant reduction in anxiety score (p=0.0075, effect size 0.21) from baseline to six weeks with a reduced anxiety score of –0.9 points. There was no significant reduction in depression (p=0.0755, effect size 0.16).

Table 11: Hospital Anxiety and Depression Scale (HADS) in Study III

Variable (N=70)	Baseline	Post	Change score	
	Mean (SD)	Mean (SD)	(95 % CI)	*P value*
Anxiety (HADS-A)	7.2 (4.4)	6.3 (4.2)	-0.9 (-1.55 to -0.25)	0.0070
Depression (HADS-D)	5.3 (3.8)	4.7 (3.5)	-0.59 (-1.23 to 0.06)	0.0755

Quality of life

Table 12 presents the HRQOL results. There was a significant change in the EWB parameter (p<0.0001, effect size 0.29) when comparing baseline to the six-week evaluation and a significant decrease in SWB (p=0.0036, effect size 0.24). There was no significant improvement or decline, however, in general HRQOL, fatigue, or on the FACT-L subscales (i.e. PWB, FWB, EWB, SWB and LCS).

Table 12: Functional Assessment of Cancer Therapy (FACT-L) in Study III

Variable (N=70)	Baseline	Post	change score	
	Mean (SD)	Mean (SD)	(95 % CI)	*P value*
FACT-L Total score	94.4 (18.9)	96.0 (18.4)	1.60 (-1.34 to 1.62)	0.2815
Physical Well-being	20.4 (5.0)	20.8 (4.9)	0.36 (-0.78 to 1.5)	0.5314
Social Well-being	23.9 (4.5)	22.7 (5.4)	-1.22 (-2.03 to -0.41)	<0.0001
Functional well-being	16.5 (5.9)	17.0 (5.5)	0.50 (-0.46 to 1.46)	0.3031
Emotional well-being	15.2 (5.0)	16.6 (4.4)	1.44 (0.75 to 2.13)	0.0036
Lung cancer subscale	18.4 (4.8)	18.9 (4.6)	0.52 (-0.41 to 1.46)	0.2683
Trial outcome index	55.3 (13)	56.7 (12.8)	1.38 (-0.96 to 3.72)	0.2422

Adverse events

No SAE were reported, but during the pre-screening process before the supervised training, 10 patients were excluded from the physical training component (one to two exercise sessions out of twelve) due to fever, dizziness, pain or bodily discomfort.

EXHALE: Exercise as a strategy for rehabilitation in advanced-stage lung cancer patients: A randomised clinical trial comparing the effects of 12 weeks' supervised exercise intervention versus usual care for advanced-stage lung cancer patients (Study IV)

At present (February 2015), 139 patients with inoperable lung cancer have finished the baseline test and have been randomised in Study IV. Seventy patients (35 women and 35 men; average age 67 in an age range of 40-84) have been allocated to the exercise intervention. Sixty-eight patients have been allocated to the control group (33 women and 35 men; average age of 65 in an age range of 45-81). No SAE or AE during the exercise intervention have been reported to date.

DISCUSSION

Discussion of findings

Safety and feasibility

Study II of this thesis confirms that training is safe and feasible for patients with inoperable lung cancer. This is consistent with other similar studies [51-58].

Safety

During Study II and III we did not find any exercise-related SAE or AE [56], which is in line with other published studies [54, 55]. Studies by Temel et al. and Glattki et al. do not describe any information about SAE or AE [51, 53]. There are several factors that can affect the number of exercise-related SAE and AE for this patient population: pre-screening prior to test and the exercise sessions (disease burden); side effects from treatment; supervised vs. home-based training; and intensity of training.

In order to prevent SAE and AE it is important to screen patients who participate in exercise. In addition to any exclusion criteria, it is important to evaluate the individual patient before each exercise / test session. In Study we tested whether pre-screening I [44], inspired by Winningham et al. [1], before each exercise session and test session could prevent or reduce the risk of exercise-related SAE and AE in a heterogeneous group of cancer patients. Pre-screening was carried out by a study nurse who also participated in the daily training. During the pre-screening patients were excluded from the daily training if the following criteria were met: temperature >38; diastolic blood pressure <45 or >110; resting HR <110; infection requiring treatment; leukocytes <1 bn/l; and platelets < 50 bn/l. The pre-screening procedure is described in Study I [44].We found that pre-screening was a useful tool for detection and prevention to reduce the risk of SAE and AE. Both the pre-screening and observation carried out by the nurse during training have been shown to have a positive impact on the patients' sense of safety during tests and exercise [64, 84]. This model has also been applied in Study II, III and IV. Like Study II other studies have also used pre-screening procedure before exercise and test sessions [51, 55-58].

Similar to Study II [56], the training of patients with advanced, inoperable lung cancer (IIIa-IV) is used by Temel et al., Cheville et al., Hwang et al. and Henke et al. [51, 52, 57, 58]. The other studies have included patients with lung cancer in various stages (I-IV) [53, 54].

Whether patients trained under supervised conditions or not played a role in the reporting of SAE and AE. The probability of acute injures being reported is likely to be significantly higher under supervised conditions than if the patient trains at home. As mentioned previously, the study nurse participated the supervised training in Study II. The training programme in the intervention in Study II comprised a combination of supervised training and training at home. During home-based training patients were to contact exercise team immediately if there were any SAE, and if there were any AE they were to record them in order to report them the next time they came in for supervised training. Adherence to home-based training was low (8.7%) in our study. This is in

contrast to studies by Cheville et al. and Kuehr et al. [52, 55], which are the only studies that have used home-based training for this group of patients. In Cheville et al.'s study, which had an adherence of 85%, project staff contacted the patients every other week and asked about pain, neurological symptoms, fatigue and other problems related to the training programme [52]. In Kuehr et al.'s study, which had an adherence of 77%, the patients had to provide an assessment of their current pain, fatigue, emotional status and nausea on a visual analogue scale (VAS) after each training session [55].

The training intensity is likely to have an impact on the number of SAE and AE because the intensity of the training is related to the strain the body is put under. In Study I we evaluated a training intervention in a heterogeneous group of cancer patients that also included the intensity at which the patients could train. We found that high-intensity interval training does not provoke SAE or AE. This type of training was used in Study II, III and IV. The training intensities specified in the published studies vary greatly, but regardless of the training intensity, no SAE or AE are reported. The intensity of the cardiovascular training varied from 85-95% of the maximal HR to 50-80% of the maximal HR [51, 56-58]. The remaining studies do not specify the intensity [52, 54, 55]. The variation in intensity in these studies is also significant for strength training and is from 70-90% to 50-60% of their maximal strength [51, 56, 57]). The remaining studies either did not specify the intensity or they did not have a strength component in the intervention [52-55].

Based on Study II and the published studies [51-58], the findings indicate that patients with inoperable lung cancer can safely participate in interventions with training. The published studies, however, differ with regard to training intensity, number of components in the training (cardiovascular or strength), supervised training versus home-based training, and the use of chemotherapy. None of the above studies provide an explicit account of the presence of SAE [51-58] .

Feasibility

In Study II the completion rate was 73% [56]. In the published studies there is a significant variation in completion rate from 44% in Temel et al. to 85% in Cheville et al. [51-54, 57-59]. Studies by Hummler et al. and Glattki et al. do not specify the completion rate [53, 54]. The total number of patients enrolled in the published studies [51-58], including patients with lung cancer in the earlier stages (I-III) and 32 patients with colon cancer from Cheville et al.'s study, is 326 [52, 54, 55]. Hummler et al. and Glattki et al., however, do not provide dropout and completion rates [53, 54]. This brings the number of enrolled patients where dropouts are reported down to 230.

There were 68 patients who dropped out of the interventions for the following reasons: death (14); worsening of the disease (37); pneumonia (2); pain (2); lack of motivation (13); changes residence (8). The mean completion rate for all of the studies was approximately 68%, which is slightly below the level intervention studies have shown from previous studies of patients with other cancer diagnoses.

Physical capacity, functional capacity and muscle strength

Physical capacity

Because patients enrolled in Study II are also included in data from Study III, the results for the physiological outcomes (physical capacity, functional capacity and muscle strength) will be discussed in relation to Study III.

In Study III the enrolled patients achieved a significant increase in VO_2max (p=0.0003) of 0.1 l/O_2/min This is comparable to a study by Hwang et al., where the intervention group achieved a significant improvement (p=0.005) of 1.7 ml/O_2/min/kg compared to the control group, which experienced a decrease of 0.4 ml/O_2/min/kg [58]. Only Study III and Hwang et al.'s study used VO_2max as an outcome [58, 67]. In the Hwang et al. study, patients with inoperable lung cancer were randomised to an eight-week (3 x weekly) exercise intervention comprising 30-40 minutes of walking or bike training at 80% of VO_2max or to a control group where patients could receive instruction with a resistance band if desired. Even though the Hwang et al. study is an RCT, their results must be assessed with caution as a selection bias cannot be excluded [58]. After randomisation, where 12 patients were assigned to each group, two patients from the control group were moved to the intervention group upon their request and one patient was moved from the intervention group to the control group. The training intensity in both studies was 80-90% of VO_2max. Study III and Hwang et al.'s study indicates that it is likely that six to eight weeks of cardiovascular training has an effect on VO_2max [58]. This finding should be tested in a larger population of inoperable lung cancer patients in a randomised design [68].

Functional capacity

Patients in Study III achieved significant improvement in the 6MWD (p<0.0001) of 33 metre (m), which is comparable to other studies in which 6MWD was measured [51, 53, 55, 57]. Temel et al. showed average improvement (from 410 to 435 m), which was not significantly different compared to the control group [51]. However, studies by Henke et al., Glattki et al. and Kuehr et al. found significant improvement in the 6MWD [53, 55, 57]. In an RCT, Henke et al. found an increase of

19 m in the intervention group and a decrease of 47 m in the control group [57]. In this case, however, there is a significant difference in baseline values between the two groups, 378 m vs. 240 m respectively. In a study by Glattki et al. the patients achieved the largest increase, 41 m, and in a study by Kuehr et al. they achieved an increase of 32 m[53, 55]. When the baseline values in the five studies are compared, the baseline value (527 m) of patients in Study III is higher than in the other studies. This could be a result of all our patients being eligible for chemotherapy, which means their WHO - performance status was either 0 or 1.We excluded patients with bone and brain metastases, and comorbidities such as clinically symptomatic heart disease and myocardial infarction within the past three months, which corresponds to exclusion in most of the other studies [51, 53, 55, 57]. Henke et al., however, did not mention, for example whether or not patients with bone and brain metastases were excluded [57].

Based on the findings from Study III and the other studies published [53, 55, 57], it can be concluded that patients with inoperable lung cancer can increase their functional capacity with physical training concomitant with cytotoxic treatment. This could potentially have clinical significance because studies have found that patients with inoperable lung cancer who have a high functional level live significantly longer than patients with a low functional level. Randomised trials are necessary to clarify this [60, 61].

Muscle strength

Study III shows a significant increase ($p<0.05$) in all muscle groups, which is consistent with other studies using this group of patients [51, 55, 57]. These studies, however, exercise and measure in different ways. In Study III and in a study by Temel et al., patients trained on strength training machines based on 1RM measurements [51]. In studies by Henke et al. and Kuehr et al., patients trained using different strength resistance bands [55, 57]. Kuehr et al. measured strength using a hand-held dynamometer [55], while Henke et al. assessed strength based on the number of repetitions completed for each exercise [57].

In contrast to Study III, where there was a significant increase in all muscle groups, Temel et al. only found a significant increase ($p<0.05$) in one muscle group (elbow extension) [51]. A probable explanation for this difference could be that the patients in Study III trained at 70-90% of 1RM, while patients in the Temel et al. study trained at 60% of 1RM [51].

Kuehr et al.'s [55] study showed a significant increase in all muscle groups ($p<0.05$). Patients were measured with a handheld dynamometer and trained for eight weeks, where the first week of

intervention was supervised during the patient's hospitalisation and the remaining seven weeks of training took place at home.

Henke et al.'s study is the only one out of the four mentioned that is randomised [57]. The patients were randomised either to the intervention group, which walked, did stair workouts and strength training, or to the control group, which did conventional physical therapy if the patient had been referred for that. The period of intervention began the day the patient received chemotherapy for the first time and ended after the third cycle of chemotherapy. The patients in the intervention group achieved significantly increased strength (p <0.05) compared to the control group for two of the four exercises (bridging, abdominal). The control group had a significant decrease in all exercises (p<0.05). There were significant differences between the two groups as the control group had significantly lower baseline values than the intervention group.

The findings from the above-mentioned studies show that 1) patients with inoperable lung cancer can improve their strength with strength training and that 2) patients who do not strength train lose strength during three chemotherapy cycles [57]. Collins et al. point out in a systematic review a prevalence of sarcopenia (loss of muscle mass) in patients with lung cancer and found that it frequently occurred regardless of the patient's body mass index and was associated with poorer physical function and survival [85]. This could indicate that strength training in this patient population has a beneficial effect. This relationship is explored in Study IV.

Anxiety and depression

In Study III the enrolled patients with inoperable lung cancer reduced their symptoms of anxiety (p=0.007), while symptoms of depression did not show a significant reduction (p=0.07). This finding is in part in contrast to Temel et al.'s study, which did not find a significant reduction in either anxiety or depression [51].

One possible explanation for the reduced symptoms of anxiety in Study III is that there may be an association between experiencing an improvement in both physical and functional capacity. The assumption can be made that the patients who consented to participating in an intervention like Study III had the belief that the intervention would improve their level of cardiovascular fitness, functional level and muscle strength. When this expectation is met, patients change their perception of their own situation. This is supported by a our qualitative interview study conducted among the patient population enrolled in Study II [66]. The patients emphasised, for example that they had signed up for the programme to improve their poor physical fitness.

Another possible explanation in the reduction of patient symptoms of anxiety in Study III is that the patients who were part of the intervention participated in relaxation training, which has been shown to reduce symptoms of anxiety and depression in various cancer patient populations [86-88]. There are several studies that have shown that an increase in anxiety and depression in patients with inoperable lung cancer is associated with impaired HRQOL, poor prognosis, decreased adherence to treatment and reduced survival [39, 89, 90]. The prognostic implications of our findings in Study III are being examined in the randomised Study IV [68].

Quality of life

Study III did not find a significant improvement in the overall HRQOL (total FACT-L score), which is consistent with the other exercise studies in patients with inoperable lung cancer [51, 55, 57, 58]. One reason for the lack of progress in HRQOL in patients with inoperable lung cancer may be that shortly prior to the intervention patients are informed upon diagnosis that the disease is incurable. With this knowledge in mind, it is perhaps unrealistic for the patient to experience that six weeks of exercise intervention will improve HRQOL.

Study III showed a significant improvement in the EWB parameter (p=0.003) and a significant reduction in the SWB parameter (p<0.001). This is in line with Temel et al., Henke et al. and Kuehr et al., who also found significant changes in the individual parameters in the questionnaires used (FACT-L, EORTC QLQ-C30 - LC13) [51, 55, 57]. Temel et al. found significant improvement in the LCS FACT-L parameters (p<0.05) and Henke et al. found improvement in physical functioning (p=0.025); haemoptysis (p=0.019); pain in arms or shoulder (p=0.048); peripheral neuropathy (p=0.050); and cognitive functioning (p=0.050) (EORTC QLQ-C30 - LC13) [51, 57]. In addition, Kuehr et al. found a significant reduction in the total FACT-L score (p=0.03), while Hwang et al. did not find significant changes (EORTC-QLQ-LC13) [55, 58].

We found significant improvement in the EWB parameter, which comprises six items that are directed at the patients' belief in their own ability to deal with their illness, as well as concerns related to worsening of the disease and death. This indicates that patients strengthen their ability to cope with their own situation, which is in keeping with Gralla et al., who examined the concerns that had the greatest impact on HRQOL in a cross-sectional study of 660 lung cancer patients [91]. The most prevalent concern was the fear of losing independence and not being able to perform daily activities. In Study III, the enrolled patients improved their level of fitness, functionality and strength significantly, which is likely what makes it possible to maintain normal function. This is also supported by a our qualitative interview study of the patient population included in Study II,

which showed that patients participated in the training to allow them to do something about symptoms they felt affected their daily lives [66].

A negative finding in Study III was that enrolled patients had a reduction in SWB, which is covered by seven items directed at the patient's relationships with family and friends. One possible explanation for this reduction is that they trained in groups with patients in the same position. We have previously shown that patients with inoperable lung cancer experience a strong sense of solidarity with other patients during and after training. This shared understanding of their destiny opens their eyes to the reluctance and lack of empathy they feel from family and friends [66]. This is confirmed by other studies that have examined the importance of the stigmatisation patients with lung cancer experience [92, 93]. Regardless of whether their lung cancer is tobacco related or not, they experience shame and this is found to have a negative impact on their relationships with family and friends [94].

Whether or not an exercise intervention has the capacity to change HRQOL significantly for patients with inoperable lung cancer remains to be tested in a larger randomised design. The results from Study III and the other published articles [51, 55, 57], however, indicate that patients achieve significant changes in the individual parameters, each of which has an impact on HRQOL.

Methodological considerations

The purpose of this thesis is to investigate the effect of a combined exercise and relaxation intervention targeting patients with inoperable lung cancer. We have therefore chosen a quantitative prospective experimental design and divided the study into three phases. The intervention and the measuring techniques were tested in Study I in a prospective study, where the intervention and the methods were tested on a heterogeneous group of patients with different cancer diagnoses in various stages of the disease. Phase I (Study II) was designed as a prospective experimental feasibility study focusing on safety and practicability. In phase II (Study III) the intervention was tested on a group of lung cancer patients and potential gains were recorded. Finally, to assess the size of the effect (Study IV) a RCT is being undertaken in phase III and its size is based on a strength calculation derived from phase II findings.

Internal validity

Several important factors influence the internal validity of the studies in this thesis. VO_2max is a shared outcome in Study I, II and IV and a primary outcome in Study III and IV. The gold standard

for measuring VO_2max is the direct watt-max test, where the inhaled and exhaled gases are analysed while the test subject bikes on a stationary cycle ergometer until fatigued with a gradually increased load measured in watts [95]. Study I tested the indirect watt-max test for measuring VO_2max developed by Andersen et al. [73]. The indirect watt-max test was carried out in the same manner as the direct watt-max test, but without an analysis of the exhaled and inhaled gases. The watt load was instead measured and noted in seconds from the point at which the test subject started and then stopped (MPO). These values were then put into the formula developed by Andersen et al.: VO_2max=0.16+(0.0117xMPO) [73]. It is debatable whether the indirect test of VO_2max is a precise measure of the individual patient's VO_2max, and this may have resulted in an inaccurate estimation of VO_2max. An improvement in the indirect watt-max test could be an indication of the patient becoming accustomed to and feeling more comfortable with the test. In this thesis, however, we focus on changes in VO_2max after the exercise intervention, and changes of this nature are likely to be valid as the uncertainty of the indirect test for the same person also applies at baseline and for the final test; however, an underestimation of the change cannot be ruled out (attenuation due to measurement error). In order to optimise the validity of the primary outcome in Study IV the direct measurement of VO_2max is being used.

Muscle strength was measured by means of 1RM. Our qualitative study of the same patient population as the one used in Study I showed that patients felt comfortable about being tested maximally for both cardiovascular and muscle strength during chemotherapy, which is why this design was used in Study II, III and IV [64].

Functional capacity, an expression of Vo_2max, muscle strength and functionality, reflects a person's ability to translate VO_2max and muscle strength into daily life activities [96]. The 6MWD was used to measure functional capacity, as recommended by ATS [75]. The test, which was used in Study II and III, was done on a course measuring 30 m, but courses measuring 20 m and 50 m can also be used [75]. The rationale for measuring functional capacity in patients with advanced-stage lung cancer is described in two studies, where a high physical function has been found to have prognostic value [60, 61]. Kasymjanova et al. found that the distance a newly diagnosed patient with advanced-stage lung cancer could walk for the 6MWD had a bearing on disease progression and survival [60]. Jones et al. also found that the 6MWD was an independent prognostic factor for survival and that every extra 50 m a patient could walk at baseline significantly reduced the risk of death [61].

To assess HRQOL and cancer-related symptoms, we chose to use FACT-L in Study II, III and IV. Even though FACT-L has been used in other exercise studies on patients with lung cancer the questionnaire is not designed to detect changes in HRQOL that result from an exercise intervention [51, 52, 55]. This may mean that problems and concerns affecting HRQOL in patients with lung cancer who take part in exercise studies are not addressed in FACT-L. HADS was used to assess the patients' anxiety and depression [79] . There is the risk of recall bias when PRO is used. A bias of this nature cannot be excluded from the studies in this thesis since patients were asked to fill out both FACT-L and HADS based on experiences from the past week. Nor can we rule out that response bias may have influenced the PRO results in Study II and III.

An additional factor of importance to the internal validity is that the project team that carried out the physical training comprised the same project team who were responsible for the composition of the intervention and for the data collection. The statisticians who performed the analyses were not a part of the project team and did not have contact with the patients. The qualitative analyses done on the patient population in Study I and II were also conducted by researchers who were not directly involved in carrying out the intervention [64, 97]. In order to improve the internal validity of Study IV the collection of data and the data analysis (baseline test, 12-week test) are being carried out by researchers who are blinded to the allocation (intervention, control) of patients [68].
It has not been the intention of nor possible for this thesis to distinguish or isolate the potential impact of each of the intervention components. The intervention was designed as a single package comprising exercise (cardiovascular and strength training) and relaxation training. Patients were encouraged to participate in the entire package and could not opt out of individual components. The assumption has been made, however, that improvement in the physical parameters is not due to the relaxation training.

External validity

A major factor in the external validity is generalisability. Patients in Study I, II and III were included in a single group design and the lack of a control group has certainly reduced the external validity. The results from Study III are based on 71 out of 114 enrolled patients with inoperable lung cancer, which is why these results are not generalisable to all patients with inoperable lung cancer but reflect the effect on a select group of patients. Study III did a dropout analysis of the patients who did not complete the intervention as well as a final test on all outcomes (Table 13). The dropout analysis showed that the patients who dropped out had a significantly lower baseline

6MWD, a significantly lower level of anxiety and a significantly higher baseline EWB than the patients who completed the final test. The reason for this significant diversity is not known, but it could be due to a type I error, and therefore this will be examined in study IV, though this requires an additional authorization that will be sought from Ethics Review Committee for the Capital Region of Denmark.

Another important factor that may have affected the external validity is recruitment / selection bias. A total of 713 patients with inoperable lung cancer were screened for participation. Based on the exclusion criteria, 344 patients were excluded. Out of the remaining 369 patients with inoperable lung cancer 114 patients wished to participate in the study (Study III). It is likely that the people who participated in the intervention had more energy or motivation to participate than the ones who did not wish to participate in the training. The number of dropouts in Study III, however, showed that 43 patients did not complete the intervention, which means that even among the patients who were motivated to begin the intervention, a third dropped out. This could indicate that this patient group is difficult to retain due to advanced illness and full-blown symptoms.

The individual components (cardiovascular, strength and relaxation) in the intervention and an exact description of them (intensity, frequency, duration) play a role with regard to generalisability. The training components in the intervention can relatively easily be reproduced and thus raise the external validity.

Table 13: Dropout analysis in Study III

Variable	Two measurents				Dropouts				Difference		
	N	Mean	SD		N	Mean	SD		diff	95% CI	
VO_2max	71	1.30	0.43		43	1.22	0.5		0.0807	-0.0878	0.2491
leg	71	71.1	30.3		43	62.3	30.5		8.8012	-2.8253	20.4277
Chest	71	28.9	13.0		43	29.8	12.2		-0.9523	-5.8300	3.9253
Lat	71	34.4	13.5		43	35.4	13.2		-0.9704	-6.1029	4.1622
knee	71	36.5	12.1		43	36.9	9.8		-0.3534	-4.6909	3.9840
abd	70	38.0	13.4		43	37.7	8.9		0.2817	-4.2881	4.8516
back	71	26.8	9.6		43	28.3	8.1		-1.4248	-4.9008	2.0511
6mwt	71	520.3	136.6		43	453.2	186.1		67.1146	6.9999	127.2
fev1_	71	1.89	0.74		43	1.87	0.97		0.0269	-0.2820	0.3357
HADS_A	70	7.2	4.4		34	4.6	3.5		2.5395	0.8392	4.2398
HADS_D	70	5.3	3.8		34	4.1	3.1		1.1681	-0.3279	2.6641
FACT total	70	94,4	18,9		34	97,2	19,4		-2,8062	-10,7192	5,1069
FACT_PWB	70	20.4	5.0		34	19.9	6.4		0.5389	-1.7309	2.8088
FACT_EWB	70	15.2	5.0		34	18.0	4.4		-2.7706	-4.7668	-0.7744
FACT_FWB	70	16.5	5.9		34	17.4	6.1		-0.9840	-3.4622	1.4942
FACT_SWB	70	23.9	4.5		34	23.6	4.9		0.3768	-1.5400	2.2935
FACT_LCS	70	18.3	4.8		34	18.4	5.2		0.0328	-2.0036	2.0691
FACT_TOI	70	55.3	13.0		34	55.7	14.2		-0.4123	-5.9733	5.1486

The composition of the project team, the cross-disciplinary combination of physical therapist and project nurse, and the team's experience could play a role in being able to reproduce the findings in this thesis. The role of the project team can be seen as a balancing act between promoting a safe environment for patients by having the relevant clinical competencies, i.e. knowledge about the patients' disease and treatment process, and still motivating the patient during exercise sessions and "enforcing" the requirements. A less experienced team or one with a different composition may also influence the results. This is also applied for group training, which under the right circumstances (facilitated by the project team) creates increased adherence to the training and motivates patients to put in more effort during training [62, 63, 66]. The project team must deliberately create a group dynamic in which the training and a sense of community are in focus and not the lung cancer disease. This helps create the atmosphere of a fitness centre (exercise equipment, sportswear, loud music) and not a hospital (hospital gowns, uniformed personnel, silence).

CONCLUSION

The purpose of this thesis was to investigate whether an exercise intervention comprising both supervised training and home-based training combined with relaxation exercises was safe and beneficial for patients with inoperable lung cancer undergoing chemotherapy.

To conclude Study I and Study II in this thesis, we can document that the patients with inoperable lung cancer are able to complete a six-week exercise and relaxation intervention without exercise-related SAE. Based on the results of the feasibility study (Study II), we also found that adherence to the home-based training component was low, which is why that component was taken out of the intervention.

We can furthermore conclude that patients with inoperable lung cancer can increase VO_2max (p=0.005), functional capacity (6MWD, p<0.0001) and muscle strength (p<0.0001) significantly. Patients are thus not only able to maintain their level of physical capacity but also to improve it. We found that the intervention significantly reduced the patients' level of anxiety. The patients did not improve their HRQOL significantly, but we did observe a significant improvement in EWB.

The magnitude of the effect of the combined exercise and relaxation intervention is being tested in an RCT (Study IV). This type of study will contribute new knowledge, and if the findings from Study III can be replicated, strongly support the recommendation of physical training in combination with relaxation for patients with inoperable lung cancer undergoing chemotherapy.

CLINICAL AND RESEARCH PERSPECTIVES

The results of this thesis have shown that an exercise intervention combined with relaxation in patients with advanced lung cancer (IIIb-IV) is feasible. The thesis has shown that it is safe for patients with inoperable lung cancer to complete the training. Patients can increase their physical capacity, functional capacity and muscle strength. The significance of these findings has not been definitively studied and documented in large randomised trials and there are still no studies that examine the effect of physical exercise on complementary treatment to chemotherapy.

Study IV [68] is designed as an RCT with VO_2 peak as its primary outcome. From a strength calculation made based on the findings from Study III, 108 patients with inoperable lung cancer will be enrolled in either an exercise intervention combined with relaxation or a control group that receives usual care. Because 40% of the enrolled patients in Study III dropped out from baseline to test 2 we have chosen to double the number of enrolled patients to 216. We have also expanded the

intervention to 12 weeks instead of six. Study IV began inclusion of patients in 2012 and at the end of 2014 there were 135 patients with inoperable lung cancer enrolled. In Study IV we have chosen to include more methods for monitoring HRQOL, symptoms and side effects, as well as to directly test VO_2 peak.

Study IV will enable us to determine whether the beneficial effects found in Study III were obtained due to patient selection. Regardless of whether the results remain positive or not, Study IV will contribute new knowledge to a relatively unexplored area within exercise for patients with inoperable lung cancer.

An important finding from this thesis is the improvement of essential physical parameters where the loss of important physical functions can be prevented or reduced. As mentioned earlier patients with lung cancer state that their greatest worry influencing HRQOL is a losing independence and not being able to perform daily activities. With an improvement in the physical parameters combined with a reduction in the level of anxiety the patients' explicit desire to succeed in maintaining independence and their level of daily activity is met regardless of poor prognosis and symptom burden.

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Appendix

LUFT

Lungekræft og Fysisk Træning.
Et træningstilbud til lungekræftpatienter i kemoterapi

FACT-L
Spørgeskema

Udfyldes af personale

Patient ID: _____

Start ☐ **6 uger** ☐

Dato: _____

Indtastet ☐

FACT-L (Version 4)

Nedenfor er anført en række udsagn, som andre mennesker med din sygdom har sagt, er vigtige. **Ved at sætte en ring omkring ét 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.**

	FYSISK VELBEFINDENDE	**Slet ikke**	**En lille smule**	**I nogen grad**	**En hel del**	**Meget**
GP1	Jeg mangler energi	0	1	2	3	4
GP2	Jeg har kvalme	0	1	2	3	4
GP3	På grund af min fysiske tilstand har jeg svært ved at opfylde min familie/mine nærmestes behov	0	1	2	3	4
GP4	Jeg har smerter	0	1	2	3	4
GP5	Jeg er generet af bivirkninger af behandlingen	0	1	2	3	4
GP6	Jeg føler mig syg	0	1	2	3	4
GP7	Jeg er tvunget til at være sengeliggende noget af tiden	0	1	2	3	4

	SOCIALT/FAMILIEMÆSSIGT VELBEFINDENDE	**Slet ikke**	**En lille smule**	**I nogen grad**	**En hel del**	**Meget**
GS1	Jeg føler, jeg har et tæt forhold til mine venner	0	1	2	3	4
GS2	Jeg får følesesmæssig støtte fra min familie/mine nærmeste	0	1	2	3	4
GS3	Jeg får støtte fra mine venner	0	1	2	3	4
GS4	Min familie/mine nærmeste har accepteret min sygdom	0	1	2	3	4
GS5	Jeg er tilfreds med den måde, vi taler om sygdommen på i familien/blandt mine nærmeste	0	1	2	3	4
GS6	Jeg føler mig tæt knyttet til min partner (eller den person, der er min bedste støtte)	0	1	2	3	4
Q1	*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.*					
GS7	Jeg er tilfreds med mit sexliv	0	1	2	3	4

FACT-L (Version 4)

Ved at sætte en ring omkring ét 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	Slet ikke	En lille smule	I nogen grad	En hel del	Meget
GE1	Jeg er ked af det	0	1	2	3	4
GE2	Jeg er tilfreds med den måde, jeg klarer min sygdom på	0	1	2	3	4
GE3	Jeg er ved at give op i kampen mod min sygdom	0	1	2	3	4
GE4	Jeg føler mig nervøs	0	1	2	3	4
GE5	Jeg er bekymret for at dø	0	1	2	3	4
GE6	Jeg er bekymret for, at min tilstand vil forværres	0	1	2	3	4

	FUNKTIONELT VELBEFINDENDE	Slet ikke	En lille smule	I nogen grad	En hel del	Meget
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-L (Version 4)

Ved at sætte en ring omkring ét 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	Slet ikke	En lille smule	I nogen grad	En hel del	Meget
B1	Jeg bliver let forpustet	0	1	2	3	4
C2	Jeg taber mig	0	1	2	3	4
L1	Jeg tænker klart	0	1	2	3	4
L2	Jeg har hostet	0	1	2	3	4
B5	Jeg er generet af hårtab	0	1	2	3	4
C6	Jeg har en god appetit	0	1	2	3	4
L3	Jeg har trykken i brystet	0	1	2	3	4
L4	Jeg har let ved at trække vejret	0	1	2	3	4
Q3	Har du nogensinde røget? Nej___ Ja___ Hvis ja:					
L5	Jeg fortryder, at jeg har røget	0	1	2	3	4

HAD
Spørgeskema

Udfyldes af personale

Patient ID: _____

Start ☐ **Post** ☐

Dato: _____

Indtastet ☐

CIRE

CIRE forskergruppe / OKT 2011

Dette spørgeskema er udformet med henblik på at hjælpe læger med at finde ud af, hvordan du har det.

Læs hvert spørgsmål og sæt kryds ved det svar, der kommer tættest på, hvordan du har haft det i den sidste uge.

1. Jeg føler mig anspændt:

☐1 Næsten hele tiden

☐2 Meget af tiden

☐3 Engang imellem

☐4 Slet ikke

2. Jeg nyder stadig de ting, som jeg tidligere har nydt:

☐1 Helt, som jeg plejer

☐2 Ikke helt så meget

☐3 Kun lidt

☐4 Næsten ikke

3. Jeg er bange for, at der skal ske noget frygteligt:

☐1 Helt bestemt og meget voldsomt

☐2 Ja, men det er ikke så slemt

☐3 Lidt, men det bekymrer mig ikke

☐4 Slet ikke

4. Jeg kan le og se det morsomme i en situation:

☐1 Lige så meget, som jeg plejer

☐2 Ikke helt så meget nu

☐3 Helt klart ikke så meget nu

☐4 Slet ikke

5. Jeg gør mig bekymringer:

☐1 En stor del af tiden

☐2 Meget af tiden

☐3 Engang imellem, men ikke så tit

☐4 Kun lejlighedsvis

6. Jeg føler mig glad

☐1 Slet ikke

☐2 Ikke så tit

☐3 Nogle gange

☐4 Det meste af tiden

Fortsæt venligst på næste side

→

7. Jeg kan sidde roligt og føle mig afslappet

☐1 Helt bestemt

☐2 Som regel

☐3 Ikke så tit

☐4 Slet ikke

8. Jeg føler det som om jeg fungerer langsommere:

☐1 Næsten hele tiden

☐2 Meget ofte

☐3 Nogle gange

☐4 Slet ikke

9. Jeg føler mig bange, som om jeg har "sommerfugle i maven":

☐1 Slet ikke

☐2 Lejlighedsvis

☐3 Temmelig tit

☐4 Meget ofte

10. Jeg har mistet interessen for mit udseende:

☐1 Fuldstændig

☐2 Jeg er ikke så omhyggelig, som jeg burde være

☐3 Måske er jeg knap så omhyggelig som før

☐4 Jeg er lige så omhyggelig, som jeg altid har været

11. Jeg føler mig rastløs, som om jeg hele tiden skal være i bevægelse:

☐1 Virkelig meget

☐2 Temmelig meget

☐3 Ikke særlig meget

☐4 Slet ikke

12. Jeg glæder mig til ting, som skal ske:

☐1 Lige så meget som før

☐2 Noget mindre, end jeg plejer

☐3 Helt klart mindre end tidligere

☐4 Næsten ikke

13. Jeg får en pludselig fornemmelse af panik:

☐1 Særdeles tit

☐2 Temmelig ofte

☐3 Ikke særlig ofte

☐4 Slet ikke

14. Jeg kan nyde en god bog eller et radio/TV-program:

☐1 Ofte

☐2 Nogle gange

☐3 Ikke særlig tit

☐4 Meget sjældent

SF 36
Spørgeskema

Udfyldes af personale

Patient ID: _____

Start ☐ **Post** ☐

Dato: _____

Indtastet ☐

CIRE

CIRE forskergruppe / OKT 2011

Dette spørgeskema handler om din opfattelse af dit helbred.

Oplysningerne vil give et overblik over, hvordan du har det, og hvor godt du er i stand til at udføre dine daglige gøremål.

Besvar hvert spørgsmål ved at sætte kryds ved det svar, der passer bedst på dig. Hvis du er i tvivl om, hvordan du skal svare, svar da venligst så godt du kan.

---

1. Hvordan synes du dit helbred er alt i alt?

(Sæt kun ét kryds)

- Fremragende ☐ 1
- Vældig godt ☐ 2
- Godt ☐ 3
- Mindre godt ☐ 4
- Dårligt ☐ 5

---

2. Sammenlignet med for ét år siden, hvordan er dit helbred alt i alt nu?

(Sæt kun ét kryds)

- Meget bedre nu end for ét år siden ☐ 1
- Noget bedre nu end for ét år siden ☐ 2
- Nogenlunde det samme ☐ 3
- Noget dårligere nu end for ét år siden ☐ 4
- Meget dårligere nu end for ét år siden ☐ 5

3. **De følgende spørgsmål handler om aktiviteter i dagligdagen. Er du på grund af dit helbred begrænset i disse aktiviteter? I så fald, hvor meget?**

(Sæt ét kryds i hver linie)

	Ja, meget begrænset	Ja, lidt begrænset	Nej, slet ikke begrænset
Krævende aktiviteter, som fx at løbe, løfte tunge ting, deltage i anstrengende sport	☐ 1	☐ 2	☐ 3
Lettere aktiviteter, såsom at flytte et bord, støvsuge eller cykle	☐ 1	☐ 2	☐ 3
At løfte eller bære dagligvarer	☐ 1	☐ 2	☐ 3
At gå **flere** etager op ad trapper	☐ 1	☐ 2	☐ 3
At gå **én** etage op ad trapper	☐ 1	☐ 2	☐ 3
At bøje sig ned eller gå ned i knæ	☐ 1	☐ 2	☐ 3
Gå **mere end én kilometer**	☐ 1	☐ 2	☐ 3
Gå **nogle hundrede meter**	☐ 1	☐ 2	☐ 3
Gå **100 meter**	☐ 1	☐ 2	☐ 3
Gå i bad eller tage tøj på	☐ 1	☐ 2	☐ 3

---

4. **Har du inden for de sidste 4 uger haft nogen af følgende problemer med dit arbejde eller andre daglige aktiviteter på grund af dit fysiske helbred?**

(Sæt ét kryds i hver linie)

	JA	NEJ
Jeg har skåret ned på den **tid**, jeg bruger på arbejde eller andre aktiviteter	☐ 1	☐ 2
Jeg har **nået mindre**, end jeg gerne ville	☐ 1	☐ 2
Jeg har været begrænset i hvilken **slags** arbejde eller andre aktiviteter, jeg har kunnet udføre	☐ 1	☐ 2
Jeg har haft **besvær** med at udføre mit arbejde eller andre aktiviteter (fx krævede det en ekstra indsats)	☐ 1	☐ 2

5. **Har du inden for de sidste 4 uger haft nogen af følgende problemer med dit arbejde eller andre daglige aktiviteter på grund af følelsesmæssige problemer?**

(Sæt ét kryds i hver linie)

	JA	NEJ
Jeg har skåret ned på den **tid**, jeg bruger på arbejde eller andre aktiviteter	☐ 1	☐ 2
Jeg har **nået mindre**, end jeg gerne ville	☐ 1	☐ 2
Jeg har udført mit arbejde eller andre aktiviteter mindre **omhyggeligt**, end jeg plejer	☐ 1	☐ 2

---

6. **Inden for de sidste 4 uger hvor meget har dit fysiske helbred eller følelsesmæssige problemer vanskeliggjort din kontakt med familie, venner, naboer eller andre?**

(Sæt kun ét kryds)

- Slet ikke ☐ 1
- Lidt ☐ 2
- Noget ☐ 3
- En hel del ☐ 4
- Virkelig meget ☐ 5

---

7. **Hvor stærke fysiske smerter har du haft i de sidste 4 uger?**

(Sæt kun ét kryds)

- Ingen smerter ☐ 1
- Meget lette smerter ☐ 2
- Lette smerter ☐ 3
- Middelstærke smerter ☐ 4
- Stærke smerter ☐ 5
- Meget stærke smerter ☐ 6

8. **Inden for de sidste 4 uger hvor meget har fysiske smerter vanskeliggjort dit daglige arbejde** *(både arbejde uden for hjemmet og husarbejde)*?

(Sæt kun ét kryds)

- Slet ikke ☐ 1
- Lidt ☐ 2
- Noget ☐ 3
- En hel del ☐ 4
- Virkelig meget ☐ 5

---

9. **Disse spørgsmål handler om, hvordan du har haft det i de sidste 4 uger.**

Hvor stor en del af tiden i de sidste 4 uger -

(Sæt ét kryds i hver linie)

	Hele tiden	Det meste af tiden	En hel del af tiden	Noget af tiden	Lidt af tiden	På intet tids-punkt
har du følt dig veloplagt og fuld af liv?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du været meget nervøs?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du været så langt nede, at intet kunne opmuntre dig?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du følt dig rolig og afslappet?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du været fuld af energi?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du følt dig trist til mode?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du følt dig udslidt?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du været glad og tilfreds?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
har du følt dig træt?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

10. **Inden for de sidste 4 uger, hvor stor en del af tiden har dit fysiske helbred eller følelsesmæssige problemer gjort det vanskeligt at se andre mennesker** *(fx besøge venner, slægtninge osv.)*?

(Sæt kun ét kryds)

- Hele tiden ☐ 1
- Det meste af tiden ☐ 2
- Noget af tiden ☐ 3
- Lidt af tiden ☐ 4
- På intet tidspunkt ☐ 5

---

11. **Hvor rigtige eller forkerte er de følgende udsagn for dit vedkommende?**

(Sæt ét kryds i hver linie)

	Helt rigtigt	Over-vejende rigtigt	Ved ikke	Over-vejende forkert	Helt forkert
Jeg bliver nok lidt lettere syg end andre	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Jeg er lige så rask som enhver anden, jeg kender	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Jeg forventer, at mit helbred bliver dårligere	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Mit helbred er fremragende	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

EORTC-C30-QLQ

Spørgeskema

Udfyldes af personale

Patient ID: _____

Start ☐ **Post** ☐

Dato: _____

Indtastet ☐

CIRE

_____

EORTC QLQ-C30 (version 3.0)

Vi er interesserede i at vide noget om Dem og Deres helbred. Vær venlig at besvare alle spørgsmålene selv ved at sætte en ring omkring det svar (tal), som passer bedst på Dem. Der er ingen "rigtige" eller "forkerte" svar. De oplysninger, som De giver os, vil forblive strengt fortrolige.

Skriv venligst Deres forbogstaver her: |_|_|_|_|

Deres fødselsdato (dag, måned, år): |_|_| |_|_| |_|_|_|_|

Dato for udfyldelse af dette skema (dag, måned, år): 31 |_|_| |_|_| |_|_|_|_|

	Slet ikke	Lidt	En del	Meget
1. Har De nogen vanskeligheder ved at udføre anstrengende aktiviteter, som f.eks. at bære en tung indkøbstaske eller en kuffert?	1	2	3	4
2. Har De nogen vanskeligheder ved at gå en lang tur?	1	2	3	4
3. Har De nogen vanskeligheder ved at gå en kort tur udendørs?	1	2	3	4
4. Er De nødt til at ligge i sengen eller at sidde i en stol om dagen?	1	2	3	4
5. Har De brug for hjælp til at spise, tage tøj på, vaske Dem eller gå på toilettet?	1	2	3	4

I den forløbne uge:

	Slet ikke	Lidt	En del	Meget
6. Var De begrænset i udførelsen af enten Deres arbejde eller andre daglige aktiviteter?	1	2	3	4
7. Var De begrænset i at dyrke Deres hobbyer eller andre fritidsaktiviteter?	1	2	3	4
8. Havde De åndenød?	1	2	3	4
9. Har De haft smerter?	1	2	3	4
10. Havde De brug for at hvile Dem?	1	2	3	4
11. Har De haft besvær med at sove?	1	2	3	4
12. Har De følt Dem svag?	1	2	3	4
13. Har De savnet appetit?	1	2	3	4
14. Har De haft kvalme?	1	2	3	4
15. Har De kastet op?	1	2	3	4

Vær venlig at fortsætte på næste side

I den forløbne uge:	Slet ikke	Lidt	En del	Meget
16. Har De haft forstoppelse?	1	2	3	4
17. Har De haft diarré (tynd mave)?	1	2	3	4
18. Var De træt?	1	2	3	4
19. Vanskeliggjorde smerter Deres daglige gøremål?	1	2	3	4
20. Har De haft svært ved at koncentrere Dem om ting som f.eks. at læse avis eller se fjernsyn?	1	2	3	4
21. Følte De Dem anspændt?	1	2	3	4
22. Var De bekymret?	1	2	3	4
23. Følte De Dem irritabel?	1	2	3	4
24. Følte De Dem deprimeret?	1	2	3	4
25. Har De haft svært ved at huske?	1	2	3	4
26. Har Deres fysiske tilstand eller medicinske behandling vanskeliggjort Deres familieliv?	1	2	3	4
27. Har Deres fysiske tilstand eller medicinske behandling vanskeliggjort Deres omgang med andre mennesker?	1	2	3	4
28. Har Deres fysiske tilstand eller medicinske behandling medført økonomiske vanskeligheder for Dem?	1	2	3	4

Ved de næste 2 spørgsmål bedes De sætte en ring omkring det tal mellem 1 og 7, som passer bedst på Dem

29. Hvordan vil De vurdere Deres samlede helbred i den forløbne uge?

1	2	3	4	5	6	7
Meget dårligt						Særdeles godt

30. Hvordan vil De vurdere Deres samlede livskvalitet i den forløbne uge?

1	2	3	4	5	6	7
Meget dårlig						Særdeles god

EORTC QLQ - LC13

Patienter fortæller undertiden, at de har følgende symptomer eller problemer. Anfør venligst, i hvilket omfang De har haft disse symptomer eller problemer inden for den forløbne uge. Besvar spørgsmålene ved at sætte en ring omkring det tal, som passer bedst til dem.

I den forløbne uge:		**Slet ikke**	**Lidt**	**En del**	**Meget**
31.	Hvor meget har De hostet ?	1	2	3	4
32.	Har De hostet blod op ?	1	2	3	4
33.	Har De haft åndenød i hvile ?	1	2	3	4
34.	Har De haft åndenød når De gik ?	1	2	3	4
35.	Har De haft åndenød, når De gik op ad trapper ?	1	2	3	4
36.	Har De haft ømhed i munden eller på tungen ?	1	2	3	4
37.	Har De haft svært ved at synke ?	1	2	3	4
38.	Har De haft stikken og prikken i hænder eller fødder ?	1	2	3	4
39.	Har De haft af hårtab ?	1	2	3	4
40.	Har De haft smerter i brystkassen ?	1	2	3	4
41.	Har De haft smerter i Deres arm eller skulder ?	1	2	3	4
42.	Har De haft smerter i andre dele af kroppen ?	1	2	3	4
	Hvis Ja, hvor ? _____				
43.	Har De taget noget medicin for smerter?				
	1. Nej **2. Ja**				
	Hvis ja, hvor meget hjalp det ?	1	2	3	4

Pittsburgh Sleep Quality Index (PSQI)

Udfyldes af personale

Patient ID: _____

Start ☐ **6 uger** ☐ **12 uger** ☐

Dato: _____

Indtastet ☐

CIRE

_____

Pittsburgh Sleep Quality Index (PSQI) oversat til dansk

Validering af oversættelse til dansk
Oversættelse fra engelsk til dansk: Mette Thorlund Haahr
Oversættelse fra dansk til engelsk: Karine Madsen
Dansk/engelsk konsensus check: Matthew Liptrot

Navn_____ ID#_____Dato_____ Alder_____

Instruktion:

De følgende spørgsmål drejer sig om dine vanlige sovevaner **i den sidste måned.** Dine svar skal give det bedste billede af dine sovevaner i løbet **af de fleste** dage og nætter i den sidste måned. Vær venlig at besvare **alle** spørgsmålene.

1: I gennem den sidste måned, hvornår er du almindeligvis gået i seng?

Vanlige sengetid_____

2: I gennem den sidste måned, hvor lang tid (i minutter) har det almindeligvis taget dig at falde i søvn?

Antal minutter_____

3: I gennem den sidste måned, hvornår er du almindeligvis stået op om morgenen?

Vanlige stå op tid_____

4: I gennem den sidste måned, hvor mange natlige timer af *egentlig* søvn, har du fået? (Dette er eventuelt anderledes end det faktiske antal timer, du har ligget i sengen)

Timer af *egentlig* søvn per nat_____

For hver af de sidste spørgsmål sæt kun ét kryds ved det bedst mulige svar. Vær venlig at besvare **alle** spørgsmålene.

5: I gennem den sidste måned, hvor ofte har du haft problemer med at sove på grund af at du .....

(a) ikke kan falde i søvn inden 30 min

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(b) vågner om natten eller tidlig morgen

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(c) er nødt til at gå på toilettet en eller flere gange

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(d) har besvær med at trække vejret ordentligt

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(e) hoster eller snorker højlydt

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(f) har det for koldt

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(g) har det for varmt

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(h) har mareridt

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(i) har smerter

Ikke i gennem den sidste måned	Mindre end en gang om ugen	En eller to gange om ugen	Tre eller flere gange om ugen
☐	☐	☐	☐

(j) Andre end de nævnte grunde. Vær venlig at beskrive dem

_____

_____

Hvor mange gange igennem den sidste måned har du haft problemer med at sove på grund af dette

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

6: I gennem den sidste måned, hvordan vurderer du din overordnede søvnkvalitet?

- Meget god ☐
- Rimelig god ☐
- Rimelig dårlig ☐
- Meget dårlig ☐

7: I gennem den sidste måned, hvor ofte har du taget medicin (på recept eller i håndkøb) for at hjælpe dig med at sove?

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

8: I gennem den sidste måned, hvor ofte har du haft problemer med at holde dig vågen i mens du kører bil, at du spiser et måltid mad, eller er i gang med sociale aktiviteter?

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

9: I gennem den sidste måned, hvor stort et problem har det været for dig at opretholde nok entusiasme til at få tingene gjort?

- Ingen problem overhovedet ☐
- Et ubetydelig problem ☐
- Til tider et betydende problem ☐
- Ofte betydende problem ☐

10: Har du en sengepartner eller deler værelse med en anden person?

- Ingen sengepartner eller deler værelse ☐
- Har partner eller beboer i et andet værelse ☐
- Partner i samme værelse men ikke i samme seng ☐
- Partner i samme seng ☐

11: Hvis du har en sengepartner eller deler værelse med en anden person, spørg ham/hende om hvor ofte du i gennem den sidste måned har……

(a) snorket højlydt.

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

(b) haft lange pauser i vejrtrækningen, når du sover.

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

(c) sparket eller spjættet med benene, imens du sover.

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

(d) haft episoder af disorientering eller forvirring, imens at du sover.

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

(e) haft andre forstyrrelser imens du sover. Vær venlig at beskrive:

Hvor ofte har du i gennem den sidste måned oplevet dette

Ikke i gennem den sidste måned		Mindre end en gang om ugen		En eller to gange om ugen		Tre eller flere gange om ugen	

Social Støtte
Tredje netværk

Udfyldes af personale

Patient ID: _____

Start □ **Post** □

Dato: _____

Indtastet □

CIRE

_____

CIRE forskergruppe / OKT 2011

Nedenfor finder du en række udsagn vedrørende støtte, som man kan få fra sine omgivelser. I princippet er der ved hvert udsagn 7 svarmuligheder. Læs venligst hvert udsagn og sæt en cirkel omkring det tal, der bedst passer på dig. Der er ingen rigtige eller forkerte svar. Det er

dit eget indtryk, der gælder.

1 = Passer slet ikke		**5 = Passer en smule**
2 = Passer som oftest ikke	**4 = neutral**	**6 = Passer som oftest**
3 = Passer af og til ikke		**7 = Passer fuldstændigt**

1. Der er en speciel person i mit liv, som altid er der, når jeg har brug for hende/ham	→	1	2	3	4	5	6	7
2. Der er en speciel person i mit liv, som jeg kan dele mine glæder og sorger med	→	1	2	3	4	5	6	7
3. Min familie prøver virkelig at hjælpe mig	→	1	2	3	4	5	6	7
4. Min familie giver mig den følelsesmæssige hjælp og støtte, som jeg har brug for	→	1	2	3	4	5	6	7
5. Der er en speciel person i mit liv, som er en virkelig støtte for mig og som jeg kan regne med.	→	1	2	3	4	5	6	7
6. Mine venner prøver virkelig at hjælpe mig	→	1	2	3	4	5	6	7
7. Jeg kan regne med mine venner, når noget går galt	→	1	2	3	4	5	6	7
8. Jeg kan tale med min familie om mine problemer	→	1	2	3	4	5	6	7
9. Jeg har venner, som jeg kan dele mine glæder og sorger med	→	1	2	3	4	5	6	7
10 Der er en speciel person i mit liv, som jeg kan dele mine følelser med	→	1	2	3	4	5	6	7

1 = Passer slet ikke		**5 = Passer en smule**
2 = Passer som oftest ikke	**4 = neutral**	**6 = Passer som oftest**
3 = Passer af og til ikke		**7 = Passer fuldstændigt**

11.	Min familie er villig til at hjælpe mig, når jeg skal træffe beslutninger	→	1	2	3	4	5	6	7
12.	Jeg kan tale med mine venner om mine problemer	→	1	2	3	4	5	6	7
13.	Jeg har mulighed for at drøfte beslutninger med andre kræftpatienter	→	1	2	3	4	5	6	7
14.	Jeg kan tale med andre kræftpatienter om mine erfaringer og problemer	→	1	2	3	4	5	6	7
15.	Jeg har mulighed for at dele mine glæder og sorger med andre kræftpatienter	→	1	2	3	4	5	6	7
16.	Der er andre kræftpatienter, som giver mig den hjælp og støtte, som jeg har brug for	→	1	2	3	4	5	6	7
17.	Jeg er en del af fællesskabet med andre kræftpatienter	→	1	2	3	4	5	6	7
18.	Samvær med andre kræftpatienter giver mig optimisme og håb	→	1	2	3	4	5	6	7
19.	Der er andre kræftpatienter, som inspirerer mig til at være fysisk aktiv	→	1	2	3	4	5	6	7

Skema for Sygdoms-
og behandlingsvariable

Patient ID: _____

Start ved diagnose ☐

Inklusion i intervention ☐

1 år fra inklusion eller ved frafald (omfatter død eller ophørt deltagelse) ☐

Dato: _____

Indtastet ☐

Navn:

CPR-NR.:

Adresse:

Cancersygdom: _____

Dato for diagnose: _____

Diagnose: _____

ICD-O: _____

Diagnosedato (kriterier skal specificeres):

_____

_____

TNM stadie for solide tumorer:

_____

_____

Lokalisation, hvis dette ikke fremgår entydigt af diagnosekode og TNM:

_____

_____

Behandling

Radioterapi	Ja	Nej
	☐1	☐2

Kemoterapi	Ja	Nej
	☐1	☐2

Hvis ja, specificeres om der er givet

Potentiel neurotoksicitet

Taxaner	Ja	Nej
	☐1	☐2
Vinca-alkaloider	Ja	Nej
	☐1	☐2
Platinoler	ja	nej
	☐1	☐2

Potentiel lungetoksicitet

Bleomycin	ja	nej
	☐1	☐2

Potentiel kardiotoxicitet

Anthracykliner	ja	nej
	☐1	☐2

Kirurgi	Åben	lukket (kikkert)
	☐1	☐2

Anden onkologisk behandling	ja	nej
	☐1	☐2

Hvis ja, specificer:

_____

_____

Funktionsniveau

Lansky (børn)	0-100:	_____
Karnofsky (hæmatologi)	0-100 %:	_____
WHO score (Voksne onkologi)	0-4 (5):	_____

LUFT

Lungekræft og Fysisk Træning.
Et træningstilbud til lungekræftpatienter i kemoterapi

1

Spørgeskema vedrørende Socio-økonomiske forhold

Udfyldes af personale

Patient ID: _____

Start ☐ **6 uger** ☐ **12 uger** ☐

Dato: _____

Indtastet ☐

OPLYSNINGER OM DIG SELV

Fødselsdato (DD. MM. ÅR) _____

Mand ☐1

Kvinde ☐2

Vægt .....

Højde .....

Hvilket land er du født i?

Danmark ☐1

Øvrige Vestlige lande (Vesteuropa, Canada, USA, Australien og New Zealand) ☐2

Ikke-vestlig (Øvrige lande) ☐3

Hvad er din ægteskabelige status?

Gift/Samboende ☐1

Enlig/fraskildt/enke ☐2

Har du hjemmeboende børn?

☐1 Ja ☐2 Nej

Bor du i?

Leje bolig ☐1

Ejerbolig ☐2

Andel ☐3

Andet ☐4

Hus, Antal værelser _____

Ryger du?

Ja, dagligt, mindre end 5 stk	☐1
Ja, mellem 5 og 10 stk	☐2
Ja, mellem 10 og 15 stk	☐3
Ja, mellem 15 og 20 stk	☐4
Ja, over 20 stk	☐5
Nej, jeg er holdt op inden for det sidste halve år	☐6
Nej, jeg er holdt op for længe siden	☐7
Nej, jeg har aldrig røget	☐8

Hvor mange genstande drikker du typisk, på en uge?

(Øl, Vin/ Hedvin, Spiritus)

Antal genstande ……

Hvor ofte får du 6 genstande eller mere ved en enkelt lejlighed?

Aldrig	☐1
Sjældnere end én gang om måneden	☐2
Månedligt	☐3
Ugentligt	☐4
Dagligt eller næsten dagligt	☐5

Hvilken uddannelse er den højeste, som du har gennemført?

Mindre end 9.klasse ☐1
Afsluttet 9. el.10. klasse ☐2
Gymnasial uddannelse ☐3
Erhvervsuddannelse /læring/ faglig uddannelse ☐4
Kort videregående uddannelse (*under* 3 år) ☐5
Mellemlang videregående uddannelse (3-4 år) ☐6
Langvarig videregående uddannelse (5 *år* og derover) ☐7

Hvad er din beskæftigelsessituation?

Lønmodtager i arbejde eller selvstændig ☐1
Arbejdsløs (evt. i aktivering) ☐2
Sygedagpenge/revalidering/fleksjob ☐3
Efterløn/pension ☐4
Under uddannelse ☐5
Andet
Stillingsbetegnelse……

Er du sygemeldt fra din nuværende beskæftigelsessituation?

☐1 Nej ☐2 Ja, fuldtid ☐3 Ja, deltid

Hvor stor er husstandsindkomsten?

Under 200.000 ☐1
Mellem 200.000 – 300.000 ☐2
Mellem 300.000 – 400.000 ☐3
Mellem 400.000 – 500.000 ☐4
Mellem 600.000 – 700.000 ☐5
Mellem 700.000 – 800.000 ☐6
Over 800.000 – ☐7

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

Ikke fysisk belastende – overvejende stillesiddende ☐1
(fx skole, kontor, chauffør etc.)

Moderat fysisk belastende – involverer nogen fysisk aktivitet ☐2
(fx går, løfter, bærer let, etc.)

Meget fysisk belastende – overvejende tungt arbejde ☐3
(arbejde fx jord og beton, gartner etc.)

BEHANDLING OG TERAPI

Er du i kemoterapi? ☐1 Ja ☐2 Nej ☐3 Ved ikke

Er du i stråleterapi? ☐1 Ja ☐2 Nej ☐3 Ved ikke

Er du i hormonbehandling? ☐1 Ja ☐2 Nej ☐3 Ved ikke

Går du i individuel terapi (psykolog/psykiater)? ☐1 Ja ☐2 Nej

……

……

Tager du noget medicin udover det du har fået i afdelingen. ☐1 Ja ☐2 Nej
(Navn, Alternativ behandling)

……

……

……

FYSISK AKTIVITET

Inden du fik din kræftdiagnose,

Cyklede du da dagligt (fx til og fra arbejde)? ☐$_1$ Ja ☐$_2$ Nej

Hvis ja, angiv antal minutter (dagligt) ……

Dyrkede du da ***let anstrengende*** sport? ☐$_1$ Ja ☐$_2$ Nej

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

Hvis ja, angiv hvor mange timer om ugen ……

Dyrkede du da ***meget anstrengende*** sport? ☐$_1$ Ja ☐$_2$ 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) ☐$_1$

II ***Gå- og/eller cykelture*** *under* 3 timer om ugen ☐$_2$

III ***Regelmæssig fysisk aktiv*** *mindst* 3 timer om ugen ☐$_3$

IV ***Hård fysisk træning*** *mere end* 4 timer om ugen ☐$_4$

Hvilket fysisk aktivitetsniveau passer bedst på dig i dag?

I ***Stillesiddende***
(Læser, ser fjernsyn eller anden stillesiddende beskæftigelse) ☐$_1$

II ***Gå- og/eller cykelture*** *under* 3 timer om ugen ☐$_2$

III ***Regelmæssig fysisk aktiv*** *mindst* 3 timer om ugen ☐$_3$

IV ***Hård fysisk træning*** *mere end* 4 timer om ugen ☐$_4$

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

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 ☐$_1$

Det er tilstrækkeligt som det sker nu ☐$_2$

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

Ja ☐$_1$

Nej ☐$_2$

Ved ikke ☐$_3$

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 kræftpatienter* 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* forhindrer 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? ☐$_1$ Ja ☐$_2$ Nej

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

(Du må gerne sætte flere krydser)

Utilpashed	☐$_1$
Manglende fysisk overskud	☐$_2$
Manglende motionstilbud som passer til mig	☐$_3$
Økonomisk hensyn	☐$_4$
Mangler en træningspartner/træningspartnere	☐$_5$
Usikkerhed på, hvad jeg *kan*	☐$_6$
Usikkerhed på, hvad jeg *må*	☐$_7$
Travlhed i hverdagen	☐$_8$

Hvordan vurderer du dit eget helbred?

Virkelig godt	☐$_1$
Godt	☐$_2$
nogenlunde	☐$_3$
Dårligt	☐$_4$

Meget dårligt ☐5

LUFT

Lungekræft og Fysisk Træning.
Et træningstilbud til lungekræftpatienter i kemoterapi

2

Spørgeskema vedrørende Socio-økonomiske forhold

Udfyldes af personale

Patient ID: _____

Start ☐ **6 uger** ☐ **12 uger** ☐

Dato: _____

Indtastet ☐

OPLYSNINGER OM DIG SELV

Vægt .....

Højde .....

Hvad er din ægteskabelige status?

Gift/Samboende ☐*1*

Enlig/fraskildt/enke ☐*2*

Har du hjemmeboende børn?

☐1 Ja ☐2 Nej

Bor du i?

Leje bolig ☐1

Ejerbolig ☐2

Andel ☐3

Andet ☐4

Hus, Antal værelser _____

Ryger du?

Ja, dagligt, mindre end 5 stk	☐1
Ja, mellem 5 og 10 stk	☐2
Ja, mellem 10 og 15 stk	☐3
Ja, mellem 15 og 20 stk	☐4
Ja, over 20 stk	☐5
Nej, jeg er holdt op inden for det sidste halve år	☐6
Nej, jeg er holdt op for længe siden	☐7
Nej, jeg har aldrig røget	☐8

Hvor mange genstande drikker du typisk, på en uge?

(Øl, Vin/ Hedvin, Spiritus)

Antal genstande ……

Hvor ofte får du 6 genstande eller mere ved en enkelt lejlighed?

Aldrig	☐1
Sjældnere end én gang om måneden	☐2
Månedligt	☐3
Ugentligt	☐4
Dagligt eller næsten dagligt	☐5

Hvad er din beskæftigelsessituation?

Lønmodtager i arbejde eller selvstændig	☐1
Arbejdsløs (evt. i aktivering)	☐2
Sygedagpenge/revalidering/fleksjob	☐3
Efterløn/pension	☐4
Under uddannelse	☐5

Andet

Stillingsbetegnelse……

Er du sygemeldt fra din nuværende beskæftigelsessituation?

☐1 Nej ☐2 Ja, fuldtid ☐3 Ja, deltid

BEHANDLING OG TERAPI

Er du i kemoterapi? ☐$_1$ Ja ☐$_2$ Nej ☐$_3$ Ved ikke

Er du i stråleterapi? ☐$_1$ Ja ☐$_2$ Nej ☐$_3$ Ved ikke

Er du i hormonbehandling? ☐$_1$ Ja ☐$_2$ Nej ☐$_3$ Ved ikke

Går du i individuel terapi (psykolog/psykiater)? ☐$_1$ Ja ☐$_2$ Nej

……

Tager du noget medicin udover det du har fået i afdelingen. ☐$_1$ Ja ☐$_2$ Nej

(Navn, Alternativ behandling)

……

……

……

Nedenfor er angivet nogle kategorier til beskrivelse af ***fysisk aktivitetsniveau.***

Hvilket fysisk aktivitetsniveau passer bedst på dig i dag?

I	***Stillesiddende*** (Læser, ser fjernsyn eller anden stillesiddende beskæftigelse)	☐$_1$
II	***Gå- og/eller cykelture*** *under* 3 timer om ugen	☐$_2$
III	***Regelmæssig fysisk aktiv*** *mindst* 3 timer om ugen	☐$_3$
IV	***Hård fysisk træning*** *mere end* 4 timer om ugen	☐$_4$

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

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 ☐$_1$

Det er tilstrækkeligt som det sker nu ☐$_2$

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

Ja ☐$_1$

Nej ☐$_2$

Ved ikke ☐$_3$

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 kræftpatienter* 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* forhindrer 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? ☐$_1$ Ja ☐$_2$ Nej

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

(Du må gerne sætte flere krydser)

Utilpashed	☐$_1$
Manglende fysisk overskud	☐$_2$
Manglende motionstilbud som passer til mig	☐$_3$
Økonomisk hensyn	☐$_4$
Mangler en træningspartner/træningspartnere	☐$_5$
Usikkerhed på, hvad jeg *kan*	☐$_6$
Usikkerhed på, hvad jeg *må*	☐$_7$
Travlhed i hverdagen	☐$_8$

Hvordan vurderer du dit eget helbred?

Virkelig godt	☐$_1$
Godt	☐$_2$
nogenlunde	☐$_3$
Dårligt	☐$_4$
Meget dårligt	☐$_5$

TRÆNINGS-ØVELSER FOR LUNGEPATIENTER

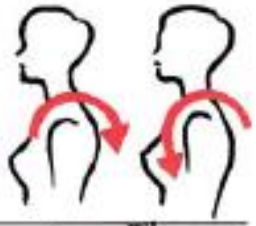
Danmarks Lungeforening

SIDDENDE ØVELSER PÅ TABURET.

Øvelser for skulderbæltet i roligt tempo.

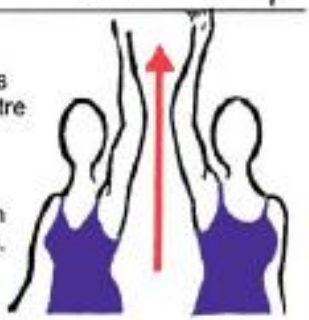
1.
Løft skiftevis højre skulder, venstre skulder og begge skuldre.

2.
Rul skuldrene fremad (op, frem, ned, bagud), og derefter baglæns (op, bagud, ned, frem).



3.
Træk armene vandret bagud, skiftevis med strakte og bøjede albuer.

4.
Stræk skiftevis højre og venstre arm op mod loftet, så meget at du mærker, at din side strækkes.



Udspænding af nakkemusklerne i roligt tempo.

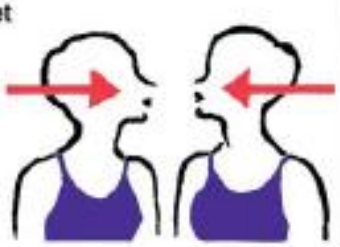
1.

Tag først nogle dybe vejrtrækninger med hænderne på maven; pust ud med spidse læber.

2.

Bøj hovedet til højre, øret mod skulder, eventuelt hjælp med hånden; hold stillingen et øjeblik og skift til venstre side.

3.
Drej hovedet og se mod højre side, drej hovedet og se mod venstre side.

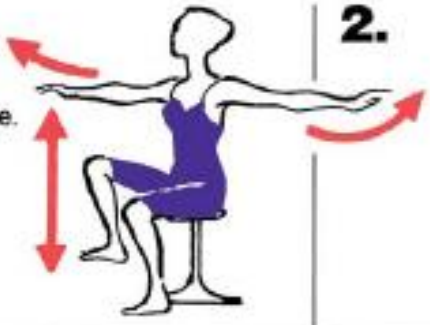


4.

Bøj hovedet frem, læg hænderne på baghovedet og hold stillingen et øjeblik.

Øvelser for benene i hurtigt tempo.

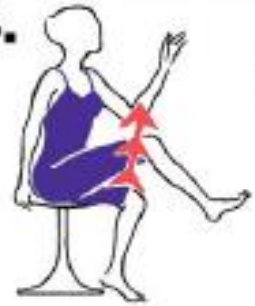
1.
Tramp i gulvet og sving løst med armene.



2.
Stræk skiftevis højre og venstre knæ til vandret.

3.
Stræk skiftevis højre og venstre ben ud til siden.

4.
Før højre albue til venstre knæ og omvendt.



STÅENDE ØVELSER

Øvelser for armene og brystkassen

1.

Sving armene frem og tilbage, start med højre arm fremme, venstre arm bagud.

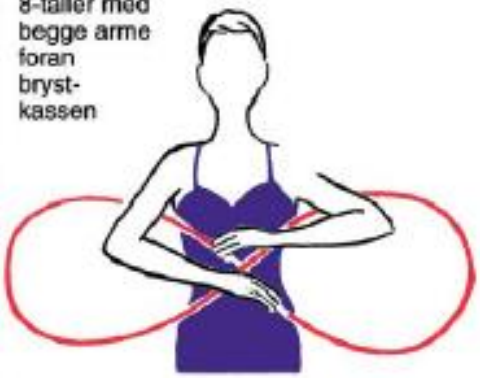
2.

Træk begge arme skråt opad og bagud, skiftevis til højre og venstre side.

STÅENDE ØVELSER

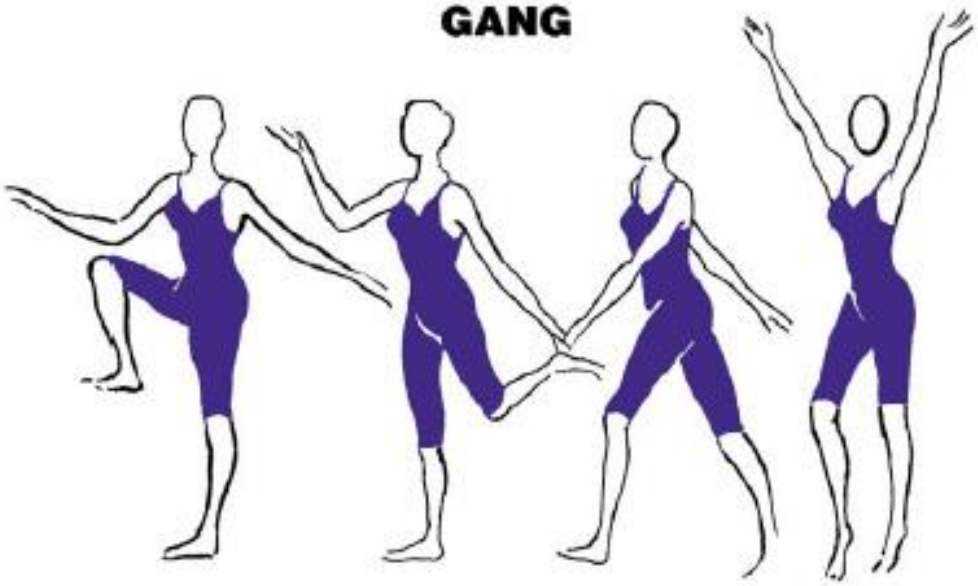
3.
Bøj til siden, eventuelt med armen over hovedet.

4.
Tegn liggende 8-taller med begge arme foran bryst-kassen



Øvelserne udføres med vægtoverføring fra det ene ben til det andet, og husk at give efter i knæene!

GANG



Almindelig fremad, på tæer, på hælene, på fodens inderside, på fodens yderside, med høje knæløft, med spark bagud, sidelæns, baglæns, med chassétrin..... o.s.v.
Husk de løse armsving under gangen!

Udarbejdet af fysioterapeuterne på Hillerød Sygehus. April 1999. Genoptrykt april 2007. Ebo Grafisk A/S, Roskilde.

Hjemmetræning

Dato	11-okt	12-okt	13-okt	14-okt	15-okt		18-okt	19-okt	20-okt	21-okt	22-okt
År	2009	2009	2009	2009	2009		2009	2009	2009	2009	2009
Træningsdag	1 Mandag	2 Tirsdag	3 Onsdag	4 Torsdag	5 Fredag		6 Mandag	7 Tirsdag	8 Onsdag	9 Torsdag	10 Fredag
Trappetræning 3 x 5 min eller 15 min											
Gangtræning : 1 gang daglig a 20 min											
Øvelsesprogram											

Dato	25-okt	26-okt	27-okt	28-okt	29-okt		01-nov	02-nov	03-nov	04-nov	05-nov
År	2009	2009	2009	2009	2009		2009	2009	2009	2009	2009
Træningsdag	11 Mandag	12 Tirsdag	13 Onsdag	14 Torsdag	15 Fredag		16 Mandag	17 Tirsdag	18 Onsdag	19 Torsdag	20 Fredag
trappetræning 3 x 5 min eller 15 min											
Gangtræning : 1 gang daglig a 20 min											
Øvelsesprogram											

Dato	08-nov	09-nov	10-nov	11-nov	12-nov		13-nov	14-nov	15-nov	16-nov	17-nov
År	2009	2009	2009	2009	2009		2009	2009	2009	2009	2009
Træningsdag	21 Mandag	22 Tirsdag	23 Onsdag	24 Torsdag	25 Fredag		26 Mandag	27 Tirsdag	28 Onsdag	29 Torsdag	30 Fredag
Trappetræning 3 x 5 min eller 15 min											
Gangtræning : 1 gang daglig a 20 min											
Øvelsesprogram											