

**Tabel 7. Uitgangsvraag 6 – Welke vorm van revalidatie kan klachten voorkomen/verminderen tijdens de ziekte- en symptoomgerichte palliatieve fase?**

Study (trial) ID	Study type	Source of funding/ conflicts of interest	Setting	Hypotheses	Eligibility criteria	Sample size/ Lost to follow up	Duration of the Study	Randomization method	Patient characteristics and group comparability	Interventions and compliance	Control/ Comparator (including duration, dose)	Primary Outcome Measure (s) Secondary Outcome Measure (s)	Effect size – Primary outcome(s) Effect size – Secondary outcome (s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
Brown 2006	Stratified RCT	Linse Bock Foundation and Saint Mary's Hospital Sponsorship Board. No indication of conflicts of interest	Division of Radiation Oncology Mayo Clinic Rochester	To examine the effect of participation in a structured, multidisciplinary intervention on fatigue for advanced cancer patients	Inclusion criteria: adult advanced cancer patients planned to undergo radiation therapy – cancer diagnosis within the last 12 months, expected survival of at least 6 months, but 5-year survival probability $\leq$ 50%, treatment recommendation of radiation therapy for at	Randomized: Intervention: 57; control: 58 Completed week 4 assessment: Intervention: 46; control: 54	4 weeks intervention. Completion of questionnaires at week 4, 8, and 27	Stratification for tumor type, age, gender, and ECOG score, using a minimization procedure that balances the marginal distributions	Comparable groups. 35% women, 80% over 50 years, 60% on current chemotherapy, mean radiotherapy dose 5322 cGy in 29 fractions, 80% married, 55% employed, median hemoglobin 12,3, mean MMSE 28,7, mean POMS 68, mean SDS 66, mean LASA 54, mean STAI 55	Participants attended 8 90-minute sessions over 4 weeks. Manual about the sessions. Each sessions had a theme focusing on quality of life. Begin: 20 minutes exercise, followed by educational information, cognitive-behavioral strategies, discussion, and support. Motion,	No intervention, standard care	Primary: single-item Linear Analogue Self Assessment (LASA) fatigue questionnaire. Secondary: Profile of Mood States (POMS), Fatigue-Inertia Subscale and Vigor-Activity Subscale, Spielberger's State-Trait Anxiety Inventory (STAI), Symptom Distress Scale (SDS)	No significant differences in mean fatigue scores between arms at any week. There were trends not reported favoring the standard treatment (less fatigue when no intervention)	Overall quality of life improved in the intervention arm (i.e. primary endpoint of the initial study, but not reported in detail in this article)	Randomized study, but not blinded (full blinding is not possible because of the intervention, but the investigators could have been blinded). Total number of participants is not that high	B

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					least 2 weeks. Exclusion criteria: MMSE < 20, ECOG ≥ 3, active alcohol or substance dependence (except nicotine), active thought disorder, suicidal plans, participation in psychosocial research trial					stretching, functional exercises. Individualized home program. End of session: relaxation exercise						
Cristopher 2004	Pilot, pre-post study in one group	No information	Oncology Community Outreach Program, University of Massachusetts	To evaluate the impact of a community-based 12-week exercise program on physical and psychosocial well-being in	Participants of fall and winter exercise programs. Women that survived cancer. No criteria about life expect-	21 patients (12 fall exercise, 9 winter exercise)	12 week exercise program, pre- en post-test questionnaires	No randomization	All women, al-most all breast cancer patients, mean age 60 years, al-most all white patients, 80%	12 week exercise program, twice a week, low-impact aerobics, toning, flexibility exercises,	No control group	Psychosocial Adjustment to Illness Scale (PAIS-SR), Profile of Mood States-short form (POMS-SF), Symp-	Almost no statistically significant differences were found. In the group that attended the fall exercise statistically	No other outcomes	No comparative design, weak description of important parameters, e.g. exercise program, patient recruitment,	C

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				women cancer survivors	any				married, mean time since diagnosis 44 months, mean time since treatment ended 22 months	relaxation techniques		Tom Distress Scale (SDS), Piper Fatigue Scale (PFS), Quality of Life-Cancer Survivors Scale (QOL-CS)	significant improvement was measured on subscales (domestic environment, psychosocial distress, and social well-being)		poor article, very few patients, no distinction in cancer stage and life expectancy	
Cramp 2008	Cochrane systematic review	No external sources of support, internal source: faculty health social care, University West England, no indications of conflict of interest	-	To evaluate the effect of exercise on cancer-related fatigue during and after cancer treatment	Only RCTs were included. Adults of any age, regardless of gender, tumour type, tumour stage, type of cancer treatment. Patients could be in active treatment, in long-term follow-up or receiving	28 RCTs included, total 2083 patients	-	-	Most patients had breast cancer, stages of cancer varied, stages of treatment varied, most patients were women, mean age 39-69 years	Any exercise intervention aimed to reduce fatigue associated with cancer	No exercise, usual care, alternative treatment	Patient-reported fatigue (multiple scales), exercise maintenance on follow-up, attrition, time spent exercising, aerobic capacity, quality of life measures, anxiety, depression, self-efficacy	Less fatigue in patients that were in the intervention group (SMD -0.23; 95% BI -0.33 - 0.13). Post test changes: intervention more effective (SMD -0.23; 95% BI -0.36 - -0.09) In breast	Only meta-analyses reported in this evidence table. To report valid results of single studies (that are mentioned in the review), one should have more information of those single trials collected	Good Cochrane systematic review. Value for this guideline however limited, because of no distinction in analyses in subgroups of cancer stage (although these data are collected	A1

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London 2005	Prospective observational study	Robert Wood Johnson Foundation Promoting Excellence National Program Office, Supportive Care of the Dying	CALL Care sites, facilities of supportive care for the dying: a coalition for compassionate care	To evaluate the CALL-intervention in patient with life-threatening cancer, cardiac illness, respiratory conditions or dementia	Cancer stage IV, Car-diac illness stage III or IV or ejection fraction $\leq$ 25%, Dementia stage 6 or 7 of FAST, Respiratory illness Karnofsky score $<$ 50 or required oxygen for activities of daily living	295 patients at enrollment, no completed questionnaires at 18 months (94 patients died during the study)	18 months	No randomization	Mean age 72 years, 62% female, 88% whites, 41% lived at home with family, 21% alone at home, and 26% in a nursing home	CALL Care Approach: a variety of services (e.g. coordinate physician visits, connect with spiritual care provider, educate patient and family, plan for universal activities, pro-active bereavement follow-up), coordinated by a specific multidisciplinary CALL Care team	No control group	Scores on Modified City of Hope Patient Questionnaire (55 items on physical, emotional/relationship, spiritual, health-care experience, and health care providers communication) at enrollment, 1, 3, 6, 9, 12, 15, and 18 months	comparing this effect was even bigger Comparing the enrollment score and the last data alive there were better, but insignificant scores on fatigue and nausea, and better significant scores on mouth/ food symptoms (e.g. dry mouth, appetite changes), intestinal problems, breathing	No other outcomes	No comparative design, no information on patient recruitment, large amount of patients lost-to-follow-up, probably selective	C

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Lowe 2009	Systematic review	National Cancer Institute of Canada Canadian Cancer Society, Sociobehavioral Cancer Research Network	-	To review the evidence of physical activity as supportive care intervention in palliative cancer patients	A study had to examine a physical activity intervention in palliative cancer patients, aged 18 years or older, regardless of gender, tumor type, or type of cancer treatment. Palliative cancer was defined as progressive, incurable locally recurrent or metastatic cancer, with a life expect-	6 studies, total 84 patients. All pilot studies, some case-reports	-	-	Mean age 58 years, 64/84 women, most patients having breast cancer, followed by gastrointestinal cancer	Supervised group exercise programs and unsupervised home-based physical activity program (Duke Energizing Exercise Plan for 9 patients, Arm-chair Fitness and gentle exercise video for 38 breast cancer patients, group exercise program focused on muscle strength,	Most studies had no comparison	Primary outcomes: Patient-reported quality of life, patient-reported physical functioning, patient-reported fatigue. Secondary outcomes: objective measures of physical fitness and physical functioning, patient-reported palliative symptoms	In one of the studies significant lower decline in total well-being scores in intervention group. The only RCT showed no significant differences	No other outcomes	Systematic review of poor studies, only one RCT, rest of the studies non-comparative and even case reports. No meta-analysis. Classification on the validity is not possible due to the poor quality of the underlying studies	No level

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					tancy of less than 12 months				standing balance and aerobic endurance for 34 patients)							
Mustian 2006					Newly diagnosed cancer patients undergoing curative treatment → therefore this study is excluded for further analysis											
Oldervoll 2006	Pilot study, Phase II	Norwegian Foundation for Health and Rehabilitation and the Norwegian Cancer Society. No indication of conflict of interest	Oncological outpatient clinic at St. Olav Hospital in Trondheim and Hospice Lovenberg	To evaluate the effect of a 6-week structured exercise program on HRQOL, fatigue, and physical performance in cancer patient with	Cancer patients with a life expectancy between 3 and 12 months, Karnofsky performance score $\geq 60$ , adequate pain relief, and lived	63 patients at enrollment, 29 patients dropped out due to sudden death, or medical or social reasons. There seems to be	6 weeks	No randomization	15 males, 19 females, mean age 65 years, 88% not employed, median KPS 80, different types of cancer (16 gastro-intestinal cancer),	Exercises in groups (3-8 patients per group), twice a week, 50 minutes per session, 6 weeks long. Warm-up circuit training with 6	No control group	EORTC-QoL, Life QoL, EORTC QLQ-C30, Fatigue Questionnaire (FQ), 6 minute walk, timed sit-stand, functional	Significant improvement in emotional functioning (69 → 78, p=0,002). Fatigue score decreased: 51 → 43 (p=0,06; less fatigue).	Increase in walking distance by 29 meter (p=0,007), decrease in time sit-stand of 1 second (p=0,001)	Well-documented study, but non-comparative design. Only a few patients in the study	C

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				short life expectancy	less than 30 minutes from the hospital. Consecutive patients	selective follow-up → 34 patients in analysis			80% metastases	stations, relaxation/ stretching session. Focus on muscle strength, standing balance, and aerobic endurance		onal reach	Same trends on other scales. Physical functioning and global quality of life remained stable. Dyspnea reduced (42 → 60, p=0.006), role + social functioning improved (50 → 63, p=0.02 and 55 → 65, p=0.008).			
Porock 2000	Pre-test post-test design, pilot study	Silver Chain Nursing Foundation and Edith Cowan University	Home Hospice Care Service in Perth, Western Australia	To determine the effects of an individualized exercise program (Duke Energizing Exercise Programme)	Patients with advanced cancer, ECOG classification of 1 and more, estimated life expectancy of at least 1	11, 2 dropped out for selective reasons (feeling unwell, finishing it all too much), 6 completed	4 weeks	No randomization	9 patients, mean age 60 years, 6 female, 4 bowel cancer, 2 pancreas cancer, 7 patients with	Physiotherapist specialized in oncology and palliative care conducted home visit and educated the	No control group	Multidimensional Fatigue Inventory (MFI), Symptom Distress Scale (SDS), Hospital Anxiety and	Minimal fluctuation in the mean MFI subscale scores, quality of life scores improved from day 0 to	No other outcomes	Very few patients in the study, lack of complete data, non-comparative study	C





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Strasser 2004	Retrospective descriptive comparative study	Swiss Cancer Research	Multidisciplinary Clinic and traditional pain and symptom management clinic at the University of Texas MD Anderson Cancer Center	To characterize symptoms, recommendations, and effect of multidisciplinary team on symptom expression and overall satisfaction of patient and families. Comparison with traditional pain and symptom management	First 138 consecutive patients at the MD clinic and a consecutive sample of 77 patients seen at the PSM clinic	138 patients in MD clinic, 77 patients in PSM clinic. No lost-to-follow-up due to retrospective design	Retrospective chart analysis, + follow-up (mean 9 days) at MD Center	No randomization	Adults with primary tumors of various types. Referral to the clinics for pain control, end-of-life issues (only MD), and management of multiple symptoms (only MD), 54% female, mean age 54 years, median survival 10 weeks in MD, and 51 weeks in PSM clinic	MD Clinic has no waiting area, patients have private room with bed and bathroom. In 5 hours the patient is assessed by a physician, nurse, social worker, physical, occupational, speech therapist, pharmacist, nurse practitioner, and pastoral care worker. On-site counseling, specific education, and simple interventions	Traditional pain and symptom management given by a physician and a nurse	In MD Clinic: ad-hoc questionnaire with 7 items, to be answered on a 5-point scale, focused on satisfaction. Retrospective chart review on symptoms, results of standardized assessments, and recommendations	In the MD group patients received median 4 non-physician recommendations, in the PSM group none. In MD group significant improvement in pain, nausea, depression, anxiety, sleep, shortness of breath, and well-being, but not in fatigue, anorexia, or drowsiness. No comparative data, patients in	No other outcomes	Both groups are not comparable at baseline due to differences in the severity of the disease. Almost no comparisons have been made between the groups, so this study is best worth given a non-comparative retrospective study, however with useful information	C

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Sola 2004	Cochrane systematic review			To determine the effectiveness of non-invasive interventions delivered by health-care professionals in improving symptoms, psychosocial functioning and quality of life	Only RCT's and CCT's were included. Studies on patients of either sex and any age diagnosed with lung cancer (also with some patients with other thoracic cancer) at any stage of their illness	9 studies	-	-	No aggregate data on patient characteristics, no specific data for those patients in the palliative phase of their disease, all patients had lung cancer	Various interventions have been studied in the RCT's and CCT's, divided in 6 groups: Nursing interventions to manage breathlessness, nursing programs, nutrit-	-	Well-being (subjective or objective perception of improvement in physical health, or of symptoms related to cancer, metastases or side effects of treatment; or improvement of psycho-	Nurse led breathing programs may produce beneficial effects. Nurse follow-up can be as effective and leads to greater patients satisfaction than physician follow-up, coun-	No other outcomes	Well designed Cochrane systematic review with extensive description of the methods, no metaanalysis	A1
										are provided. Multidisciplinary team discussion on assessment and recommendation, given to the patient. Follow-up in 1-2 weeks is provided.			the MD clinic were overall as on subscores very satisfied			

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Temel 2009	Uncontrolled feasibility study	Public funds	Hospital-based	To assess feasibility of exercise program for patients with advanced NSCLC	Patients < 12 weeks of diagnosis of non-small cell lung cancer (NSCLC)	25/14	12 weeks	None	Patients aged 48-81 with advanced NSCLC, mostly (70%) treated with chemotherapy	A Structured exercise program consisting of 16 twice weekly sessions over 12 weeks. The program took place in groups (8-10 patients) lasting 90-120 minutes. After warming up a 30 minutes aerobic	No control	Feasibility (adherence to the intervention); secondary: functional capacity (6 m walking test), quality of life (QOL), symptoms and fatigue (FACT-L)	Of 25 accrued patients, 20 completed baseline assessment and 11 attended all sessions (44% adherence); No changes in QOL, fatigue or mood. Lung cancer symptoms improved.	-	It is unclear what selection of eligible patients participated. It is unclear whether observed effect is related to the intervention	C

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Yoshioka 1994	Uncontrolled study		Hospice-based		Terminal cancer patients (<6 months to death) admitted to a hospice and provided with a rehabilitation program.	355/?	6 months		Patients aged 17-88 with terminal cancer	robic exercise. A strength component consisted of 3 sets of 10 repetitions of 6 different exercises over 30-40 minutes	No control	ADL (Barthel index). Questionnaires mailed to relatives 3 months after death.	No adherence data. Most patients experienced some relief		26% of eligible patients accrued in the study	C

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Marciniak 1996	Retrospective case series		Hospital-based		Adult cancer patients admitted for comprehensive inpatient rehabilitation	159			Patients aged 17-88, 38% of which had metastatic disease	sed bed exercises, endurance training, chesty physiotherapy, + some specific treatments No specific intervention mentioned	No control	Functional status	Functional gains between admission and discharge (mean 42.9- >56.0) (p< 0.001) Presence of metastatic disease did not influence outcome.			C
Headley 2004	Quasi-experimental study				Women ≥17 years with stage IV breast cancer	38/32		No randomization		30min. seated exercise program (armchair fitness) 3	No exercise program	Fatigue and QOL (FACIT-F); pain	Less increase in fatigue and less decline in QOL for		Unclear how patients were assigned to treatment group.	B

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					scheduled to receive chemotherapy and able to sit.					times a week. 84% adherence			experimental group		Subjects in the control group more educated and more frequently unmarried.	