Journal of Geriatric Oncology xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

Geriatric assessment with management for older patients with cancer receiving radiotherapy. Protocol of a Norwegian cluster-randomised controlled pilot study

Inga Røyset [a,b,g], Ingvild Saltvedt [a,b], Siri Rostoft [c,d], Bjørn Henning Grønberg [e,f], Øyvind Kirkevold [g,h,i], Line Oldervoll [j,k], Asta Bye [l], Jūratė Šaltytė Benth [g,m,n], Sverre Bergh [g,h], Line Melby [i], Vidar Halsteinli [o], Øystein Døhl [a,p], Tove Røsstad [k,p], Guro Falk Eriksen [d,g,q], May Ingvild Volungholen Sollid [g,i], Darryl Rolfson [r], Marit Slaaen [d,g,*]

[a] Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Science, Norwegian University of Science and Technology (NTNU), NO-7491 Trondheim, Norway
[b] Department of Geriatric Medicine, Clinic of Medicine, St. Olavs Hospital, Trondheim University Hospital, Box 3250, Torgarden, NO-7006 Trondheim, Norway
[c] Department of Geriatric Medicine, Oslo University Hospital, Pb 4956, Nydalen, NO-0424 Oslo, Norway
[d] Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Pb 1171, Blindern, NO-0318 Oslo, Norway
[e] Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Science, Norwegian University of Science and Technology (NTNU), NO-7491 Trondheim, Norway
[f] Department of Oncology, St. Olav Hospital, St. Olavs Hospital, Trondheim University Hospital, Box 3250, Torgarden, NO-7006 Trondheim, Norway
[g] The Research Centre for Age-related Functional Decline and Disease, Innlandet Hospital Trust, Box 68, NO-2312 Ottestad, Norway
[h] Norwegian Advisory Unit on Ageing and Health, Vestfold Hospital Trust, Postboks 2136, NO-3103 Tønsberg, Norway
[i] Department of Health Sciences in Gjøvik, NTNU, Box 191, N-2802 Gjøvik, Norway
[j] Center for Crisis Psychology, Faculty of Psychology, University of Bergen, PB 7807, NO-5020 Bergen, Norway
[k] Department of Public Health and Nursing, Faculty of Medicine and Health Science, NTNU, PB 8905, NO-7491 Trondheim, Norway
[l] Oslo Metropolitan University (Oslomet), Postboks 4, St. Olavs plass, NO-0130 Oslo, Norway
[m] Institute of Clinical Medicine, Campus Ahus, University of Oslo, P.O.Box 1171, NO-0318 Blindern, Norway
[n] Health Services Research Unit, Akershus University Hospital, P.O.Box 1000, NO-1478 Lørenskog, Norway
[o] Regional Center for Health Care Improvement, St. Olavs Hospital, Trondheim University Hospital, Box 3250, Torgarden, NO-7006 Trondheim, Norway
[p] Department of Health and Welfare Services, City of Trondheim, Postboks 2300, Torgarden, NO-7004 Trondheim, Norway
[q] Department of Internal Medicine, Hamar Hospital, Innlandet Hospital Trust, Skolegata 32, NO-2318 Hamar, Norway
[r] Division of Geriatric Medicine, University of Alberta, 1-198, Clinical Sciences Building, 11350 83 Ave, Edmonton, Alberta T6G 2P4, Canada

ARTICLE INFO

Article history:
Received 12 October 2021
Accepted 2 November 2021
Available online xxxx

Keywords:
Randomised controlled trial
Geriatric assessment with management
Radiotherapy
Research protocol
Pilot study

ABSTRACT

About 50% of patients with cancer are expected to need radiotherapy (RT), and the majority of these are older. To improve outcomes for older patients with cancer, geriatric assessment (GA) with management (GAM) is highly recommended. Evidence for its benefits is still scarce, in particular for patients receiving RT. We report the protocol of a cluster-randomised pilot study designed to test the effect, feasibility and health economic impact of a GAM intervention for patients ≥65 years, referred for palliative or curative RT. The randomising units are municipalities and city districts. The intervention is municipality-based and carried out in collaboration between hospital and municipal health services from the start of RT to eight weeks after the end of RT. Its main constituents are an initial GA followed by measures adapted to individual patients' impairments and needs, systematic symptom assessments and regular follow-up by municipal cancer nurses, appointed to coordinate the patient's care. Follow-up includes at least one weekly phone call, and a house call four weeks after the end of RT. All patients receive an individually adapted physical exercise program and nutritional counselling. Detailed guidelines for management of patients' impairments are provided. Patients allocated to the intervention group will be compared to controls receiving standard care. The primary outcome is physical function assessed by the European Organisation of Research and Treatment of Cancer Quality of Life Questionnaire C-30. Secondary outcomes are global quality of life, objectively tested physical performance and use of health care services. Economic evaluation will be based on a comparison of costs and effects (measured by the main outcome measures). Feasibility will be assessed with mixed methodology, based on log notes and questionnaires filled in by the municipal nurses and interviews with patients and nurses. The study is carried out at two Norwegian RT centres. It was opened in May 2019. Follow-up will proceed until June 2022. Statistical analyses will start by the end of 2021. We expect the trial

* Corresponding author at: The Research Centre for Age-related Functional Decline and Disease, Innlandet Hospital Trust, P.O Box 68, NO-2313 Ottestad, Norway.
E-mail address: marit.slaaen@sykehuset-innlandet.no (M. Slaaen).

https://doi.org/10.1016/j.jgo.2021.11.001

Please cite this article as: I. Røyset, I. Saltvedt, S. Rostoft, et al., Geriatric assessment with management for older patients with cancer receiving radiotherapy. Protocol..., J Geriatr Oncol, https://doi.org/10.1016/j.jgo.2021.11.001

to provide important new knowledge about the effect, feasibility and costs of a GAM intervention for older patients receiving RT.

Trial registration: ClinTrials.gov, ID NCT03881137, initial release 13th of March 2019.

List of Abbreviations

ADL	activities of daily living
ASCO	American Society of Clinical Oncology
BMI	body mass index
EFS	Edmonton Frail Scale
EORTC QLQ-C30	the European Organisation for Research and Treatment of Cancer Quality of life Questionnaire-C30
ESAS	Edmonton Symptom Assessment System
EQ-5D-5L	the EuroQual-5D-5L questionnaire
GA	geriatric assessment
GAM	geriatric assessment with management
GDS	geriatric depression scale
GP	general practitioner
IADL	instrumental activities of daily living
ICC	intra-cluster correlation
MNA-SF	Mini Nutritional Assessment – Short Form
PF	physical function as measured by the EORTC QLQ-C30
RCT	randomised controlled trial
RT	radiotherapy
SD	standard deviation
SPPB	Short Physical Performance Battery
TUG	Timed Up and Go
QoL	quality of life

1. Introduction

Radiotherapy (RT) is a main treatment modality in cancer, and is estimated to be needed by about 50% of all patients with cancer during their disease trajectory [1,2]. The majority, and an increasing number of these patients, are older [3].

RT may be administered with curative or palliative intent, and most often as external beam irradiation, which includes daily irradiation fractions over a period varying from one day to several weeks, depending on treatment intent, cancer type, and the organ involved. Due to smaller daily fractions and higher total doses, curative treatment usually takes more time and has more frequent and severe side effects than palliative treatment. In either case, side effects may be local, i.e., related to radiation area, or general, e.g., fatigue and physical deterioration [4]. Both acute and late side effects may occur. Acute effects are usually reversible, and most pronounced by the end of or during the first weeks after treatment. Late effects develop three months or more after treatment, and are persistent and/or progressive [4]. There is evidence suggesting that older patients benefit from RT equally compared to younger patients [5,6]. Higher incidence of co-existing problems, higher toxicity rates, and a negative impact of side effects on quality of life (QoL) and physical function are, however, serious concerns [4–7].

Geriatric assessment (GA) addresses problems that are frequent in older age [8,9] and includes systematic assessment of somatic health (such as comorbidity and nutritional status), mental health (such as cognition and depression), functional aspects (such as activities of daily living [ADL] and physical function), and social network and living situation. When followed by adequate management of identified vulnerabilities and impairments, i.e. GA with management (GAM), this approach has documented success in improving outcomes in non-cancer populations [10,11]. GA has been adapted for cancer care, and mounting evidence shows that it may identify remediable problems, improve patient-centred communication, affect oncological treatment decisions, and predict survival or adverse effects from chemotherapy and cancer surgery [8,12–16]. All GA domains cover areas where impairments may negatively affect outcomes of cancer and cancer treatment [17]. However, these impairments may also be prevented, alleviated, or improved by targeted measures, such as optimising treatment of comorbid conditions, discontinuation of inappropriate medications, nutritional counselling, and physical rehabilitation [17–20]. Thus, GAM is strongly recommended to improve treatment and care for older patients with cancer [16,21–23]. Currently, there is evidence that such an approach improves the completion rate of cancer surgery and chemotherapy, and reduces the risk of severe chemotherapy toxicity [16]. Few studies have looked at the impact on patient-centred outcomes of major importance to older patients [24], and research has hitherto mainly focused on surgical and systemic cancer treatment.

We have developed a GAM intervention for older patients with cancer receiving RT, aiming to improve their physical function and QoL. The aim of this paper is to present the protocol of a cluster-randomised pilot study, conducted to assess the effect, feasibility, and costs of the intervention.

2. Methods/Design

2.1. Aims and Objectives

The overarching aim of the pilot study is to provide the evidence needed for a future definite evaluation and implementation of a GAM intervention for older patients receiving RT on a larger scale. The primary objective is to assess potential short- and long-term effects of the intervention on patient-centred outcomes, i.e. self-reported and objectively tested physical function, global QoL and symptom occurrence. Further objectives are to assess feasibility, both at the patient- and organizational level, and to study the use of health care services and costs in comparison to standard care.

2.2. Study Design

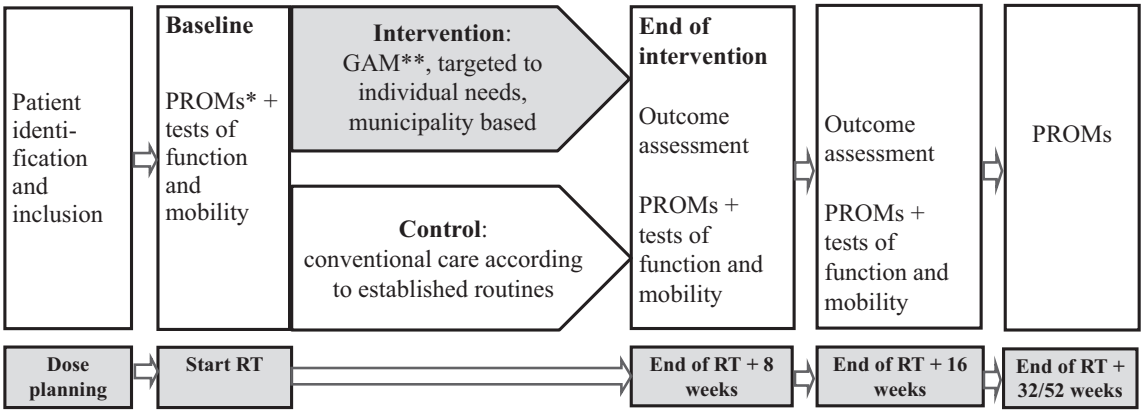
The study is a controlled cluster-randomised pilot study where municipalities or city districts were randomised to either intervention or control before the study was opened for inclusion. The intervention is a multicomponent, individually targeted GAM intervention for older patients receiving RT in terms of external beam irradiation. It is compared to conventional care (control) and applied in collaboration between hospital and municipal health service from start of RT to eight weeks after the end of treatment. The patients are followed with study specific assessments for an additional 44 weeks (Fig. 1), and for five years with respect to survival.

The study was opened in May 2019 and closed for inclusion in April 2021. Follow-up is ongoing.

2.3. Study Context

2.3.1. The Norwegian Health Care System

The context for the study conduct and the experimental intervention is the Norwegian public health service. This covers all levels of hospital services, rehabilitation, and primary health care including general practitioners (GPs), physiotherapists, home care services and nursing homes. Norway has universal health care where the government owns and manages the hospitals through four regional health authorities. These provide most hospital services and reimburse rehabilitation service to inhabitants within their respective geographical region. GPs and physiotherapists (outside hospitals) are partly reimbursed by



*PROMs = patient reported outcome measures. Also applied in both groups at the end of RT and at the end of RT + 4 weeks
** GAM = Geriatric assessment with management

Fig. 1. Overview over the study design.

governmental means. Otherwise, each municipality funds, organises, and manages all primary health service for its inhabitants. In-hospital treatment and home care nursing are free of charge, whereas limited co-payment (relative to income) is required for practical help at home. Moreover, patients pay for medications, outpatient hospital treatment, GP consultations, and physiotherapy up to a yearly limit of about 230 Euros, above which all is free.

2.3.2. The Study Centres

The study is conducted at two RT centres in two Norwegian health regions, and in collaboration with municipalities in their catchment areas. The primary RT study centre (Centre 1) is situated in a local hospital in the south-eastern Norway health region. It provides RT with palliative intent, irrespective of cancer type, to all inhabitants (approximately 346,000) in a catchment area including 42 municipalities. Curative RT is mainly administered to patients with breast, prostate, lung, and skin cancers, whereas patients with other diagnoses and those in need of specific irradiation techniques (e.g. stereotactic treatment) are referred to the health region's university hospital. The second study centre (Centre 2) is located at the university hospital in a city (207,000 inhabitants) of the central Norway health region. It provides all RT services to the inhabitants in a catchment area including 38 municipalities with approximately 470,000 inhabitants.

The two study centres differ in volume of patients, resources, and organisation. Thus, established routines for consultations and information also vary (Table 1). However, neither has implemented any routines for GA or geriatric consultations for patients with cancer, and there is a shortage of expertise in geriatric care. At the local hospital (Centre 1), a specialist in geriatric medicine is available merely two days a week, and although the university hospital (Centre 2) has a well-established department of geriatric medicine, resources are too scarce to allow any routine- or regular services for patients with cancer. Nutritionists, physiotherapists and social workers are available upon referral, but capacity is limited, and inpatients are usually prioritized. Upon referral, both centres have access to palliative care specialists, at Centre 1 by a palliative care team, and at Centre 2 by a palliative care centre.

Before study start, an experienced cancer nurse was employed as a project nurse at Centre 1, whereas a PhD student specialized in geriatric medicine filled a similar position at Centre 2. Otherwise, no extra resources were allocated to the study centres.

2.3.3. Collaborating Municipalities and Cancer Contact Nurses

At Centre 1, 30 out of 42 municipalities consented to study participation. These vary from small rural municipalities to larger ones with an urban centre. Overall, twelve municipalities have 4500 inhabitants or less, twelve comprise from about 6000 to about 14,000 inhabitants, and the remaining six have 20,000 to 35,000 inhabitants. All provide the essential primary health care services as previously described, and they all have a cancer coordinator or cancer contact nurse in their staff. These nurses, hereafter referred to as cancer contact nurses, are designated to work with patients with cancer and their next of kin, either part-time (e.g. one day a week in the smaller municipalities) or full time. Not all of them are formally educated cancer nurses, but they all have substantial experience in cancer care. Moreover, a majority participated in a foregoing observational study (Clinicaltrials.gov ID NCT03071640) by our research group and received training in geriatric methodology. The cancer contact nurses' work covers information, evaluation, and support, to some extent specialized palliative care, and conventionally also ad hoc collaboration with patient's GP, in-hospital oncologists and cancer nurses.

In the catchment area of Centre 2, the city municipality harbouring the university hospital was invited and consented to study participation. Here, home care service is organised into four distinct city districts, each with 34,000 to 50,000 inhabitants. Although their nursing staff includes some cancer nurses, none of the city districts holds designated positions for cancer contact nurses like those in the catchment area of Centre 1.

2.4. Randomisation and Concealment

Before study start, consenting municipalities and city districts were defined as clusters. In two cases, two municipalities were joined into one cluster as they shared a common cancer contact nurse. Thus, 32 clusters (28 municipality clusters and four city districts) were stratified into blocks according to number of inhabitants. Thereafter, clusters within each block were randomly assigned to either intervention or control by using a computer-generated algorithm, 16 clusters in each group. This means that eligible, consenting patients from an intervention municipality/district enter the intervention program, whereas patients from control municipalities/districts enter the control group. Consequently, when consent has been provided, the allocation is open to both the patients and their health care professionals. However, assessors of pre-defined outcomes that are not patient-reported are blinded.

2.5. Study Population

The defined inclusion criteria are: age 65 years or older, referral for palliative or curative RT, confirmed cancer diagnosis, residency in one

Table 1
Organisation at the participating study centres.

	Centre 1, at a local hospital	Centre 2, at a university hospital
Resources		
No of linear accelerators	2	4
No of oncologists (senior consultants)	2–3	3.5
No of resident physicians	1–2	2
No of radiation therapists (full time positions)	14.6	27
No of physicists	3	5
No of cancer nurses (full time positions)	1.35	0
No of individual patients each year	Approx. 700	Approx. 1300
No of patients receiving palliative radiotherapy	Approx. 300	Approx. 500
No of patients receiving curative radiotherapy	Approx. 400	Approx. 800
Routine offers to patients during treatment		
Group-wise assembly[a]	Patients with breast or prostate cancer receiving curative radiotherapy	None
Consultations with oncologist/resident physician		
At start of treatment	All patients	All patients
During treatment	Some, mainly lung and CNS cancer	Some, mainly those who undergo long term RT (>2 weeks)
By the end of treatment	All patients	All patients
Consultations with cancer nurse		
At start of treatment	All patients except those having participated in the day course	No standard routines
By the end of treatment	All patients except hospital inpatients	No standard routines Some patients are followed alternately by physicians and nurses.
Follow-up after treatment		
At the radiotherapy centre		
Telephone calls	2 weeks after radiotherapy for all patients with breast cancer having received curative treatment, 4–6 weeks after a single 8 Grey irradiation fraction	No standard routines
Outpatient consultations	For patients receiving curative treatment: after 3 and 12 months for patient with prostate cancer, and after 6 weeks for most patients with lung cancer	Some selected patients having received long term curative treatment
Other follow-up	Most patients followed by their oncologist outside the radiotherapy centre	Most patients followed by their oncologist outside the radiotherapy centre

[a] The assembly is arranged for groups of patients, and offered about 1–2 weeks prior to treatment. It includes information about the cancer disease, its treatment, and related issues given by a radiation therapist, an oncologist, a cancer nurse, a social worker, a physiotherapist and a former patient. Patients also visit the location where RT is given as well as a nearby area open for individual physical training sessions.

of the participating municipalities/city districts, fluency in Norwegian, ability to fill in self-report questionnaires, and consent to study enrolment by written, informed consent. Exclusion criteria are: life expectancy of less than three months and referral for only one palliative fraction of RT.

2.6. The Intervention Program as Planned

The intervention has two main components: 1) GAM and 2) collaboration across sectors with the municipal cancer contact nurse in a crucial coordinating position (Fig. 2).

2.6.1. The Content of the GAM Intervention

Essential GAM parts are a broad assessment by the start of RT and repeated, systematic assessments during follow-up (Table 2). The initial assessment focuses on somatic- and mental health, function, and social conditions. In accordance with recommendations for GA in oncology [8], it includes a systematic evaluation of comorbidity, medications, physical function (mobility, strength, and balance), ADL, instrumental ADL (IADL), nutritional status, cognitive function, depression, and social situation. For this purpose, we have chosen established, validated geriatric tools and methods (Table 2). The intervention also includes a systematic symptom assessment, the Edmonton Symptom Assessment System (ESAS) [25] assessing 10 common symptoms in cancer on scales ranging from zero (best) to ten (worst), and a screening tool for frailty, the Edmonton Frail Scale (EFS) [26]. Follow-up assessments include at least weekly registrations of weight and symptoms (ESAS) during the intervention period, and nutritional- and frailty screening (EFS) at the end of RT and four weeks later (Table 2). The purpose of repeating EFS is to uncover problems within new areas that may need further assessment and management. Additional follow-up assessments should be conducted in accordance with identified impairments and needs.

Following the initial assessment, individually adapted measures targeting identified impairments, symptoms, and needs are to be applied in accordance with pre-defined guidelines (Table 3), and subsequently adjusted according to repeated assessments. Furthermore, all patients are to receive a physical exercise program adapted to results of their physical performance tests (Fig. 2). The program has three parts: 1) encouragement to maintain or increase daily life physical activities; 2) participation in suitable, organised activities in accordance with preferences and available options; and 3) individual exercises for training at home at least three times a week. At home exercises are based on three schemes with different levels of difficulties (light/moderate/more strenuous), suitable for older patients. These schemes were provided by a physiotherapist before study start and were meant as templates for further adjustment. At Centre 1, two physiotherapists agreed to make these individual adjustments based on patient evaluation and results of the physical performance tests. Similar physiotherapy resources could not be allocated at Centre 2.

2.6.2. Collaboration and Coordination

Before the study was opened for inclusion, one or two (depending on availability and size of the municipality) cancer contact nurses from the intervention municipalities were appointed municipal coordinators for the patients' care and intervention programs. The tasks were included into their routine work without providing any extra resources. To compensate for the lack of nurses in similar positions in the city intervention districts, an experienced municipal nurse was contracted in a part-time position. Thus, at study enrolment, each intervention patient is to be assigned a named municipality-based contact nurse.

The GA and the follow-up assessment by the end of RT are hospital-based. Due to limited availability of other relevant expertise, it was decided that the project nurse (Centre 1) and the PhD student (Centre

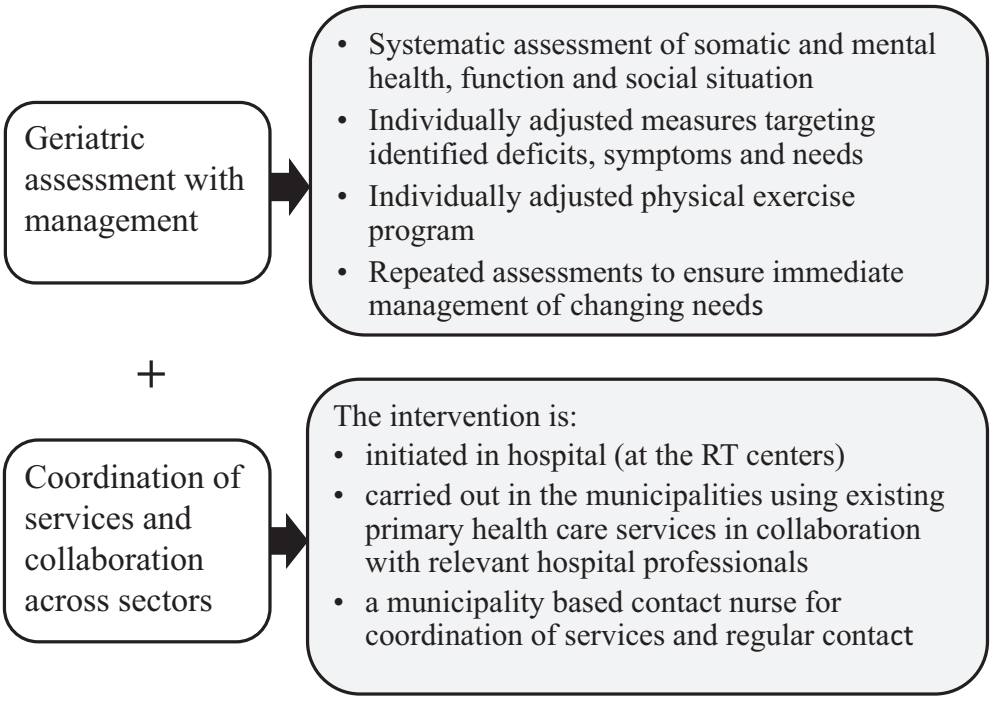


Fig. 2. The main constituents of the intervention program.

2) should conduct these assessments and initiate each patient's interventions. Following the GA, targeted measures are to be decided in collaboration with the patient's oncologist, seeking advice or contribution from other hospital specialists whenever needed (Table 3, guidelines). Next, the GA findings and undertaken measures are to be conveyed to the patient's cancer contact nurse, to ensure targeted follow-up and further involvement of relevant municipal health services. Results of the in-hospital follow-up assessment are to be handled accordingly. The municipal contact nurses are scheduled to follow the patients with regular consultations from start to end of intervention. As a minimum, this is a weekly telephone call including the basic pre-planned assessments, and a house call with a more thorough assessment four weeks after the end of RT (Table 2). Through a pre-study seminar and meetings approximately every third month, the cancer contact nurses are encouraged to use their clinical judgment and experience and make additional contacts with the patients when considered necessary. In all working hours, the project nurse and/or the PhD student are to be available for questions and support, or to help arrange contact with other hospital professionals.

2.7. Control Group

Patients from control municipalities/city districts receive current standard care. This means full access to all hospital and municipality services, as initiated by health professionals who according to standard routines provide their treatment and care. Opposed to the control city districts (Centre 2), the control municipalities in the catchment area of Centre 1 all have a municipal cancer contact nurse available. In standard care, these are involved ad hoc and mainly for palliative patients, i.e. when hospital professionals find referrals needed, or the patients themselves contact these nurses.

2.8. Outcome Assessment

An overview of the overall data collection in both study groups are presented in Table 4. The effectiveness of the intervention will be tested using patient-reported measures, physical performance tests, and registration of use of health care services. The pre-defined primary time point for outcome assessment is eight weeks post-RT. Physical function (PF) measured by the European Organisation for Research and Treatment of Cancer (EORTC) Quality of life Questionnaire-C30 (QLQ-C30) [39] is the defined primary outcome. Secondary outcomes are QoL assessed by the QLQ-C30 global QoL scale and EuroQoL-5D-5L (EQ-5D-5L) [40], physical performance assessed by the Short Physical Performance Battery (SPPB) [34], grip strength measured by a dynamometer [36], cost-effectiveness, use of health care services (hospital in- and outpatient services and municipality services), and trend in PF and QoL during follow-up. Other pre-defined outcomes are mobility assessed by the Timed Up and Go (TUG) test and the one legged balance test [35,41], symptom occurrence (fatigue, pain, dyspnoea, and sleeping disturbances) and emotional function assessed by the QLQ-C30, and nutritional abnormalities assessed by body mass index (BMI), weight loss and loss of appetite (subscale of the QLQ-C30). Patient-reported outcomes (QLQ-C30 and EQ-5D-5L) are assessed at baseline, at the end of RT, and thereafter four, eight, sixteen, 32 and 52 weeks after RT. Physical performance tests are applied at baseline and eight and sixteen weeks after the end of RT (Table 4). At baseline, the tests are conducted by the project nurse or PhD student, whereas municipal physiotherapists, blinded to the patients' study allocation, conduct the follow-up tests.

Economic evaluation will be based on a comparison of costs and effects as measured by the main outcome measures, EQ-5D-5L in particular. Costs include direct costs associated with GAM (intervention costs), as well as costs related to hospital admissions, home care and nursing home care. Data on service utilization will be obtained from national registers, and hospital and municipal registers, respectively (Table 4).

For evaluation of intervention feasibility, we will use the first four topics in the RE-AIM (reach, efficacy, adaption, implementation, and maintenance) framework [42,43]. We will use both qualitative and quantitative data. Quantitative data will include simple counting of withdrawals and included patients from those eligible, but will mainly be based on weekly log notes by the cancer contact nurses who administered the intervention. These notes comprise information on whether the scheduled contacts have taken place or not, time spent, results of the planned assessments (if actually performed) (Table 2), and registration of all measures that have been recommended or initiated, as well as adherence to these measures. Qualitative data will include individual

Table 2
Overview over systematic assessments during the intervention program, terminating 8 week after end of radiotherapy.

Area	All study participants[a]	Intervention patients					
	Baseline at the radiotherapy (RT) centre	Baseline (at the RT centre)	Weekly, during RT[b]	End RT (at the RT centre)	End RT + 1, 2 and 3 weeks[b]	End RT + 4 weeks[b]	End RT + 5, 6, 7 and 8 weeks[b]
Somatic health							
Clinical status		Blood pressure and extra lab tests[c]					
Overall frailty	Edmonton Frail Scale (EFS) [26]			EFS		EFS	
Symptoms		Edmonton Symptom Assessment System (ESAS) [25]	ESAS	ESAS	ESAS	ESAS	ESAS
Comorbidity	Charlson Comorbidity Index [27]	Old Americans' Resource Survey (OARS) [28]					
Medication	Number (EFS)	Registration of all medications (ATC codes)		All medications		All medications	
Nutritional status	Weight and height, weight loss (EFS)	Mini Nutritional Assessment- Short Form (MNA-SF) [29]	Weight	MNA-SF and weight	Weight	MNA-SF and weight	Weight
Mental health							
Cognition	Mini-Cog [30]						
Depression		Geriatric Depression Scale (GDS)-15 [31]					
Function							
Daily life activity	EFS items	Lawton index [32] Barthel index [33]					
Mobility, strength, balance	Short Physical Performance Battery (SPPB) [34] Timed Up and Go (TUG) [35] Grip strength [36] Falls			SPPB[d]			
Physical activity	Items from HUNT 3[e] [37]						
Social conditions							
Social	Civil status, living conditions, available help, home care, Oslo Social Support Scale [38]						
Measures applied and adherence to the intervention program							
Log notes[f]		X	X	X	X	X	X
Questionnaires filled in by municipal nurses			X		X	X	X

[a] Registrations performed to enable an adequate comparison of patients' characteristics between control and intervention for subsequent analyses,
[b] Registrations performed by the municipality based cancer contact nurse.
[c] Extra lab tests: HbA1c = glycated haemoglobin, FT4 = free thyroxine 4, THS = thyroid stimulating hormone, B12 = vitamin B12.
[d] SPPB repeated only for patients receiving >12 RT fractions.
[e] HUNT3 = the third Norwegian Trøndelag Health Survey.
[f] Log notes filled in by the project nurse/PhD student (baseline and end RT) or the municipality based cancer contact nurse (during and after RT)

interviews with patients and focus group interviews with cancer contact nurses. Patients to be interviewed are selected through purposive sampling from the intervention group, with the aim to attain diversity in centre site, age, gender, treatment aim and diagnosis, whereas all cancer contact nurses administering the intervention are invited. The interviews will be analysed using thematic analysis [44].

2.9. Sample Size

Pre-study sample size estimations were based on a cluster-randomised controlled trial (RCT) with 32 clusters. A total of 53 patients distributed in sixteen clusters (proportionally to cluster size) in each group would enable the detection of a clinically significant difference (twelve points) in the physical functioning QLQ-C30 scale at week eight with a standard deviation (SD) of 24 in each group at the significance level of 5% and with a power of 80%, assuming an intra-cluster correlation (ICC) of 10%. The ICC is assumed to be relatively small as the intervention primarily is applied by municipal cancer nurses with similar training in collaboration with hospital specialists, thus similar to all intervention patients. Power calculation was performed for analysis of covariance, adjusting difference between groups for baseline values, and assuming the correlation between baseline and follow-up measurements to be 0.5. According to a former study on older cancer patients performed by this research group, we would expect an attrition of about 15–20% at sixteen weeks of follow-up post RT. To take this into account, and as it was paramount to ensure that all municipalities are represented by included patients, we aimed at increasing sample size by about 28% and include 81 patients in each group, i.e. a total of 162 patients.

2.10. Statistical Analysis

Primary analysis will assess the difference between the control- and the intervention group in PF measured by the QLQ-C30 questionnaire eight weeks after end of RT. Longitudinal analysis of covariance will be performed by estimating a linear mixed model with fixed effects for baseline values, time and interaction between time and group variable. The model will include random effects for patients nested within study cluster. The difference between the control and the intervention group in the secondary outcomes will be assessed by the same method as described for the primary analysis. Furthermore, the differences between the control- and the intervention group in trend in the primary outcome (PF) and all continuous secondary outcomes throughout the follow-up period will be assessed by linear mixed model with fixed effects for baseline values, time and interaction between time and group variable. The model will include random effects for patients nested within study

Table 3
Guidelines for initiation of targeted measures in accordance with identified impairment.

	«Cut offs» indicating needs for attention or measures	Suggested measures
Somatic health		
Extra lab tests	Tests outside normal range	• Notify treating oncologist to undertake required measures, including referral to patient's GP or other specialist (for instance to correct B12 deficiency or hypothyroidosis).
Blood pressure	Mild to moderate hypertension (140–179/90–109)	• Ensure that controls are scheduled according to pre-defined intervals.
	Serious hypertension	• Immediately notify treating oncologist to undertake required measures, including referral to other specialist.
	Low blood pressure (< 100–110 systolic)	• Check for orthostatism or syncope. If present: notification of treating oncologist.
Symptoms	ESAS scores >4 for any symptom[a]	• Notify treating oncologist (or GP if registered by municipal nurse) to initiate treatment according to a Norwegian renowned handbook of palliative care, or eventually, referral to palliative care team.
Comorbidities		
Hearing	Impaired	• Notify treating oncologist to consider needs of additional work-up. • Discuss need for hearing aids with patient and refer to relevant instances, e.g. hospital hearing centre, nearest public assistive technology centre, and local branches of the Norwegian Association for the Hearing Impaired, which may notify peers for assistance.
Vision	Impaired	• If known eye disease: check control routines. No known eye disease: consider referral to optician or ophthalmologist. Consider need for visual aids including magnifiers.
Other comorbidities	Comorbidity affecting ADL[b] or IADL[c] >3 comorbid conditions receiving active treatment Additionally: according to clinical judgment	• Notify treating oncologist, and eventually discuss with or refer to relevant specialists for work up and optimisation of treatment.
Medication		
	Use of - medications with interactions classified as "should be avoided" - «STOP» medications or > 7 regular medication	• A review of patients' medication must be considered. Notify treating oncologist to decide whether this should be done by the oncologist, or by referral to another hospital specialist or patients' GP.
	- > 5 regular medications + comorbidity affecting ADL/IADL or symptoms requiring new medication[d]	• For all patients: ensure that their lists of medications are updated and that hospital-, GP-,and eventually home care lists correspond.
Nutrition		
	MNA-SF 12–14 points (normal)[e]	• Encourage patients to continue their eating habits and intake. Weekly weight, and if changes, repeat MNA-SF and apply measure in accordance with new results.
	MNA-SF 8–11 points (risk of undernutrition)	• Assess food intake and symptoms (ESAS).* • Make an individually adjusted action plan, based on the guidelines (step 1) provided by the nutritionist (includes 5–6 meals per day, shortening of nightly fasting hours, actions to alleviate nutritional impact symptoms and to enrich intake). Weekly weight.
	MNA-SF < 8 points (undernourished)	• Map food intake in relation to energy need (30 kcal/kg), and assess symptoms. • Make an individually adjusted action plan based on the guidelines provided by the nutritionist (step 2) including actions from step 1, further enrichment of intake and nutritional supplements.
		• For both patients at risk and undernourished: consider social actions (hospice, day care centre, company at meals, food delivery through home care services etc.
Mental health		
Cognition	Mini-Cog score below 4	• Seek comparative information from next of kin (requires patient's consent). • Evaluate score in relation to GDS[f] and ESAS results: any impact of anxiety/depression? • *Re*-evaluate list of medications: medications that may influence cognition? • Notify the treating oncologist about results for relevant actions. • Consider measures such as help to administer medication, technical aids, home care etc. • Repeat Mini-Cog by the end of RT to assess if impairments are persistent. If so, contact patient's GP or home care dementia service for further work up.
Depression	GDS-15 score 5–8 (mild depression) [f]	• Discuss reasons and potential (non-drug) measures with the patients. Relevant measures may be talks with oncologist/GP or municipal cancer nurse/psychiatric nurse, or social measures (day centre, volunteers for visits, organised activities). • Repeat evaluation/GDS-15 assessment after about 2 weeks. If scores have increased, evaluate measures used and suggest others (+ see scores >8). If scores are stable or better, continue the applied measures with further follow-up from the municipal contact nurse.
	GDS-15 score > 8 (moderate to severe depression)	• Notify the treating oncologist or the patient's GP for additional work-up and treatment.
Function		
Daily life activity	Inability in any ADL[b]	• First, check if identified needs are already taken appropriately care of. • Refer patient to municipal home care service for evaluation. Relevant measures are home care nursing, participation in home care rehabilitation program, at home facilitation (evaluation by occupational therapist) including technical aids and security alarm. • If problem is incontinence: check for use of diuretics and if this might be changed, if blood sugar is satisfactory and if there might be urinary infections or retention. Ensure that necessary aids are available.
	Inability in any IADL[c]	• First, check if identified needs are already taken appropriately care of. If not, adequate measures must be applied depending on nature and cause of problems. Measures similar to those addressing ADL deficiency may be relevant, as may also help with administration of medication, practical help at home, food delivery, admittance to municipal day care centre, financial support for transportation, help from local volunteer centre.

(continued on next page)

Table 3 (*continued*)

	«Cut offs» indicating needs for attention or measures	Suggested measures
Mobility	SPPB[g], Timed Up and Go, grip strength Patients reporting dizziness, instability, fall within the last six months or with Timed Up and Go (TUG) > 14	• Physical exercise program adjusted to results of performance tests. • Check for orthostatism, syncope as a reason for falls, and use of drugs affecting the cardiovascular system or CNS. In case of such findings, notify the treating oncologist to undertake appropriate measure, including referral to other specialists. • Other relevant measures are walking aids, referral to municipal home care rehabilitation, security alarm at home, at home facilitation and fall prevention (evaluation by occupational therapist). Training of strength and balance must be underlined in the individually adjusted physical exercise program.
Social conditions		
Social conditions		• Apply measures in accordance with patient's needs and preferences. Alternatives are home care nursing (if additional needs to take care of), day care centres including hospice day care when available, volunteers and social offers in the patient's municipality.

[a] ESAS = Edmonton Symptom Assessment System.
[b] ADL = Activities of Daily Living.
[c] IADL = Instrumental Activities of Daily Living.
[d] based on ESAS scores.
[e] MNA-SF = Mini Nutritional Assessment Short Form.
[f] GDS-15 = 15 item Geriatric Depression Scale.
[g] SPPB = Short Physical Performance Battery.

cluster. Differences between groups in dichotomous outcomes will be assessed by generalized linear model with the same fixed and random effects as described above. Primarily, all analyses will be performed on intention-to-treat principle. As sensitivity analysis, a per-protocol approach including only data from patients complying with protocol, will be conducted. We will also use the statistical approach as described for the primary and secondary analyses to compare the intervention group to a retrospective, matched controlled group from a previous observational study (NCT03071640). Additional pre-planned analyses, including exploratory and health economic analyses are published on ClinicalTrials.gov, identifier NCT03881137.

Table 4
Overview over the data collection and outcome assessments, both study groups.

Registrations	Baseline (at the start of RT)[a]	At the end of RT	Weeks after the end of RT				
			4	8	16	32	52
Collected through patient interview by project nurse/PhD student							
Sociodemographics	X						
Weight, weight loss/height/BMI[b]	X	X		X	X		
Falls last six months	X						
Travel distance from home to RT centre	X						
Means of transportation/travel time	X						
Collected by project nurse/PhD student from treating oncologist/hospital records							
Information on cancer disease and treatment	X	X					
ECOG performance status[c]	X						
Result of routine lab tests	X						
Charlson Comorbidity Index	X						
Planned and received RT regimen	X	X					
Performance tests conducted by the project nurse/PhD at baseline, by local physiotherapists during follow-up							
SPPB[d], Timed Up and Go, One legged balance test, Grip strength	X			X	X		
Mini-Cog (cognitive screening)	X						
Edmonton Frail Scale	X						
Questionnaires (patient-reported)							
EORTC QLQ-C30[e]	X	X	X	X	X	X	X
EQ-5D-5L[f]	X	X	X	X	X	X	X
Oslo Social Support scale	X						
Physical Activity	X			X	X		X
Stays in rehabilitation institutions				X	X		X
Official Norwegian registries and patients' medical records							
Use of all hospital and primary health care service	Throughout the overall follow-up						

[a] RT = radiotherapy.
[b] BMI = Body mass index.
[c] ECOG performance status = Eastern Cooperative Oncology Group performance status.
[d] SPPB = Short Physical Performance Battery.
[e] EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer (EORTC) Quality of life Questionnaire-C30.
[f] EQ-5D-5L = The EuroQol 5D-5L questionnaire.

2.11. Study Conduct, Time Schedule and Current Status

Patient enrolment is completed. In accordance with protocol, eligible patients were identified at referral to RT, consecutively recruited, and received oral and written information from the project nurse or PhD student at the first consultation (dose planning). Eligibility was confirmed by the treating physicians. For those who consented, baseline registrations were performed as close to start of RT as possible. Due to practical constraints, a window of three days for patients receiving less than 15 irradiation fractions and six days for patients receiving a higher number were allowed. The project nurse or PhD student performed the tests at baseline and end of RT. They were also responsible for all data collection and for handing out self-report questionnaires at these time points (Table 4). Thus, in accordance with protocol, there was a brief contact with patients in the control group after enrolment, whereas intervention patients entered the intervention program as described. Follow-up questionnaires after completion of RT are administered by post with a pre-paid return envelope attached.

Patient enrolment was scheduled for one year from May 2019. In February 2020, 10 municipalities had either withdrawn from the study, or could be expected to include fewer patients than pre-planned. Thus, samples size had to be re-assessed. Based on the primary end-point, the original assumptions, and the reduced number of clusters and number of patients in some clusters, new estimates indicated that at least 69 patients should be included in each group. Considering attrition, we now estimated that a total of 186 patients, i.e. 93 patients in each group, would be required to show a statistically significant difference between groups.

Shortly after this revision was made, the COVID-19 pandemic forced us to pause the inclusion. The study group decided to re-open in late September 2020, and the inclusion was continued until April 2021. At this point, 178 patients were included, and we anticipated to have secured the minimum number of evaluable patients required for the primary endpoint analyses. Due to extensive radiation schedules,

however, the primary endpoint was not reached for all patients until late July 2021. Data collection continues, and follow-up is expected to be completed by June 2022. Statistical analyses will start by the end of 2021.

2.12. Ethics

The study, including the revised sample size estimates, is approved by the Regional Committee for Medical Research Ethics, Health Region South-East (REK HSØ) and the Data Protection Official for Research at both study centres, and is registered at ClinialTrials.gov (ID NCT03881137). It is performed according to the rules of the Helsinki declaration. All patients provide written, informed consent, and participation does not inflict upon their cancer treatment and does not imply any health risks or deviation from good clinical practice.

3. Discussion

Based on previous research showing the benefits of GAM in non-oncological settings [10,11], the documented impact of GA for older patients with cancer [45], and recommendations and guidelines from the geriatric-oncological community [22,23], we designed a pilot study to assess the effect, feasibility and costs of GAM for patients undergoing RT. To our knowledge, this is one of the first studies in Europe to examine this. We chose to design the study as a cluster-RCT. This decision was based on the crucial role of municipal cancer contact nurses in the intervention program. To avoid contamination of the control group, it was paramount that control- and intervention patients were not handled by the same primary health care professionals, and this could only be achieved by randomising municipalities and city districts. Based on the American Society of Clinical Oncology (ASCO) guidelines for geriatric oncology, we chose 65 years as the cut-off for inclusion into the study [22].

Although GAM has proven successful in other contexts [10,11], there is no universally accepted recipe for how such an intervention should be performed and implemented in a population receiving RT. To be feasible and efficient, adjustments according to the patient population, health care organisation, and available resources are necessary [16]. As RT is mainly provided as outpatient treatment, and the adverse effects tend to be most pronounced by the end of, or after treatment, the intervention program is municipality-based, and performed in collaboration between hospital- and primary care services during and after RT. The intervention was developed by our interdisciplinary study group in close collaboration with user representatives, hospital- and primary health care professionals. It is based on general GAM principals taking advantage of former studies evaluating GAM interventions in older, non-cancer patients, [10,46,47] and results from observational studies targeting older patients with cancer [48,49] performed by members of our study group. In consistency with the results of others [7,50,51], we have previously shown that physical impairments and symptom burden have a significant impact on cancer patients' QoL and physical function during treatment and follow-up [49]. Accordingly, physical activity and systematic symptom assessment are known to improve function and QoL in cancer patients [52–54]. Supported by this, and a recent publication showing that older cancer survivors are prone to accelerated physical decline [55], an individually adapted physical exercise program and repeated symptom assessment are central parts of our intervention program. Nutritional impairments are of major importance for the well-being and treatment outcomes of older patients with cancer [49,56], hence we have emphasized nutritional counselling for all, repeated nutritional assessments, and a thorough follow-up of patients' weight. Another important feature of our intervention is the involvement of the municipal cancer contact nurses. This will strengthen the collaboration and coordination between health care sectors, which is a major challenge, especially for older patients with complex needs [57]. Overall, we believe that the intervention program will be beneficial for all eligible older patients, irrespective of health status. In contrast to other studies on GAM, we have not limited our intervention to those who are frail [58]. Supporting this are also findings from a GAM intervention addressing older patients with hip fractures, where the authors surprisingly found that the intervention effect was most pronounced in the younger participants with higher pre-fracture IADL function [47].

Several aspects of the study design may be discussed. Firstly, and although we believe that cluster-randomisation was the best option to ensure a proper distinction between intervention and control during and after RT, this design raises some concerns since the patients' allocation is open to all parties involved. For the patients themselves, it may potentially affect their outcome ratings, but a more substantial worry may be that the PhD student and the project nurse assess both intervention and control patients at enrolment, and also initiate the intervention. Unfortunately, this was a pre-requisite since resources otherwise were limited. Due to training ahead of study start, we find it unlikely that their assessments per se will be biased, but as they are deeply familiar with the intervention program and exposed to assessment results, there is a potential for non-protocol co-intervention for control patients [59]. Apart from this, we do not believe that the lack of blinding affects control patients' care since their care takers are neither familiar with GA nor the intervention program. Secondly, it may be criticised that our intervention does not involve a multidisciplinary geriatric team. We chose to use a low-touch intervention in order to increase feasibility. This includes established methods to systematically assess all recommended GA domains [16,22], and detailed guidelines for the management of identified impairments with a purpose of not burdening hospital specialists, not routinely involved in the patients' care, with referrals for problems that could otherwise be handled (Table 3). However, the project nurse and the PhD student have complementary expertise and closely co-operate despite being at two different centres. This should ensure a broad approach to the patients' needs, but may also increase the risk of discrepancies in patient management between centres. Thirdly, we have chosen to include patients receiving both palliative and curative treatment, and no cancer type is excluded. Although favouring the generalizability of the results, this will inevitably lead to a heterogeneous cohort. Taking the cluster-randomisation into consideration, there is a risk that the control and intervention group will differ on important characteristics. According to the pre-planned statistical analyses, baseline differences on outcome variables will be taken into account, but major differences on patient characteristics may also have to be considered in exploratory analyses.

In conclusion, the design and conduct of the present study are largely pragmatic. Efforts have been made to take advantage of existing health services without allocation of additional resources. We strongly believe that this will increase the generalizability of our results and facilitate subsequent implementation into clinical practice. Unfortunately, all health services have been seriously affected by the COVID-19 pandemic during a major part of the study conduct, but we are still convinced that the study will provide important information about the effect and feasibility of a GAM intervention for older patients receiving RT. Furthermore, the completeness of Norwegian public health registries will ensure reliable data for a health economic analysis.

Ethics Approval and Consent to Participate

The study is approved by the Regional Committee for Medical Research Ethics, Health Region South-East (REK HSØ), Norway, registration identity 2018/2515A/13475. All participating patients provide written, informed consent.

Consent for Publication

All authors have approved the final version. Participating patients provide consent to data being used in publications. Confidentiality is guaranteed.

Availability of Data and Materials

No data are presently available, and according to Norwegian regulations, data cannot be transferred or made publicly available due to privacy concerns, i.e. before the study is fully terminated and all data anonymised.

The original protocol is available upon request. The overarching project structure is written in English, but to make the protocol easily available for our municipal co-workers, details are written in Norwegian.

Funding

The study is made possible by the Dam Foundation (grants number ref 19-3656) via the Norwegian Cancer Society (ref. 247593001) (both Norwegian non-profit organisations), Innlandet Hospital Trust (grant number 150406), the Liaison Committee for Education, Research and Innovation in Central Norway (grant number 19/4740-3), and The Joint Research Committee between St. Olav's hospital and the Faculty of Medicine and Health Sciences, NTNU – The Norwegian University of Science and Technology (FFU) (grant number 2018/42795).

Authors' Contributions

All authors have contributed to the design, planning and/or conduct of the study and will all continue to contribute until the study is completed. All authors have also contributed to the preparation and revision of the paper, and have approved the final manuscript. The first author (IR) has a main responsibility for the study conduct, have enrolled all patients from one of the two study centres, performed the assessments and collected all data related to these patients. The last author drafted the first version of the manuscript and is the project leader.

Declaration of Competing Interest

There are no conflicts of interest connected with this manuscript.

Acknowledgements

We would like to thank all patients and all municipal cancer nurses who participate in the study. Without their contribution, the study would not have been possible. We are also grateful for the help received from secretaries, nurses, radiation therapists and oncologists at the two study centres during the study conduct. A special thank is given to our project nurse, Bodil Kolsgaard, for her dedication, efficiency, flexibility and excellent work. Many thanks also to the physiotherapists, Aina Strøm, Marte Mørk Furunes, Anette Moen Eskilt, who provided the schemes for our physical exercise program and have further adapted these to each individual intervention patient at study centre 1. Finally, thanks to the local physiotherapists in each municipality who perform the physical performance tests of all patients during the follow-up.

References

[1] Barton MB, Jacob S, Shafiq J, Wong K, Thompson SR, Hanna TP, et al. Estimating the demand for radiotherapy from the evidence: a review of changes from 2003 to 2012. Radiother Oncol. 2014;112(1):140–4.
[2] Asli LM, Kvaløy SO, Jetne V, Myklebust T, Levernes SG, Tveit KM, et al. Utilization of radiation therapy in Norway after the implementation of the national cancer plan—a national, population-based study. Int J Radiat Oncol Biol Phys. 2014;90(3):707–14.
[3] Cancer in Norway 2018. Cancer incidence, mortality, survival and prevalence in Norway. https://www.kreftregisteret.no/globalassets/cancer-in-norway/2018/cin2018.pdf: The Norwegian Cancer Registry; 2019 (cited 2021 10.08).
[4] O'Donovan A, Leech M, Gillham C. Assessment and management of radiotherapy induced toxicity in older patients. J Geriatr Oncol. 2017;8(6):421–7.
[5] Bayman N, Alam N, Faivre-Finn C. Radiotherapy for lung cancer in the elderly. Lung Cancer. 2010;68(2):129–36.
[6] VanderWalde NA, Fleming M, Weiss J, Chera BS. Treatment of older patients with head and neck cancer: a review. Oncologist. 2013;18(5):568–78.
[7] Mohile SG, Heckler C, Fan L, Mustian K, Jean-Pierre P, Usuki K, et al. Age-related differences in symptoms and their interference with quality of life in 903 cancer patients undergoing radiation therapy. J Geriatr Oncol. 2011;2(4):225–32.
[8] Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol. 2014;32(24):2595–603.
[9] Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752–62.
[10] Prestmo A, Hagen G, Sletvold O, Helbostad JL, Thingstad P, Taraldsen K, et al. Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial. Lancet. 2015;385(9978):1623–33.
[11] Ellis G, Whitehead MA, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ. 2011;343:d6553.
[12] Feng MA, McMillan DT, Crowell K, Muss H, Nielsen ME, Smith AB. Geriatric assessment in surgical oncology: a systematic review. J Surg Res. 2015;193(1):265–72.
[13] Puts MT, Hardt J, Monette J, Girre V, Springall E, Alibhai SM. Use of geriatric assessment for older adults in the oncology setting: a systematic review. J Natl Cancer Inst. 2012;104(15):1133–63.
[14] Puts MT, Tapscott B, Fitch M, Howell D, Monette J, Wan-Chow-Wah D, et al. A systematic review of factors influencing older adults' decision to accept or decline cancer treatment. Cancer Treat Rev. 2015;41(2):197–215.
[15] Mohile SG, Epstein RM, Hurria A, Heckler CE, Canin B, Culakova E, et al. Communication with older patients with cancer using geriatric assessment: a cluster-randomized clinical trial from the National Cancer Institute Community Oncology Research Program. JAMA Oncol. 2020;6(2):196–204.
[16] Rostoft S, O'Donovan A, Soubeyran P, Alibhai SMH, Hamaker ME. Geriatric assessment and management in cancer. J Clin Oncol. 2021;39(19):2058–67.
[17] Pal SK, Katheria V, Hurria A. Evaluating the older patient with cancer: understanding frailty and the geriatric assessment. CA Cancer J Clin. 2010;60(2):120–32.
[18] Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, et al. Reducing inappropriate polypharmacy: the process of deprescribing. JAMA Intern Med. 2015;175(5):827–34.
[19] Salakari MR, Surakka T, Nurminen R, Pylkkanen L. Effects of rehabilitation among patients with advances cancer: a systematic review. Acta Oncol. 2015;54(5):618–28.
[20] Paccagnella A, Morassutti I, Rosti G. Nutritional intervention for improving treatment tolerance in cancer patients. Curr Opin Oncol. 2011;23(4):322–30.
[21] Hurria A, Wildes T, Blair SL, Browner IS, Cohen HJ, Deshazo M, et al. Senior adult oncology, version 2.2014: clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2014;12(1):82–126.
[22] Mohile SG, Dale W, Somerfield MR, Schonberg MA, Boyd CM, Burhenn PS, et al. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. J Clin Oncol. 2018;36(22):2326–47.
[23] Magnuson A, Allore H, Cohen HJ, Mohile SG, Williams GR, Chapman A, et al. Geriatric assessment with management in cancer care: current evidence and potential mechanisms for future research. J Geriatr Oncol. 2016;7(4):242–8.
[24] Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. N Engl J Med. 2002;346(14):1061–6.
[25] Hui D, Bruera E. The Edmonton symptom assessment system 25 years later: past, present, and future developments. J Pain Symptom Manage. 2017;53(3):630–43.
[26] Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing. 2006;35(5):526–9.
[27] Sundararajan V, Quan H, Halfon P, Fushimi K, Luthi JC, Burnand B, et al. Cross-national comparative performance of three versions of the ICD-10 Charlson index. Med Care. 2007;45(12):1210–5.
[28] Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. J Gerontol. 1981;36(4):428–34.
[29] Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T, et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. J Nutr Health Aging. 2009;13(9):782–8.
[30] Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. J Am Geriatr Soc. 2003;51(10):1451–4.
[31] Sheikh J, Yesavage J. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clin Gerontol. 1986;5(1–2):165–73.
[32] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9(3):179–86.
[33] Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J. 1965;14:61–5.
[34] Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med. 1995;332(9):556–61.
[35] Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.
[36] Norman K, Stobaus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clin Nutr. 2011;30(2):135–42.
[37] Krokstad S, Langhammer A, Hveem K, Holmen TL, Midthjell K, Stene TR, et al. Cohort profile: the HUNT study, Norway. Int J Epidemiol. 2013;42(4):968–77.
[38] Dalgard OS, Dowrick C, Lehtinen V, Vazquez-Barquero JL, Casey P, Wilkinson G, et al. Negative life events, social support and gender difference in depression: a multinational community survey with data from the ODIN study. Soc Psychiatry Psychiatr Epidemiol. 2006;41(6):444–51.
[39] Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-

of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365–76.
[40] Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20(10):1727–36.
[41] Rikli R, Busch S. Motor performance of women as a function of age and physical activity level. J Gerontol. 1986;41(5):645–9.
[42] Forman J, Heisler M, Damschroder LJ, Kaselitz E, Kerr EA. Development and application of the RE-AIM QuEST mixed methods framework for program evaluation. Prev Med Rep. 2017;6:322–8.
[43] Glasgow RE, Estabrooks PE. Pragmatic applications of RE-AIM for health care initiatives in community and clinical settings. Prev Chronic Dis. 2018;15:E02.
[44] Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77–101.
[45] Hamaker ME, Schiphorst AH, ten Bokkel Huinink D, Schaar C, van Munster BC. The effect of a geriatric evaluation on treatment decisions for older cancer patients—a systematic review. Acta Oncol. 2014;53(3):289–96.
[46] Saltvedt I, Jordhoy M, Opdahl Mo ES, Fayers P, Kaasa S, Sletvold O. Randomised trial of in-hospital geriatric intervention: impact on function and morale. Gerontology. 2006;52(4):223–30.
[47] Prestmo A, Saltvedt I, Helbostad JL, Taraldsen K, Thingstad P, Lydersen S, et al. Who benefits from orthogeriatric treatment? Results from the Trondheim hip-fracture trial. BMC Geriatr. 2016;16:49.
[48] Kirkhus L, Saltyte Benth J, Gronberg BH, Hjermstad MJ, Rostoft S, Harneshaug M, et al. Frailty identified by geriatric assessment is associated with poor functioning, high symptom burden and increased risk of physical decline in older cancer patients: prospective observational study. Palliat Med. 2019;33(3):312–22.
[49] Kirkhus L, Harneshaug M, Saltyte Benth J, Gronberg BH, Rostoft S, Bergh S, et al. Modifiable factors affecting older patients' quality of life and physical function during cancer treatment. J Geriatr Oncol. 2019;10(6):904–12.
[50] Kenis C, Decoster L, Bastin J, Bode H, Van Puyvelde K, De Greve J, et al. Functional decline in older patients with cancer receiving chemotherapy: a multicenter prospective study. J Geriatr Oncol. 2017;8(3):196–205.
[51] Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc JF, Ceccaldi J, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol. 2013;31(31):3877–82.
[52] Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc. 2010;42(7):1409–26.
[53] Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc. 2019;51(11):2375–90.
[54] Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. J Clin Oncol. 2016;34(6):557–65.
[55] Siddique A, Simonsick EM, Gallicchio L. Functional decline among older cancer survivors in the Baltimore longitudinal study of aging. J Am Geriatr Soc. 2021. https://doi.org/10.1111/jgs.17369.
[56] Ryan AM, Prado CM, Sullivan ES, Power DG, Daly LE. Effects of weight loss and sarcopenia on response to chemotherapy, quality of life, and survival. Nutrition. 2019;67–68:110539.
[57] Steihaug S, Johannessen AK, Ådnanes M, Paulsen B, Mannion R. Challenges in achieving collaboration in clinical practice: the case of Norwegian health care. Int J Integr Care. 2016;16(3):3.
[58] Ommundsen N, Wyller TB, Nesbakken A, Bakka AO, Jordhoy MS, Skovlund E, et al. Preoperative geriatric assessment and tailored interventions in frail older patients with colorectal cancer: a randomized controlled trial. Colorectal Dis. 2018;20(1):16–25.
[59] Kyte D, Ives J, Draper H, Keeley T, Calvert M. Inconsistencies in quality of life data collection in clinical trials: a potential source of bias? Interviews with research nurses and trialists. PLoS One. 2013;8(10):e76625.