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Enhanced involvement of general practitioners in cancer rehabilitation: a randomised controlled trial.

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Abstract

Objective: To test the hypothesis that a multimodal intervention giving the general practitioner (GP) an enhanced role in cancer rehabilitation improves patients' health-related quality of life and psychological distress.

Design: Cluster randomised controlled trial. All general practices in Denmark were randomised to an intervention group or to a control group. Patients were subsequently allocated to intervention or control (usual procedures) based on the randomisation status of their GP.

Setting: All clinical departments at a public regional hospital treating cancer patients and all general practices in Denmark.

Participants: Adult patients treated for incident cancer at Vejle Hospital, Denmark, between 12 May 2008 and 28 February 2009. A total of 955 patients (486 to intervention, 469 to control group) registered with 323 general practices were included.

Intervention: The intervention included an interview about rehabilitation needs with a rehabilitation coordinator at the regional hospital, information from the hospital to the GP about individual needs for rehabilitation and an encouragement of the GP to contact the patient to offer his support with rehabilitation.

Main outcome measures: The primary outcome was health-related quality of life measured 6 months after inclusion using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Secondary outcomes included quality of life at 14 months and additional subscales of the EORTC QLQ-C30 at 6 and 14 months, and psychological distress at 14 months using the Profile of Mood States (POMS) scale.

Results: No effect of the intervention was observed on primary and/or secondary outcomes after 6 and 14 months.

Conclusion: A multimodal intervention aiming to give the GP an enhanced role in cancer patients' rehabilitation did not improve quality of life or psychological distress.

Trial registration: ClinicalTrials.gov, registration ID number NCT01021371.

Background

Addressing the unmet needs of individual rehabilitation of cancer patients is paramount (1-4). The underlying problems are often psychological or social and many persist after treatment or emerge late in the illness continuum (5-8). Rehabilitation is defined by WHO as "a process intended to enable people with disabilities to reach and maintain optimal physical, sensory, intellectual, psychological and/or social function" (9) which is the conceptual frame for this study. Hence, rehabilitation is a complex and long-lasting process, but evidence on how and when to identify the patients' needs, what initiatives to offer, and how to manage the efforts is sparse (2;10-13).

General practice is characterised by continuity with frequent encounters with each patient, covering wide-ranging issues (14). Hence, general practitioners (GPs) generally have profound knowledge about the patients' prior health status, mental vulnerability and social network. General practice may, therefore, be able to initiate the rehabilitation process and take on the task of coordinating or providing the rehabilitation services needed, but currently the role of GPs is not well-defined (15-23). Studies do, however, show that GPs are willing to undertake these tasks and that the patients wish that their GPs were more proactive in doing so (24-25).

The objective of this trial was to investigate the effect of a multimodal intervention giving the GP an enhanced role in improving patients' health-related quality of life and psychological distress following cancer. To validate our results we conducted subgroup analyses of the large and homogeneous group of breast cancer patients.

Material and methods

We conducted a cluster randomised, controlled trial where all general practices in Denmark were randomised to an intervention group or to a control group by means of the unique provider number of each practice. Patients were subsequently allocated according to the randomisation of their GP. Feasibility of the intervention and the study details have previously been published (26).

Participants

All adult patients (≥18 years) newly diagnosed with cancer and admitted to Vejle Hospital between 12 May 2008 and 28 February 2009 were assessed for eligibility. Patients were included if treated at Vejle Hospital for a cancer diagnosed within the last 3 months and if listed with a general practice. Patients with carcinoma in situ or non-melanoma skin cancers were not included (Figure 1).

Two rehabilitation coordinators, both nurses with oncological experience, assessed all patients for eligibility and managed the intervention. The patients were sampled across departments, type of cancer, stage, and potential rehabilitation needs by use of the electronic patient files (26).

Setting

The study was conducted at Vejle Hospital, a public general hospital in the region of Southern Denmark (1.2 million inhabitants) (27). Cancer patients were allocated from all of Denmark.

The Danish publicly funded healthcare system ensures free access to general practice which is responsible for primary care needs, and GPs function as gatekeepers to

the rest of the healthcare system. More than 98% of all Danish residents are registered with a general practice. On average each GP meets 9 incident cancer patients during one year (28).

GPs' opportunities to refer patients to relevant rehabilitation services vary between the different municipalities, just as the availability of private patient associations and other relief organisations. These conditions might influence the quality of the rehabilitation interventions offered.

The intervention

The intervention comprised a patient interview about rehabilitation needs performed by the rehabilitation coordinators, followed by information to the GP about the patient's individual rehabilitation needs and cancer patients' rehabilitation needs in general. The core of the information was that the GP was encouraged to contact the patient to facilitate a rehabilitation process (Figure 2).

The patient interviews were conducted according to an interview guide (29) and based on a checklist of general needs and problems among cancer patients (Figure 3). Interviews were most often conducted at the hospital, but in some cases by phone. During the interview, the concept of rehabilitation was explained and the individual needs for physical, psychological, sexual, social, work- and economy-related rehabilitation were identified. It was explained that physical, psychological, sexual, social, work-related and financial issues (1-4;30) might occur at any time and change during the disease trajectory (7-8). In order to address these problems, patients were advised to consult their GP during treatment and after discharge.

Following each interview, the patient's GP was informed about the patient's actual problems and needs for rehabilitation and encouraged to be proactive, i.e. the GP was encouraged to contact the patient personally to offer support and guidance in order to identify and address actual and future needs for rehabilitation. Subsequently, the GP received an e-mail summarising the information, supplemented by general information about cancer patients' needs and problems (Figure 3). The information was personally conveyed by phone, if possible, and always sent electronically along with the more general information. Patients and GPs in the control group received the usual care and were not contacted by the rehabilitation coordinators (26).

Outcomes and sampling of data

The primary outcome was health-related quality of life measured 6 months after inclusion using the Global Health Status of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (31;32). The secondary outcomes were psychological distress at 14 months assessed by the 6 scales of the Profile of Mood States (POMS) (33) (depression/dejection, anger/hostility, tension/anxiety, vigour/activity, fatigue/inertia and confusion/bewilderment), and the Global Health Status at 6 months and functional (physical, emotional, role, cognitive or social functioning) and symptom scales (fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea or financial difficulties) of the EORTC QLQ-C30 at 6 and 14 months.

Data were sampled in identical ways irrespective of allocation status by use of patient questionnaires administered to patients alive at 6 and 14 months after inclusion. Non-responders were sent one reminder after 3 weeks (26).

Sample size

The sample size was estimated based on the primary outcome measure. According to the EORTC Tables of Reference Values (34) for all cancer patients, all stages, the Global Health Status is normally distributed with a mean of 61.3 and an SD of 24.2. A change of at least 8 units was assumed to be clinically relevant (34;35).

If the lowest acceptable statistical power was 80%, then, based on the two-sample t-test with a type 1 error alpha=0.05, the sample size was calculated to be 144 patients per group. The study was subject to clustering because the unit of randomisation was at the level of the GP, whereas the primary outcome measure was at the level of the patient. A strong effect on outcome of the individual practice was expected, but no data supported estimation of cluster effect. To allow maximum clustering it was attempted to include patients to each group from a minimum of 144 practices.

Randomisation

Prior to study start, all 2181 general practices in Denmark were randomly allocated to the intervention or control group by the unique provider number of each practice using a computerised random-number generator in the statistical program Stata version 10.0 (StataCorp, College Station, TX, USA). Hence, randomisation was performed at practice level meaning that all GPs working under the same provider number were allocated to the same group. Consequently, spill-over effect between GPs and patients from the same practice was minimised.

Blinding

The study was not blinded. The list of randomisation was available to the RCs during assessment of patient eligibility. Allocation status was obvious during intervention.

Statistical analysis

Baseline patient characteristics were described using descriptive statistics in order to present the distribution of age, sex and cancer type. We conducted intention to treat analyses and numerical outcomes of the RCT were analysed using a multi-level linear model, accounting for possible cluster effects caused by the cluster randomisation. All secondary outcomes were adjusted for confounding effect of age and sex. Missing values were regarded as missing at random.

The statistical analyses were performed using Stata version 11.0 (StataCorp, College Station, TX, USA).

Development and piloting of questionnaires and intervention

Before designing the intervention we established a theoretical basis through review of papers, reports and textbooks about the problems faced by cancer patients and GPs with respect to individual rehabilitation and continuity across healthcare sectors (1-3;16-24;36).

The questionnaires and the procedures of identification, assessment and inclusion of patients were pilot tested prior to study start. The procedures have been described in detail (26).

Results

In total 955 patients fulfilled the criteria for inclusion and 486 patients were allocated to the intervention group and 469 to the control group (Figure 1). The patients were registered with 323 general practices. Patients were on average aged 63 years at baseline and 72% were female. The most frequent cancer localisations were breast (43%) and lung (15%). The intervention and control groups showed similar baseline characteristics (Table 1). For the primary outcome, Global Health Status at 6 months, we obtained data from 281 patients from 131 practices in the intervention group and 297 patients from 125 practices in the control group, in total 612 of 858 (71%) patients (95%-confidence interval for ICC 0.000 - 0.103) (Figure 1).

The intervention had no statistically significant impact on the primary or on the secondary outcomes (Tables 2 and 3). Adjustment for age and sex of the secondary outcomes showed results similar to the unadjusted analysis. Intention to treat analyses on all outcomes of the group of breast cancer patients showed no statistical differences between patients in the intervention and control group (mean difference in primary outcome of 1.77 (-3.2 to 6.8)). Per protocol analyses on all outcomes were used to analyse if the personal telephone contact to the GP was crucial. The patients receiving all elements of the intervention showed no statistically significant difference when compared to the control group (mean difference in primary outcome of -4.43 (-9.7 to 0.8)).

Discussion

Principal findings

This intervention including a hospital-based patient interview about rehabilitation, individual and general information to the GP and an encouragement to contact the patient and

facilitate a process of rehabilitation did not improve quality of life or relieve psychological distress of patients newly diagnosed with cancer.

Strengths and weaknesses of the study

The study included 955 patients and the pre-study power calculation and the precision of the statistical estimates indicate that the study could have detected relevant effects of the intervention. The confidence interval of the difference in global health status after 6 months ranged between -2.4 and 4.9 units. Clinically relevant differences have been suggested to correspond to at least 8 units (34;35).

An important question is whether any spill-over effects may have improved care for the patients in the control group, leading to an apparently smaller impact of the intervention. Information about the study and the concept of rehabilitation was given to the staff at the involved departments at Vejle Hospital during the inclusion period, but the intervention was managed by the two rehabilitation coordinators without influence on the care provided for the patients in the control group. The cluster randomisation was performed to ensure that GPs only cared for patients in either the intervention or the control group. GPs in the control group were not informed about the study and we have no reason to believe that information about the study was disseminated between GPs in the two groups.

Another question is whether we used the most relevant outcome measures. Process measures are often used to evaluate interventions. However, despite successful implementation of interventions, the impact on patients' wellbeing is often sparse. Hence, we deliberately chose patients' quality of life as the primary outcome. Further, the EORTC

QLQ-C30 and the POMS questionnaires are both well-validated instruments to evaluate change of quality of life in cancer patients and psychological distress in general (31-35).

The intervention was designed to support rehabilitation irrespective of the character of the problem, cancer type, age and sex. We included patients with various cancer types, different prognosis, health problems and needs of supportive care. The inhomogeneity of the study population might have diluted effects in groups of patients with specific problems or diagnoses. It cannot be ruled out that a similar intervention might have effect on subgroups of patients with specific cancers or special needs. However, no effect was observed when analysing the large and rather homogeneous group of breast cancer patients.

The intervention included a personal telephone contact to the patients' GP but some GPs were not reachable (26). A priori we assumed that this personal contact could be of major importance, but per protocol analysis showed no differences in outcomes for patients where the rehabilitation coordinators managed to reach the GP by phone.

Relations to other studies

To our knowledge, only three papers have specifically evaluated the impact of GP involvement in cancer rehabilitation in a randomised design (17;36-37). A shared care programme (n=250) conducted in Denmark in 2003 included transfer of knowledge from oncologists to GPs, improved communication between parties, and active patient involvement (17). This intervention had a positive impact on patient evaluation of cooperation between primary and secondary healthcare sectors, but not on quality of life. A Norwegian study from 2005 (n=91) evaluated the effect of an invitation to a 30-minute consultation with the patient's GP, aiming at creating a closer and more frequent contact

between patients and GPs (36). No increase in number of consultations or improvement of quality of life was observed. The latest study was conducted in Sweden in 2008 (n=481) and tested the effectiveness of individual support, group rehabilitation and a combination of the two compared to standard care (37). The individual support included individual psychological and nutritional support along with intensified primary health care, including extended information about the diagnosis, education in cancer care, and supervision of the patient's home care nurse and GP by a multi-professional oncology team. The Swedish study did not show an improvement either in quality of life or psychological well-being when compared to standard care. Further, a systematic review (38) including the three studies concluded that none of the interventions improved quality of life or patient wellbeing, but due to possible methodological problems further studies on the topic are needed.

Meaning

Interventions aiming to give the GP an enhanced role in cancer rehabilitation seem to have difficulties improving quality of life. Furthermore, a number of papers evaluating the effect of various other types of interventions aiming to improve quality of life of cancer patients (39-44) have demonstrated that this may be difficult in general. To better understand the intervention and the impact on GP and patient behaviour further studies will include evaluation of process measures like GP proactivity, patient participation in different rehabilitation activities, and GP and patient satisfaction.

Future studies should evaluate the importance of the organisation of cancer treatment and rehabilitation. Is an unclear organisation with many partners (hospital departments, GPs, municipalities and private organisations) an impediment to effective

rehabilitation? A well-organised system with defined roles and easy referral to various elements of rehabilitation (specialised physiotherapy, social counselling, psychological advice etc.) may be of importance for the effect of a GP intervention. To improve rehabilitation it may also be important to develop screening tools that support identification of patients with special needs. Initiatives supporting the GPs in undertaking a proactive role for patients with special needs should be considered. The effect of interventions should, however, be carefully evaluated in order to ensure efficient use of resources before implementation.

Figure 1. Study flow.

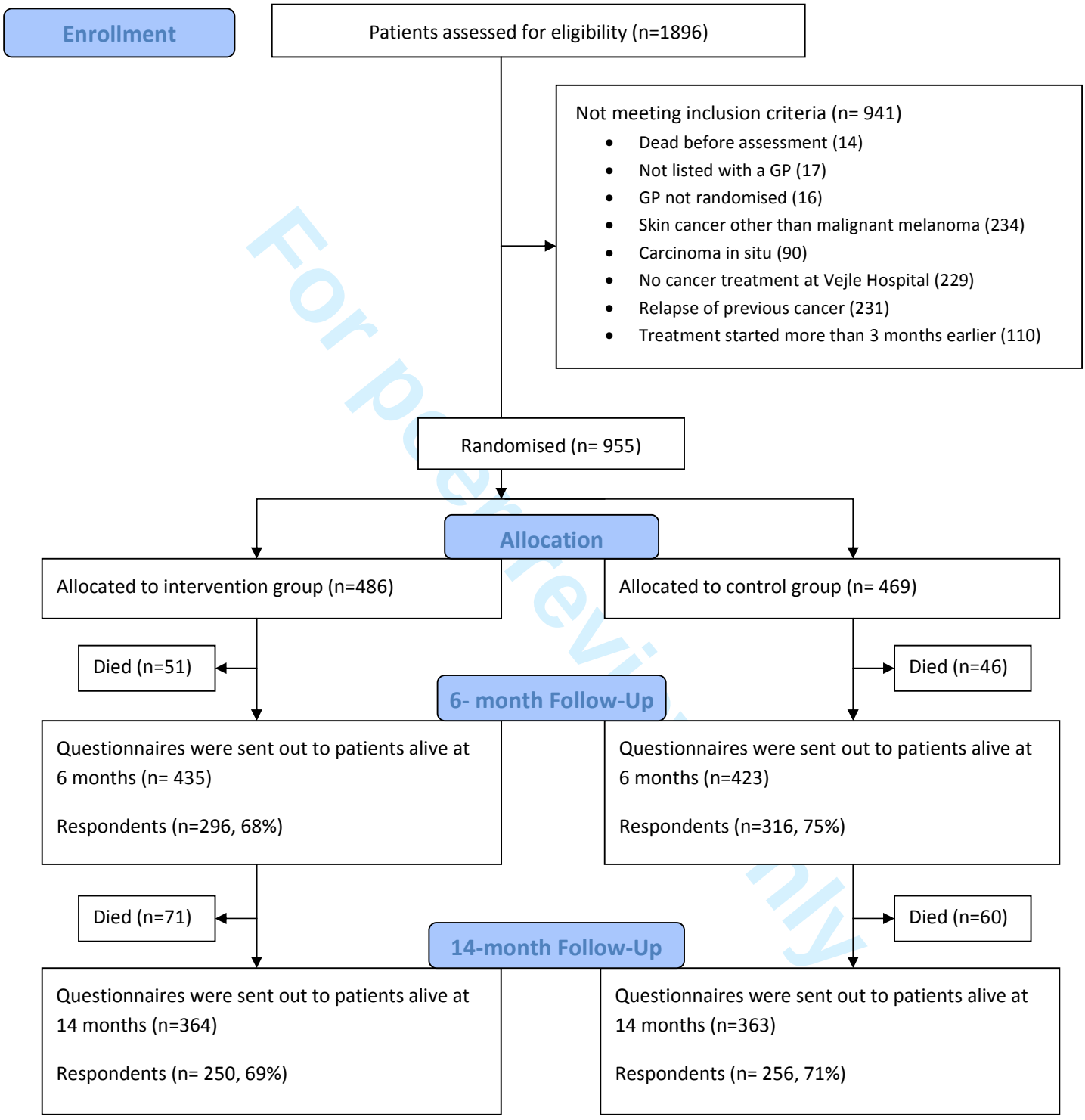

Figure 2. General needs and problems among cancer patients.

Psychological level	• Fear of death or recurrence • Guilt feelings about being sick • Anger at general practitioner or "system" for not having taken action soon enough • Troubles adjusting to new self-image • Sense of being left in limbo after discharge from the hospital • Risk of developing depression • Reconsiderations about priorities in life and how one wants to live life with or after a cancer disease • Sexual problems
Social level	• Concerns about the well-being of spouse, children and other relatives • Changed body image or sexuality • Changed position/status in marriage, in family, at work, etc. • Concerns about possible infertility caused by treatment • Information about patient associations and similar groups for patients and relatives
Physical level	• Physical capacity according to daily activities, need for special facilities, homecare, conversions of the home, etc. • Need for dietary advice, e.g. to prevent undue weight loss • Support in order to accept physical changes and late complications like tiredness, amputation, infertility, pain, etc.
Work-related level	• Concerns about losing one's job • Concerns about having to give up one's former responsibilities or change field of work due to reduced ability to work • Opportunities for financial support during sick-leave, flexible job, etc. • Support to keep in contact with workplace during sick-leave
Financial level	• Social rights like mileage allowances, reimbursement of assistive technology, etc. • Concerns about a decrease in income and consequences hereof in relation to housing, spouse, children, etc. • Conditions regarding pension or incapacity benefit

Table 1. Baseline demographic and medical characteristics for all included patients (n=955).

Demographic characteristics	Control group (n=469)	Intervention group (n=486)
Age, years		
Mean (CI)	63.6 (62.5 to 64.6)	63.2 (62.2 to 64.3)
Median	64	64
Range	21 to 98	28 to 92
Sex		
Male (%)	134 (28.6)	133 (27.4)
Female (%)	335 (71.4)	353 (72.6)
Cancer type	Numbers (%)	Numbers (%)
Cancer of breast	206 (43.9)	201 (41.4)
Cancer of lung	69 (14.7)	75 (15.4)
Malignant melanoma	44 (9.4)	35 (7.2)
Cancer of rectum/anus	33 (7.0)	45 (9.3)
Cancer of colon	29 (6.2)	39 (8.0)
Cancer of ovaries	12 (2.6)	9 (1.9)
Cancer of bilary system	7 (1.5)	8 (1.6)
Cancer of brain	6 (1.3)	8 (1.6)
Cancer of prostate	8 (1.7)	3 (0.6)
Cancer of corpus uteri	6 (1.3)	5 (1.0)
Myelomatosis	6 (1.3)	5 (1.0)
Lymphoma	3 (0.6)	4 (0.8)
Unspecified location	16 (3.4)	16 (3.3)
Other diagnoses	24 (5.1)	33 (6.8)

Table 2. Health-Related Quality of Life (EORTC QLQ-C30) outcome variables and mean differences at 6 and 14 months (95% confidence intervals).

	6 months				14 months			
Outcome variable	n	Mean (CI)	Mean difference (95% CI)	P	n	Mean (CI)	Mean difference (95% CI)	P
Global Health Status/qol								
Control group	297	68,0 (65.5 to 70.5)			246	72.8 (70.3 to 75.3)		
Intervention group	281	69,3 (66.7 to 71.9)	1.25 (-2.4 to 4.9)	0.50	240	72.1 (69.6 to 74.7)	-0.71 (-4.3 to 2.8)	0.69
Physical functioning								
Control group	294	79.0 (76.4 to 81.5)			240	81.9 (79.3 to 84-5)		
Intervention group	280	79.7(77.1 to 82.4)	0.77 (-2.9 to 4.4)	0.68	234	82.0 (79.4 to 84.6)	-0.08 (-3.6 to 3.8)	0.97
Role functioning								
Control group	291	71.3 (67.7 to 74.9)			239	78.0 (74.4 to 81.7)		
Intervention group	277	72.5 (68.8 to 76.1)	1.18 (-3.9 to 6.3)	0.65	235	78.8 (75.0 to 82.5)	0.70 (-4.5 to 5.9)	0.79
Emotional functioning								
Control group	293	80.5 (78.1 to 83.0)			240	80.7 (77.9 to 83.4)		
Intervention group	278	81.6 (79.1 to 84.1)	1.02 (-2.5 to 4.5)	0.57	238	80.8 (78.0 to 83.6)	0.12 (-3.8 to 4.1)	0.95
Cognitive functioning								
Control group	290	83.0 (80.5 to 85.5)			245	82.6 (79.7 to 85.5)		
Intervention group	278	83.9 (81.3 to 86.4)	0.88 (-2.7 to 4.5)	0.63	238	85.1 (82.1 to 88.2)	2.53 (-1.7 to 6.7)	0.24
Social functioning								
Control group	295	85.7 (83.0 to 88.4)			242	88.2 (85.4 to 91.0)		
Intervention group	280	86.0 (83.2 to 88.8)	0.28 (-3.6 to 4.2)	0.89	238	87.4 (84.6 to 90.3)	-0.77 (-4.8 to 3.2)	0.71
Fatigue								
Control group	292	37.4 (34.3 to 40.6)			244	32.1 (28.8 to 35.3)		
Intervention group	279	34.2 (30.9 to 37.4)	-3.27 (-7.8 to 1.3)	0.16	234	32.3 (28.9 to 35.6)	0.23 (-4.5 to 4.9)	0.92
Nausea and vomiting								
Control group	300	8.1 (6.1 to 10.0)			244	5.5 (3.9 to 7.2)		
Intervention group	284	8.0 (6.0 to 10.0)	-0.11 (-2.9 to 2.7)	0.94	236	5.6 (3.9 to 7.3)	0.05 (-2.3 to 2.4)	0.97
Pain								
Control group	283	23.0 (19.8 to 26.2)			241	21.9 (18.5 to 25.4)		
Intervention group	274	22.0 (18.8 to 25.3)	-0.95 (-5.5 to 3.6)	0.68	234	21.4 (17.8 to 24.9)	-0.56 (-5.5 to 4.4)	0.83
Dyspnoea								
Control group	297	17.0 (13.9 to 20.2)			245	13.2 (10.0 to 16.5)		
Intervention group	286	17.9 (14.7 to 21.2)	0.87 (-3.6 to 5.4)	0.71	233	15.4 (11.9 to 18.8)	2.11 (-2.6 to 6.8)	0.38
Insomnia								
Control group	302	27.5 (24.0 to 31.0)			248	29.6 (25.6 to 33.6)		
Intervention group	285	27.3 (23.6 to 30.9)	-0.23 (-5.3 to 4.8)	0.93	240	28.5 (24.4 to 32.6)	-1.08 (-6.8 to 4.6)	0.71
Appetite loss								
Control group	301	14.1 (11.0 to 17.2)			246	9.6 (7.1 to 12.2)		
Intervention group	288	15.9 (12.7 to 19.0)	1.79 (-2.7 to 6.2)	0.43	239	7.9 (5.4 to 10.5)	-1.67 (-5.3 to 2.0)	0.37
Constipation								
Control group	299	12.6 (9.7 to 15.5)			248	11.9 (9.0 to 14.9)		
Intervention group	284	11.3 (8.3 to 14.2)	-1.33 (-5.4 to 2.8)	0.53	236	8.9 (5.9 to 11.9)	-3.03 (-7.4 to 1.1)	0.16
Diarrhoea								
Control group	299	11.3 (8.8 to 13.9)			250	11.4 (8.5 to 14.2)		
Intervention group	284	11.4 (8.8 to 14.1)	0.08 (-3.6 to 3.8)	0.97	238	10.0 (7.0 to 13.0)	-1.38 (-5.5 to 2.8)	0.51
Financial difficulties								
Control group	297	7.6 (5.4 to 9.8)			242	6.5 (3.9 to 9.0)		
Intervention group	284	8.0 (5.7 to 10.2)	0.34 (-2.8 to 3.5)	0.83	236	6.7 (4.1 to 9.4)	0.27 (-3.4 to 4.0)	0.89
Mean values from 0 to 100. A score of 100 indicates optimal function or maximum symptom intensity (i.e. for functional measures, an increase indicates improvement, while for symptoms, an increase indicates worsening)								

Table 3. Psychological distress (POMS) at 14 months and mean differences between groups (95 confidence intervals).

Outcome variable	n	Mean range	Mean (95% CI)	Mean difference (95% CI)	P
Anger/hostility		0 to 28			
Control group	223		2.03 (1.59 to 2.48)		
Intervention group	230		1.88 (1.43 to 2.33)	-0.15 (-0.79 to 0.48)	0.64
Confusion/bewilderment		0 to 20			
Control group	229		2.45 (2.04 to 2.86)		
Intervention group	231		2.11 (1.69 to 2.53)	-0.34 (-0.92 to 0.25)	0.26
Depression/dejection		0 to 32			
Control group	223		3.85 (3.20 to 4.51)		
Intervention group	229		3.26 (2.61 to 3.92)	-0.59 (-1.52 to 0.34)	0.21
Fatigue/inertia		0 to 20			
Control group	226		4.65 (4.08 to 5.22)		
Intervention group	234		4.14 (3.02 to 4.10)	-0.51 (-1.32 to 0.29)	0.21
Tension/anxiety		0 to 24			
Control group	226		3.82 (3.28 to 4.36)		
Intervention group	233		3.56 (3.02 to 4.10)	-0.26 (-1.02 to 0.50)	0.50
Vigour/activity		0 to 24			
Control group	218		10.28 (9.51 to 11.05)		
Intervention group	228		10.09 (9.31 to 10.86)	-0.20 (-1.29 to 0.89)	0.72
Total mood disturbance		0 to 124			
Control group	200		4.87 (2.29 to 7.45)		
Intervention group	210		4.19 (1.62 to 6.76)	-0.68 (-4.32 to 2.97)	0.72

Mean values of each subscale depends on the number of items related to the individual subscale which varies from 5 to 8, each item ranging from 0 to 4. Total mood disturbance is calculated by summing up the scores on the five negative symptom subscales and subtracting the score on the one positively scored subscale, vigour/activity. A higher score indicates a higher degree of symptoms/feelings within the related subscale.

Contributors

SHB, JK, JS and DGH contributed to conception and study design. SHB, DGH, JK and JS obtained the funding. SHB, JK, JS and DGH wrote the protocol. SHB and DGH were responsible for recruitment of patients. SHB collected and managed the data. PVL was the study statistician. SHB and PVL performed the statistical analysis. SHB, PVL, JK, JS and DGH contributed to the interpretation of data. SHB drafted the first version of the manuscript. SHB, JK, JS, PVL and DGH critically reviewed, revised, and supplemented the manuscript. All authors approved the final version. SHB is the guarantor.

Licence for publication

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted

work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The study was approved by the Danish Data Protection Agency. The Regional Committee on Biomedical Research Ethics evaluated the project and concluded that the intervention did not need an approval from the Danish National Committee on Biomedical Research Ethics according to Danish law (Project-ID: S-20082000-7).

Data

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing

No additional data available.

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Checklist of items to include when reporting a cluster randomised trial

* = addition to CONSORT *Modifications to checklist in italics*			
PAPER SECTION and topic	Item	Descriptor	Reported on Page No.
TITLE & ABSTRACT	1*	How participants were allocated to interventions (e.g., "random allocation", "randomised", or "randomly assigned"), *specifying that allocation was based on clusters*	2
INTRODUCTION Background	2*	Scientific background and explanation of rationale, *including the rationale for using a cluster design.*	4+8
METHODS Participants	3*	Eligibility criteria for participants *and clusters* and the settings and locations where the data were collected.	5
Interventions	4*	Precise details of the interventions intended for each group, *whether they pertain to the individual level, the cluster level or both,* and how and when they were actually administered.	6-7
Objectives	5*	Specific objectives and hypotheses, *and whether they pertain to the individual level, the cluster level or both*.	4
Outcomes	6*	Report clearly defined primary and secondary outcome measures, *whether they pertain to the individual level, the cluster level or both*, and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	7
Sample size	7*	How *total* sample size was determined *(including method of calculation, number of clusters, cluster size, a coefficient of intracluster correlation (ICC or k), and an indication of its uncertainty*) and, when applicable, explanation of any interim analyses and stopping rules.	8
Randomisation.			5+8
Sequence generation	8*	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification, *matching*).	
Allocation concealment	9*	Method used to implement the random allocation sequence, *specifying that allocation was based on clusters rather than individuals and* clarifying whether the sequence was concealed until interventions were assigned.	
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (Masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	8-9
Statistical methods	12*	Statistical methods used to compare groups for primary outcome(s) *indicating how clustering was taken into account*; methods for additional analyses, such as subgroup analyses and adjusted analyses.	9
RESULTS Participant flow	13*	Flow of *clusters and* individual participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of *clusters and* participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	10+15 (Figure 1)
Recruitment	14	Dates defining the periods of recruitment and follow-up.	5+15 (Figure 1)
Baseline data	15*	Baseline information for each group *for the individual and cluster levels as applicable*	17 (Table 1)
Numbers analyzed	16*	Number of *clusters and* participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	10
Outcomes and Estimation	17*	For each primary and secondary outcome, a summary of results for each group measures *for the individual or cluster level as applicable*, and the estimated effect size and its precision (e.g., 95% confidence interval) *and a coefficient of intracluster correlation (ICC or k) for each primary outcome.*	10+18-19 (Table 2+3)
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed,	10

		including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	None
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	10-12
Generalisability	21*	Generalisability (external validity) *to individuals and/or clusters (as relevant)* of the trial findings.	12-13
Overall evidence	22	General interpretation of the results in the context of current evidence.	13-14

Enhanced involvement of general practitioners in cancer rehabilitation: a randomised controlled trial.

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Words: 2531

Abstract

Objective: To test the hypothesis that a multimodal intervention giving the general practitioner (GP) an enhanced role in cancer rehabilitation improves patients' health-related quality of life and psychological distress.

Design: Cluster randomised controlled trial. All general practices in Denmark were randomised to an intervention group or to a control group. Patients were subsequently allocated to intervention or control (usual procedures) based on the randomisation status of their GP.

Setting: All clinical departments at a public regional hospital treating cancer patients and all general practices in Denmark.

Participants: Adult patients treated for incident cancer at Vejle Hospital, Denmark, between 12 May 2008 and 28 February 2009. A total of 955 patients (486 to intervention, 469 to control group) registered with 323 general practices were included.

Intervention: The intervention included an interview about rehabilitation needs with a rehabilitation coordinator at the regional hospital, information from the hospital to the GP about individual needs for rehabilitation and an encouragement of the GP to contact the patient to offer his support with rehabilitation.

Main outcome measures: The primary outcome was health-related quality of life measured 6 months after inclusion using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Secondary outcomes included quality of life at 14 months and additional subscales of the EORTC QLQ-C30 at 6 and 14 months, and psychological distress at 14 months using the Profile of Mood States (POMS) scale.

Results: No effect of the intervention was observed on primary and/or secondary outcomes after 6 and 14 months.

Conclusion: A multimodal intervention aiming to give the GP an enhanced role in cancer patients' rehabilitation did not improve quality of life or psychological distress.

Trial registration: ClinicalTrials.gov, registration ID number NCT01021371.

Background

Addressing the unmet needs of individual rehabilitation of cancer patients is paramount (1-4). The underlying problems are often psychological or social and many persist after treatment or emerge late in the illness continuum (5-8). Rehabilitation is defined by WHO as "a process intended to enable people with disabilities to reach and maintain optimal physical, sensory, intellectual, psychological and/or social function" (9) which is the conceptual frame for this study. Hence, rehabilitation is a complex and long-lasting process, but evidence on how and when to identify the patients' needs, what initiatives to offer, and how to manage the efforts is sparse (2;10-13).

General practice is characterised by continuity with frequent encounters with each patient, covering wide-ranging issues (14). Hence, general practitioners (GPs) generally have profound knowledge about the patients' prior health status, mental vulnerability and social network. General practice may, therefore, be able to initiate the rehabilitation process and take on the task of coordinating or providing the rehabilitation services needed, but currently the role of GPs is not well-defined (15-23). Studies do, however, show that GPs are willing to undertake these tasks and that the patients wish that their GPs were more proactive in doing so (24-25).

The objective of this trial was to investigate the effect of a multimodal intervention giving the GP an enhanced role in improving patients' health-related quality of life and psychological distress following cancer. To validate our results we conducted subgroup analyses of the large and homogeneous group of breast cancer patients.

Material and methods

We conducted a cluster randomised, controlled trial where all general practices in Denmark were randomised to an intervention group or to a control group by means of the unique provider number of each practice. Patients were subsequently allocated according to the randomisation of their GP. Feasibility of the intervention and the study details have previously been published (26).

Participants

All adult patients (≥18 years) newly diagnosed with cancer and admitted to Vejle Hospital between 12 May 2008 and 28 February 2009 were assessed for eligibility. Patients were included if treated at Vejle Hospital for a cancer diagnosed within the last 3 months and if listed with a general practice. Patients with carcinoma in situ or non-melanoma skin cancers were not included (Figure 1).

Two rehabilitation coordinators, both nurses with oncological experience, assessed all patients for eligibility and managed the intervention. The patients were sampled across departments, type of cancer, stage, and potential rehabilitation needs by use of the electronic patient files (26).

Setting

The study was conducted at Vejle Hospital, a public general hospital in the region of Southern Denmark (1.2 million inhabitants) (27). Cancer patients were allocated from all of Denmark.

The Danish publicly funded healthcare system ensures free access to general practice which is responsible for primary care needs, and GPs function as gatekeepers to

the rest of the healthcare system. More than 98% of all Danish residents are registered with a general practice. On average each GP meets 9 incident cancer patients during one year (28).

GPs' opportunities to refer patients to relevant rehabilitation services vary between the different municipalities, just as the availability of private patient associations and other relief organisations. These conditions might influence the quality of the rehabilitation interventions offered.

The intervention

The intervention comprised a patient interview about rehabilitation needs performed by the rehabilitation coordinators, followed by information to the GP about the patient's individual rehabilitation needs and cancer patients' rehabilitation needs in general. The core of the information was that the GP was encouraged to contact the patient to facilitate a rehabilitation process (Figure 2).

The patient interviews were conducted according to an interview guide (29) and based on a checklist of general needs and problems among cancer patients (Figure 2). Interviews were most often conducted at the hospital, but in some cases by phone. During the interview, the concept of rehabilitation was explained and the individual needs for physical, psychological, sexual, social, work- and economy-related rehabilitation were identified. It was explained that physical, psychological, sexual, social, work-related and financial issues (1-4;30) might occur at any time and change during the disease trajectory (7-8). In order to address these problems, patients were advised to consult their GP during treatment and after discharge.

Following each interview, the patient's GP was informed about the patient's actual problems and needs for rehabilitation and encouraged to be proactive, i.e. the GP was encouraged to contact the patient personally to offer support and guidance in order to identify and address actual and future needs for rehabilitation. Subsequently, the GP received an e-mail summarising the information, supplemented by general information about cancer patients' needs and problems (Figure 3). The information was personally conveyed by phone, if possible, and always sent electronically along with the more general information. Patients and GPs in the control group received the usual care and were not contacted by the rehabilitation coordinators (26).

Outcomes and sampling of data

The primary outcome was health-related quality of life measured 6 months after inclusion using the Global Health Status of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (31;32). The secondary outcomes were psychological distress at 14 months assessed by the 6 scales of the Profile of Mood States (POMS) (33) (depression/dejection, anger/hostility, tension/anxiety, vigour/activity, fatigue/inertia and confusion/bewilderment), and the Global Health Status at 6 months and functional (physical, emotional, role, cognitive or social functioning) and symptom scales (fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea or financial difficulties) of the EORTC QLQ-C30 at 6 and 14 months.

Data were sampled in identical ways irrespective of allocation status by use of patient questionnaires administered to patients alive at 6 and 14 months after inclusion. Non-responders were sent one reminder after 3 weeks (26).

Sample size

The sample size was estimated based on the primary outcome measure. According to the EORTC Tables of Reference Values (34) for all cancer patients, all stages, the Global Health Status is normally distributed with a mean of 61.3 and an SD of 24.2. A change of at least 8 units was assumed to be clinically relevant (34;35).

If the lowest acceptable statistical power was 80%, then, based on the two-sample t-test with a type 1 error alpha=0.05, the sample size was calculated to be 144 patients per group. The study was subject to clustering because the unit of randomisation was at the level of the GP, whereas the primary outcome measure was at the level of the patient. A strong effect on outcome of the individual practice was expected, but no data supported estimation of cluster effect. To allow maximum clustering it was attempted to include patients to each group from a minimum of 144 practices.

Randomisation

Prior to study start, all 2181 general practices in Denmark were randomly allocated to the intervention or control group by the unique provider number of each practice using a computerised random-number generator in the statistical program Stata version 10.0 (StataCorp, College Station, TX, USA). Hence, randomisation was performed at practice level meaning that all GPs working under the same provider number were allocated to the same group. Consequently, spill-over effect between GPs and patients from the same practice was minimised.

Blinding

The study was not blinded. The list of randomisation was available to the RCs during assessment of patient eligibility. Allocation status was obvious during intervention.

Statistical analysis

Baseline patient characteristics were described using descriptive statistics in order to present the distribution of age, sex and cancer type. We conducted intention to treat analyses and numerical outcomes of the RCT were analysed using a multi-level linear model, accounting for possible cluster effects caused by the cluster randomisation. All secondary outcomes were adjusted for confounding effect of age and sex. Missing values were regarded as missing at random.

The statistical analyses were performed using Stata version 11.0 (StataCorp, College Station, TX, USA).

Development and piloting of questionnaires and intervention

Before designing the intervention we established a theoretical basis through review of papers, reports and textbooks about the problems faced by cancer patients and GPs with respect to individual rehabilitation and continuity across healthcare sectors (1-3;16-24;36).

The questionnaires and the procedures of identification, assessment and inclusion of patients were pilot tested prior to study start. The procedures have been described in detail (26).

Results

In total 955 patients fulfilled the criteria for inclusion and 486 patients were allocated to the intervention group and 469 to the control group (Figure 1). The patients were registered with 323 general practices. Patients were on average aged 63 years at baseline and 72% were female. The most frequent cancer localisations were breast (43%) and lung (15%). The intervention and control groups showed similar baseline characteristics (Table 1). For the primary outcome, Global Health Status at 6 months, we obtained data from 281 patients from 131 practices in the intervention group and 297 patients from 125 practices in the control group, in total 612 of 858 (71%) patients (95%-confidence interval for ICC 0.000 - 0.103) (Figure 1).

The intervention had no statistically significant impact on the primary or on the secondary outcomes (Tables 2 and 3). Adjustment for age and sex of the secondary outcomes showed results similar to the unadjusted analysis. Intention to treat analyses on all outcomes of the group of breast cancer patients showed no statistical differences between patients in the intervention and control group (mean difference in primary outcome of 1.77 (-3.2 to 6.8)). Per protocol analyses on all outcomes were used to analyse if the personal telephone contact to the GP was crucial. The patients receiving all elements of the intervention showed no statistically significant difference when compared to the control group (mean difference in primary outcome of -4.43 (-9.7 to 0.8)).

Discussion

Principal findings

This intervention including a hospital-based patient interview about rehabilitation, individual and general information to the GP and an encouragement to contact the patient and

facilitate a process of rehabilitation did not improve quality of life or relieve psychological distress of patients newly diagnosed with cancer.

Strengths and weaknesses of the study

The study included 955 patients and the pre-study power calculation and the precision of the statistical estimates indicate that the study could have detected relevant effects of the intervention. The confidence interval of the difference in global health status after 6 months ranged between -2.4 and 4.9 units. Clinically relevant differences have been suggested to correspond to at least 8 units (34;35).

An important question is whether any spill-over effects may have improved care for the patients in the control group, leading to an apparently smaller impact of the intervention. Information about the study and the concept of rehabilitation was given to the staff at the involved departments at Vejle Hospital during the inclusion period, but the intervention was managed by the two rehabilitation coordinators without influence on the care provided for the patients in the control group. The cluster randomisation was performed to ensure that GPs only cared for patients in either the intervention or the control group. GPs in the control group were not informed about the study and we have no reason to believe that information about the study was disseminated between GPs in the two groups.

Another question is whether we used the most relevant outcome measures. Process measures are often used to evaluate interventions. However, despite successful implementation of interventions, the impact on patients' wellbeing is often sparse. Hence, we deliberately chose patients' quality of life as the primary outcome. Further, the EORTC

QLQ-C30 and the POMS questionnaires are both well-validated instruments to evaluate change of quality of life in cancer patients and psychological distress in general (31-35).

The intervention was designed to support rehabilitation irrespective of the character of the problem, cancer type, age and sex. We included patients with various cancer types, different prognosis, health problems and needs of supportive care. The inhomogeneity of the study population might have diluted effects in groups of patients with specific problems or diagnoses. It cannot be ruled out that a similar intervention might have effect on subgroups of patients with specific cancers or special needs. However, no effect was observed when analysing the large and rather homogeneous group of breast cancer patients.

The intervention included a personal telephone contact to the patients' GP but some GPs were not reachable (26). A priori we assumed that this personal contact could be of major importance, but per protocol analysis showed no differences in outcomes for patients where the rehabilitation coordinators managed to reach the GP by phone.

Relations to other studies

To our knowledge, only three papers have specifically evaluated the impact of GP involvement in cancer rehabilitation in a randomised design (17;36-37). A shared care programme (n=250) conducted in Denmark in 2003 included transfer of knowledge from oncologists to GPs, improved communication between parties, and active patient involvement (17). This intervention had a positive impact on patient evaluation of cooperation between primary and secondary healthcare sectors, but not on quality of life. A Norwegian study from 2005 (n=91) evaluated the effect of an invitation to a 30-minute consultation with the patient's GP, aiming at creating a closer and more frequent contact

between patients and GPs (36). No increase in number of consultations or improvement of quality of life was observed. The latest study was conducted in Sweden in 2008 (n=481) and tested the effectiveness of individual support, group rehabilitation and a combination of the two compared to standard care (37). The individual support included individual psychological and nutritional support along with intensified primary health care, including extended information about the diagnosis, education in cancer care, and supervision of the patient's home care nurse and GP by a multi-professional oncology team. The Swedish study did not show an improvement either in quality of life or psychological well-being when compared to standard care. Further, a systematic review (38) including the three studies concluded that none of the interventions improved quality of life or patient wellbeing, but due to possible methodological problems further studies on the topic are needed.

Meaning

Interventions aiming to give the GP an enhanced role in cancer rehabilitation seem to have difficulties improving quality of life. Furthermore, a number of papers evaluating the effect of various other types of interventions aiming to improve quality of life of cancer patients (39-44) have demonstrated that this may be difficult in general. To better understand the intervention and the impact on GP and patient behaviour further studies will include evaluation of process measures like GP proactivity, patient participation in different rehabilitation activities, and GP and patient satisfaction.

Future studies should evaluate the importance of the organisation of cancer treatment and rehabilitation. Is an unclear organisation with many partners (hospital departments, GPs, municipalities and private organisations) an impediment to effective

rehabilitation? A well-organised system with defined roles and easy referral to various elements of rehabilitation (specialised physiotherapy, social counselling, psychological advice etc.) may be of importance for the effect of a GP intervention. To improve rehabilitation it may also be important to develop screening tools that support identification of patients with special needs. Initiatives supporting the GPs in undertaking a proactive role for patients with special needs should be considered. The effect of interventions should, however, be carefully evaluated in order to ensure efficient use of resources before implementation.

Figure 1. Study flow.

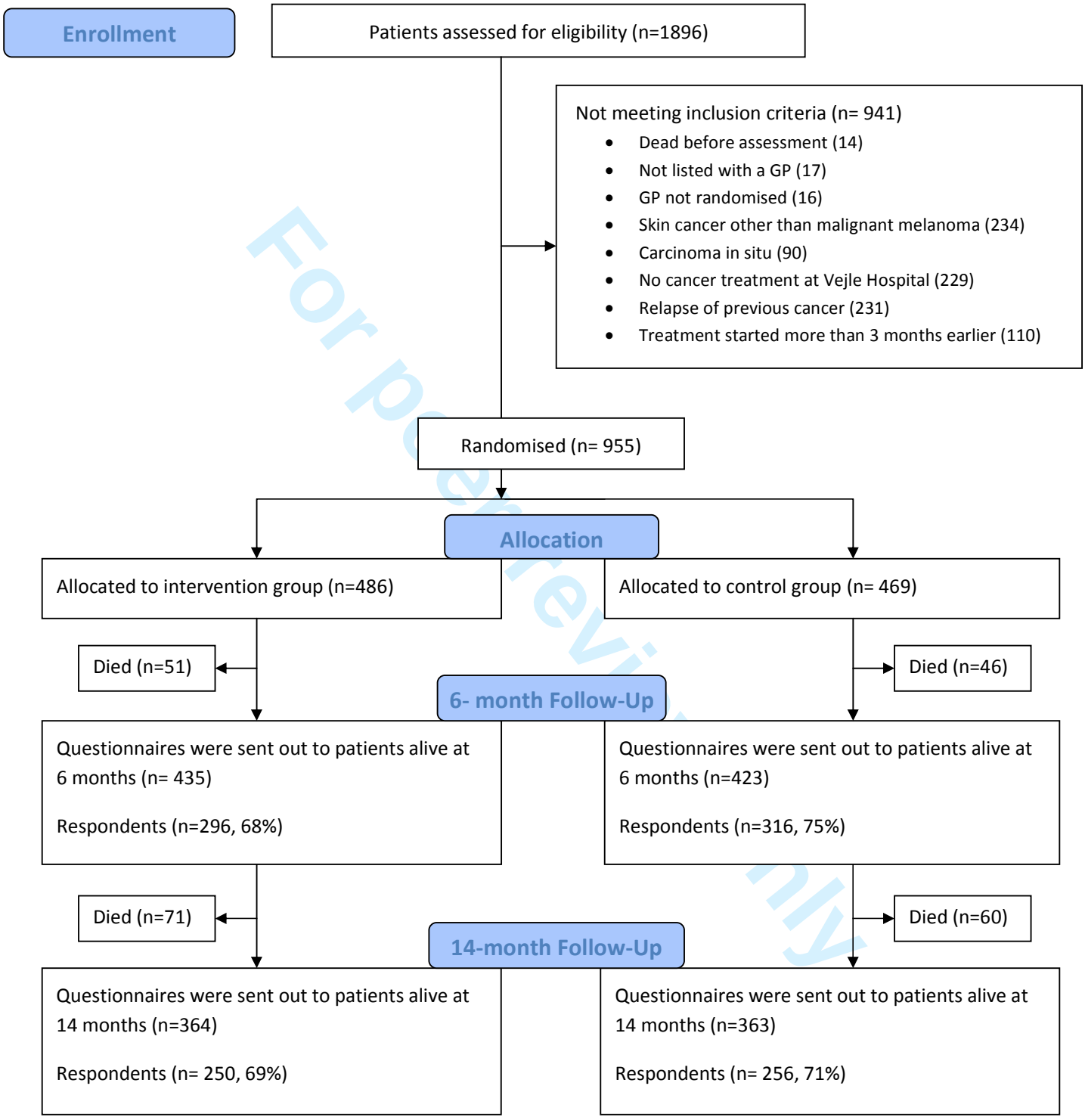

Figure 2. General needs and problems among cancer patients.

Psychological level	• Fear of death or recurrence • Guilt feelings about being sick • Anger at general practitioner or "system" for not having taken action soon enough • Troubles adjusting to new self-image • Sense of being left in limbo after discharge from the hospital • Risk of developing depression • Reconsiderations about priorities in life and how one wants to live life with or after a cancer disease • Sexual problems
Social level	• Concerns about the well-being of spouse, children and other relatives • Changed body image or sexuality • Changed position/status in marriage, in family, at work, etc. • Concerns about possible infertility caused by treatment • Information about patient associations and similar groups for patients and relatives
Physical level	• Physical capacity according to daily activities, need for special facilities, homecare, conversions of the home, etc. • Need for dietary advice, e.g. to prevent undue weight loss • Support in order to accept physical changes and late complications like tiredness, amputation, infertility, pain, etc.
Work-related level	• Concerns about losing one's job • Concerns about having to give up one's former responsibilities or change field of work due to reduced ability to work • Opportunities for financial support during sick-leave, flexible job, etc. • Support to keep in contact with workplace during sick-leave
Financial level	• Social rights like mileage allowances, reimbursement of assistive technology, etc. • Concerns about a decrease in income and consequences hereof in relation to housing, spouse, children, etc. • Conditions regarding pension or incapacity benefit

Table 1. Baseline demographic and medical characteristics for all included patients (n=955).

Demographic characteristics	Control group (n=469)	Intervention group (n=486)
Age, years		
Mean (CI)	63.6 (62.5 to 64.6)	63.2 (62.2 to 64.3)
Median	64	64
Range	21 to 98	28 to 92
Sex		
Male (%)	134 (28.6)	133 (27.4)
Female (%)	335 (71.4)	353 (72.6)
Cancer type	Numbers (%)	Numbers (%)
Cancer of breast	206 (43.9)	201 (41.4)
Cancer of lung	69 (14.7)	75 (15.4)
Malignant melanoma	44 (9.4)	35 (7.2)
Cancer of rectum/anus	33 (7.0)	45 (9.3)
Cancer of colon	29 (6.2)	39 (8.0)
Cancer of ovaries	12 (2.6)	9 (1.9)
Cancer of bilary system	7 (1.5)	8 (1.6)
Cancer of brain	6 (1.3)	8 (1.6)
Cancer of prostate	8 (1.7)	3 (0.6)
Cancer of corpus uteri	6 (1.3)	5 (1.0)
Myelomatosis	6 (1.3)	5 (1.0)
Lymphoma	3 (0.6)	4 (0.8)
Unspecified location	16 (3.4)	16 (3.3)
Other diagnoses	24 (5.1)	33 (6.8)

Table 2. Health-Related Quality of Life (EORTC QLQ-C30) outcome variables and mean differences at 6 and 14 months (95% confidence intervals).

	6 months				14 months			
Outcome variable	n	Mean (CI)	Mean difference (95% CI)	P	n	Mean (CI)	Mean difference (95% CI)	P
Global Health Status/qol								
Control group	297	68,0 (65.5 to 70.5)			246	72.8 (70.3 to 75.3)		
Intervention group	281	69,3 (66.7 to 71.9)	1.25 (-2.4 to 4.9)	0.50	240	72.1 (69.6 to 74.7)	-0.71 (-4.3 to 2.8)	0.69
Physical functioning								
Control group	294	79.0 (76.4 to 81.5)			240	81.9 (79.3 to 84-5)		
Intervention group	280	79.7(77.1 to 82.4)	0.77 (-2.9 to 4.4)	0.68	234	82.0 (79.4 to 84.6)	-0.08 (-3.6 to 3.8)	0.97
Role functioning								
Control group	291	71.3 (67.7 to 74.9)			239	78.0 (74.4 to 81.7)		
Intervention group	277	72.5 (68.8 to 76.1)	1.18 (-3.9 to 6.3)	0.65	235	78.8 (75.0 to 82.5)	0.70 (-4.5 to 5.9)	0.79
Emotional functioning								
Control group	293	80.5 (78.1 to 83.0)			240	80.7 (77.9 to 83.4)		
Intervention group	278	81.6 (79.1 to 84.1)	1.02 (-2.5 to 4.5)	0.57	238	80.8 (78.0 to 83.6)	0.12 (-3.8 to 4.1)	0.95
Cognitive functioning								
Control group	290	83.0 (80.5 to 85.5)			245	82.6 (79.7 to 85.5)		
Intervention group	278	83.9 (81.3 to 86.4)	0.88 (-2.7 to 4.5)	0.63	238	85.1 (82.1 to 88.2)	2.53 (-1.7 to 6.7)	0.24
Social functioning								
Control group	295	85.7 (83.0 to 88.4)			242	88.2 (85.4 to 91.0)		
Intervention group	280	86.0 (83.2 to 88.8)	0.28 (-3.6 to 4.2)	0.89	238	87.4 (84.6 to 90.3)	-0.77 (-4.8 to 3.2)	0.71
Fatigue								
Control group	292	37.4 (34.3 to 40.6)			244	32.1 (28.8 to 35.3)		
Intervention group	279	34.2 (30.9 to 37.4)	-3.27 (-7.8 to 1.3)	0.16	234	32.3 (28.9 to 35.6)	0.23 (-4.5 to 4.9)	0.92
Nausea and vomiting								
Control group	300	8.1 (6.1 to 10.0)			244	5.5 (3.9 to 7.2)		
Intervention group	284	8.0 (6.0 to 10.0)	-0.11 (-2.9 to 2.7)	0.94	236	5.6 (3.9 to 7.3)	0.05 (-2.3 to 2.4)	0.97
Pain								
Control group	283	23.0 (19.8 to 26.2)			241	21.9 (18.5 to 25.4)		
Intervention group	274	22.0 (18.8 to 25.3)	-0.95 (-5.5 to 3.6)	0.68	234	21.4 (17.8 to 24.9)	-0.56 (-5.5 to 4.4)	0.83
Dyspnoea								
Control group	297	17.0 (13.9 to 20.2)			245	13.2 (10.0 to 16.5)		
Intervention group	286	17.9 (14.7 to 21.2)	0.87 (-3.6 to 5.4)	0.71	233	15.4 (11.9 to 18.8)	2.11 (-2.6 to 6.8)	0.38
Insomnia								
Control group	302	27.5 (24.0 to 31.0)			248	29.6 (25.6 to 33.6)		
Intervention group	285	27.3 (23.6 to 30.9)	-0.23 (-5.3 to 4.8)	0.93	240	28.5 (24.4 to 32.6)	-1.08 (-6.8 to 4.6)	0.71
Appetite loss								
Control group	301	14.1 (11.0 to 17.2)			246	9.6 (7.1 to 12.2)		
Intervention group	288	15.9 (12.7 to 19.0)	1.79 (-2.7 to 6.2)	0.43	239	7.9 (5.4 to 10.5)	-1.67 (-5.3 to 2.0)	0.37
Constipation								
Control group	299	12.6 (9.7 to 15.5)			248	11.9 (9.0 to 14.9)		
Intervention group	284	11.3 (8.3 to 14.2)	-1.33 (-5.4 to 2.8)	0.53	236	8.9 (5.9 to 11.9)	-3.03 (-7.4 to 1.1)	0.16
Diarrhoea								
Control group	299	11.3 (8.8 to 13.9)			250	11.4 (8.5 to 14.2)		
Intervention group	284	11.4 (8.8 to 14.1)	0.08 (-3.6 to 3.8)	0.97	238	10.0 (7.0 to 13.0)	-1.38 (-5.5 to 2.8)	0.51
Financial difficulties								
Control group	297	7.6 (5.4 to 9.8)			242	6.5 (3.9 to 9.0)		
Intervention group	284	8.0 (5.7 to 10.2)	0.34 (-2.8 to 3.5)	0.83	236	6.7 (4.1 to 9.4)	0.27 (-3.4 to 4.0)	0.89
Mean values from 0 to 100. A score of 100 indicates optimal function or maximum symptom intensity (i.e. for functional measures, an increase indicates improvement, while for symptoms, an increase indicates worsening)								

Table 3. Psychological distress (POMS) at 14 months and mean differences between groups (95 confidence intervals).

Outcome variable	n	Mean range	Mean (95% CI)	Mean difference (95% CI)	P
Anger/hostility		0 to 28			
Control group	223		2.03 (1.59 to 2.48)		
Intervention group	230		1.88 (1.43 to 2.33)	-0.15 (-0.79 to 0.48)	0.64
Confusion/bewilderment		0 to 20			
Control group	229		2.45 (2.04 to 2.86)		
Intervention group	231		2.11 (1.69 to 2.53)	-0.34 (-0.92 to 0.25)	0.26
Depression/dejection		0 to 32			
Control group	223		3.85 (3.20 to 4.51)		
Intervention group	229		3.26 (2.61 to 3.92)	-0.59 (-1.52 to 0.34)	0.21
Fatigue/inertia		0 to 20			
Control group	226		4.65 (4.08 to 5.22)		
Intervention group	234		4.14 (3.02 to 4.10)	-0.51 (-1.32 to 0.29)	0.21
Tension/anxiety		0 to 24			
Control group	226		3.82 (3.28 to 4.36)		
Intervention group	233		3.56 (3.02 to 4.10)	-0.26 (-1.02 to 0.50)	0.50
Vigour/activity		0 to 24			
Control group	218		10.28 (9.51 to 11.05)		
Intervention group	228		10.09 (9.31 to 10.86)	-0.20 (-1.29 to 0.89)	0.72
Total mood disturbance		0 to 124			
Control group	200		4.87 (2.29 to 7.45)		
Intervention group	210		4.19 (1.62 to 6.76)	-0.68 (-4.32 to 2.97)	0.72

Mean values of each subscale depends on the number of items related to the individual subscale which varies from 5 to 8, each item ranging from 0 to 4. Total mood disturbance is calculated by summing up the scores on the five negative symptom subscales and subtracting the score on the one positively scored subscale, vigour/activity. A higher score indicates a higher degree of symptoms/feelings within the related subscale.

Contributors

SHB, JK, JS and DGH contributed to conception and study design. SHB, DGH, JK and JS obtained the funding. SHB, JK, JS and DGH wrote the protocol. SHB and DGH were responsible for recruitment of patients. SHB collected and managed the data. PVL was the study statistician. SHB and PVL performed the statistical analysis. SHB, PVL, JK, JS and DGH contributed to the interpretation of data. SHB drafted the first version of the manuscript. SHB, JK, JS, PVL and DGH critically reviewed, revised, and supplemented the manuscript. All authors approved the final version. SHB is the guarantor.

Licence for publication

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted

work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The study was approved by the Danish Data Protection Agency. The Regional Committee on Biomedical Research Ethics evaluated the project and concluded that the intervention did not need an approval from the Danish National Committee on Biomedical Research Ethics according to Danish law (Project-ID: S-20082000-7).

Data

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing

No additional data available.

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Enhanced involvement of general practitioners in cancer rehabilitation: a randomised controlled trial

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Enhanced involvement of general practitioners in cancer rehabilitation: a randomised controlled trial.

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Abstract

Objective: To test the hypothesis that a multimodal intervention giving the general practitioner (GP) an enhanced role in cancer rehabilitation improves patients' health-related quality of life and psychological distress.

Design: Cluster randomised controlled trial. All general practices in Denmark were randomised to an intervention group or to a control group. Patients were subsequently allocated to intervention or control (usual procedures) based on the randomisation status of their GP.

Setting: All clinical departments at a public regional hospital treating cancer patients and all general practices in Denmark.

Participants: Adult patients treated for incident cancer at Vejle Hospital, Denmark, between 12 May 2008 and 28 February 2009. A total of 955 patients (486 to intervention, 469 to control group) registered with 323 general practices were included.

Intervention: The intervention included an interview about rehabilitation needs with a rehabilitation coordinator at the regional hospital, information from the hospital to the GP about individual needs for rehabilitation and an encouragement of the GP to contact the patient to offer his support with rehabilitation.

Main outcome measures: The primary outcome was health-related quality of life measured 6 months after inclusion using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Secondary outcomes included quality of life at 14 months and additional subscales of the EORTC QLQ-C30 at 6 and 14 months, and psychological distress at 14 months using the Profile of Mood States (POMS) scale.

Results: No effect of the intervention was observed on primary and/or secondary outcomes after 6 and 14 months.

Conclusion: A multimodal intervention aiming to give the GP an enhanced role in cancer patients' rehabilitation did not improve quality of life or psychological distress.

Trial registration: ClinicalTrials.gov, registration ID number NCT01021371.

Background

Addressing the unmet needs of individual rehabilitation of cancer patients is paramount (1-4). The underlying problems are often psychological or social and many persist after treatment or emerge late in the illness continuum (5-8). Rehabilitation is defined by WHO as "a process intended to enable people with disabilities to reach and maintain optimal physical, sensory, intellectual, psychological and/or social function" (9) which is the conceptual frame for this study. Hence, rehabilitation is a complex and long-lasting process, but evidence on how and when to identify the patients' needs, what initiatives to offer, and how to manage the efforts is sparse (2;10-13).

General practice is characterised by continuity with frequent encounters with each patient, covering wide-ranging issues (14). Hence, general practitioners (GPs) generally have profound knowledge about the patients' prior health status, mental vulnerability and social network. General practice may, therefore, be able to initiate the rehabilitation process and take on the task of coordinating or providing the rehabilitation services needed, but currently the role of GPs is not well-defined (15-23). Studies do, however, show that GPs are willing to undertake these tasks and that the patients wish that their GPs were more proactive in doing so (24-25).

The objective of this trial was to investigate the effect of a multimodal intervention giving the GP an enhanced role in improving patients' health-related quality of life and psychological distress following cancer. To validate our results we conducted subgroup analyses of the large and homogeneous group of breast cancer patients.

Material and methods

We conducted a cluster randomised, controlled trial where all general practices in Denmark were randomised to an intervention group or to a control group by means of the unique provider number of each practice. Patients were subsequently allocated according to the randomisation of their GP. Feasibility of the intervention and the study details have previously been published (26).

Participants

All adult patients (≥18 years) newly diagnosed with cancer and admitted to Vejle Hospital between 12 May 2008 and 28 February 2009 were assessed for eligibility. Patients were included if treated at Vejle Hospital for a cancer diagnosed within the last 3 months and if listed with a general practice. Patients with carcinoma in situ or non-melanoma skin cancers were not included (Figure 1).

Two rehabilitation coordinators, both nurses with oncological experience, assessed all patients for eligibility and managed the intervention. The patients were sampled across departments, type of cancer, stage, and potential rehabilitation needs by use of the electronic patient files (26).

Setting

The study was conducted at Vejle Hospital, a public general hospital in the region of Southern Denmark (1.2 million inhabitants) (27). Cancer patients were allocated from all of Denmark.

The Danish publicly funded healthcare system ensures free access to general practice which is responsible for primary care needs, and GPs function as gatekeepers to

the rest of the healthcare system. More than 98% of all Danish residents are registered with a general practice. On average each GP meets 9 incident cancer patients during one year (28).

GPs' opportunities to refer patients to relevant rehabilitation services vary between the different municipalities, just as the availability of private patient associations and other relief organisations. These conditions might influence the quality of the rehabilitation interventions offered.

The intervention

The intervention comprised a patient interview about rehabilitation needs performed by the rehabilitation coordinators, followed by information to the GP about the patient's individual rehabilitation needs and cancer patients' rehabilitation needs in general. The core of the information was that the GP was encouraged to contact the patient to facilitate a rehabilitation process (Figure 2).

The patient interviews were conducted according to an interview guide (29) and based on a checklist of general needs and problems among cancer patients (Figure 2). Interviews were most often conducted at the hospital, but in some cases by phone. During the interview, the concept of rehabilitation was explained and the individual needs for physical, psychological, sexual, social, work- and economy-related rehabilitation were identified. It was explained that physical, psychological, sexual, social, work-related and financial issues (1-4;30) might occur at any time and change during the disease trajectory (7-8). In order to address these problems, patients were advised to consult their GP during treatment and after discharge. The patients gave oral consent firstly to their GPs being

informed as to their individual problems and needs and secondly to their GPs being encouraged to be proactive regarding the patients' rehabilitation.

Following each interview, the patient's GP was informed about the patient's actual problems and needs for rehabilitation and encouraged to be proactive, i.e. the GP was encouraged to contact the patient personally to offer support and guidance in order to identify and address actual and future needs for rehabilitation. Subsequently, the GP received an e-mail summarising the information, supplemented by general information about cancer patients' needs and problems (Figure 2). The information was personally conveyed by phone, if possible, and always sent electronically along with the more general information. Patients and GPs in the control group received the usual care and were not contacted by the rehabilitation coordinators (26).

Outcomes and sampling of data

The primary outcome was health-related quality of life measured 6 months after inclusion using the Global Health Status of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (31;32). The secondary outcomes were psychological distress at 14 months assessed by the 6 scales of the Profile of Mood States (POMS) (33) (depression/dejection, anger/hostility, tension/anxiety, vigour/activity, fatigue/inertia and confusion/bewilderment), and the Global Health Status at 6 months and functional (physical, emotional, role, cognitive or social functioning) and symptom scales (fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea or financial difficulties) of the EORTC QLQ-C30 at 6 and 14 months.

Data were sampled in identical ways irrespective of allocation status by use of patient questionnaires administered to patients alive at 6 and 14 months after inclusion. Non-responders were sent one reminder after 3 weeks (26).

Sample size

The sample size was estimated based on the primary outcome measure. According to the EORTC Tables of Reference Values (34) for all cancer patients, all stages, the Global Health Status is normally distributed with a mean of 61.3 and an SD of 24.2. A change of at least 8 units was assumed to be clinically relevant (34;35).

If the lowest acceptable statistical power was 80%, then, based on the two-sample t-test with a type 1 error alpha=0.05, the sample size was calculated to be 144 patients per group. The study was subject to clustering because the unit of randomisation was at the level of the GP, whereas the primary outcome measure was at the level of the patient. A strong effect on outcome of the individual practice was expected, but no data supported estimation of cluster effect. To allow maximum clustering it was attempted to include patients to each group from a minimum of 144 practices.

Randomisation

Prior to study start, all 2181 general practices in Denmark were randomly allocated to the intervention (n=1091) or control (n=1090) group by the unique provider number of each practice using a computerised random-number generator in the statistical program Stata version 10.0 (StataCorp, College Station, TX, USA). Hence, randomisation was performed at practice level meaning that all GPs working under the same provider number were

allocated to the same group. Consequently, spill-over effect between GPs and patients from the same practice was minimised.

Blinding

The study was not blinded. The list of randomisation was available to the RCs during assessment of patient eligibility. Allocation status was obvious during intervention.

Statistical analysis

Baseline patient characteristics were described using descriptive statistics in order to present the distribution of age, sex and cancer type. We conducted intention to treat analyses and numerical outcomes of the RCT were analysed using a multi-level linear model, accounting for possible cluster effects caused by the cluster randomisation. All secondary outcomes were adjusted for confounding effect of age and sex. Missing values were regarded as missing at random. We conducted complete case analyses.

The statistical analyses were performed using Stata version 11.0 (StataCorp, College Station, TX, USA).

Development and piloting of questionnaires and intervention

Before designing the intervention we reviewed papers, reports and textbooks about the problems faced by cancer patients and GPs with respect to individual rehabilitation and continuity across healthcare sectors (1-3;16-24;36).

The questionnaires and the procedures of identification, assessment and inclusion of patients were pilot tested prior to study start. The procedures have been described in detail (26).

Results

In total 955 patients fulfilled the criteria for inclusion and 486 patients were allocated to the intervention group and 469 to the control group (Figure 1). The patients were registered with 323 general practices. Patients were on average aged 63 years at baseline and 72% were female. The most frequent cancer localisations were breast (43%) and lung (15%). The intervention and control groups showed similar baseline characteristics (Table 1). For the primary outcome, Global Health Status at 6 months, we obtained data from 281 patients from 131 practices in the intervention group and 297 patients from 125 practices in the control group, in total 612 of 858 (71%) patients (95%-confidence interval for ICC 0.000 - 0.103). The percentage of missing data in the primary outcome was 5.6% (similar in the intervention and control groups).

The intervention had no statistically significant impact on the primary or on the secondary outcomes (Tables 2 and 3). Adjustment for age and sex of the secondary outcomes showed results similar to the unadjusted analysis. Intention to treat analyses on all outcomes of the group of breast cancer patients showed no statistical differences between patients in the intervention and control group (mean difference in primary outcome of 1.77 (-3.2 to 6.8)). Per protocol analyses on all outcomes were used to analyse if the personal telephone contact to the GP was crucial. The patients receiving all elements of the intervention showed no statistically significant difference when compared to the control group (mean difference in primary outcome of -4.43 (-9.7 to 0.8)).

Discussion

Principal findings

This intervention including a hospital-based patient interview about rehabilitation, individual and general information to the GP and an encouragement to contact the patient and facilitate a process of rehabilitation did not improve quality of life or relieve psychological distress of patients newly diagnosed with cancer.

Strengths and weaknesses of the study

The study included 955 patients and the pre-study power calculation and the precision of the statistical estimates indicate that the study could have detected relevant effects of the intervention. The confidence interval of the difference in global health status after 6 months ranged between -2.4 and 4.9 units. Clinically relevant differences have been suggested to correspond to at least 8 units (34;35).

An important question is whether any spill-over effects may have improved care for the patients in the control group, leading to an apparently smaller impact of the intervention. Information about the study and the concept of rehabilitation was given to the staff at the involved departments at Vejle Hospital during the inclusion period, but the intervention was managed by the two rehabilitation coordinators without influence on the care provided for the patients in the control group. The cluster randomisation was performed to ensure that GPs only cared for patients in either the intervention or the control group. GPs in the control group were not informed about the study and we have no reason to believe that information about the study was disseminated between GPs in the two groups.

Another question is whether we used the most relevant outcome measures. Process measures are often used to evaluate interventions. However, despite successful implementation of interventions, the impact on patients' wellbeing is often sparse. Hence, we deliberately chose patients' quality of life as the primary outcome. Further, the EORTC QLQ-C30 and the POMS questionnaires are both well-validated instruments to evaluate change of quality of life in cancer patients and psychological distress in general (31-35).

The intervention was designed to support rehabilitation irrespective of the character of the problem, cancer type, age and sex. We included patients with various cancer types, different prognosis, health problems and needs of supportive care. The inhomogeneity of the study population might have diluted effects in groups of patients with specific problems or diagnoses. It cannot be ruled out that a similar intervention might have effect on subgroups of patients with specific cancers or special needs. However, no effect was observed when analysing the large and rather homogeneous group of breast cancer patients.

The intervention included a personal telephone contact to the patients' GP but some GPs were not reachable (26). A priori we assumed that this personal contact could be of major importance, but per protocol analysis showed no differences in outcomes for patients where the rehabilitation coordinators managed to reach the GP by phone.

Relations to other studies

To our knowledge, only three papers have specifically evaluated the impact of GP involvement in cancer rehabilitation in a randomised design (17;36-37). A shared care programme (n=250) conducted in Denmark in 2003 included transfer of knowledge from oncologists to GPs, improved communication between parties, and active patient

involvement (17). This intervention had a positive impact on patient evaluation of cooperation between primary and secondary healthcare sectors, but not on quality of life. A Norwegian study from 2005 (n=91) evaluated the effect of an invitation to a 30-minute consultation with the patient's GP, aiming at creating a closer and more frequent contact between patients and GPs (36). No increase in number of consultations or improvement of quality of life was observed. The latest study was conducted in Sweden in 2008 (n=481) and tested the effectiveness of individual support, group rehabilitation and a combination of the two compared to standard care (37). The individual support included individual psychological and nutritional support along with intensified primary health care, including extended information about the diagnosis, education in cancer care, and supervision of the patient's home care nurse and GP by a multi-professional oncology team. The Swedish study did not show an improvement either in quality of life or psychological well-being when compared to standard care. Further, a systematic review (38) including the three studies concluded that none of the interventions improved quality of life or patient wellbeing, but due to possible methodological problems further studies on the topic are needed.

Meaning

Interventions aiming to give the GP an enhanced role in cancer rehabilitation seem to have difficulties improving quality of life. Furthermore, a number of papers evaluating the effect of various other types of interventions aiming to improve quality of life of cancer patients (39-44) have demonstrated that this may be difficult in general. To better understand the intervention and the impact on GP and patient behaviour further studies will include

evaluation of process measures like GP proactivity, patient participation in different rehabilitation activities, and GP and patient satisfaction.

Future studies should evaluate the importance of the organisation of cancer treatment and rehabilitation. Is an unclear organisation with many partners (hospital departments, GPs, municipalities and private organisations) an impediment to effective rehabilitation? A well-organised system with defined roles and easy referral to various elements of rehabilitation (specialised physiotherapy, social counselling, psychological advice etc.) may be of importance for the effect of a GP intervention. To improve rehabilitation it may also be important to develop screening tools that support identification of patients with special needs. Initiatives supporting the GPs in undertaking a proactive role for patients with special needs should be considered. The effect of interventions should, however, be carefully evaluated in order to ensure efficient use of resources before implementation.

Figure 1. Study flow.

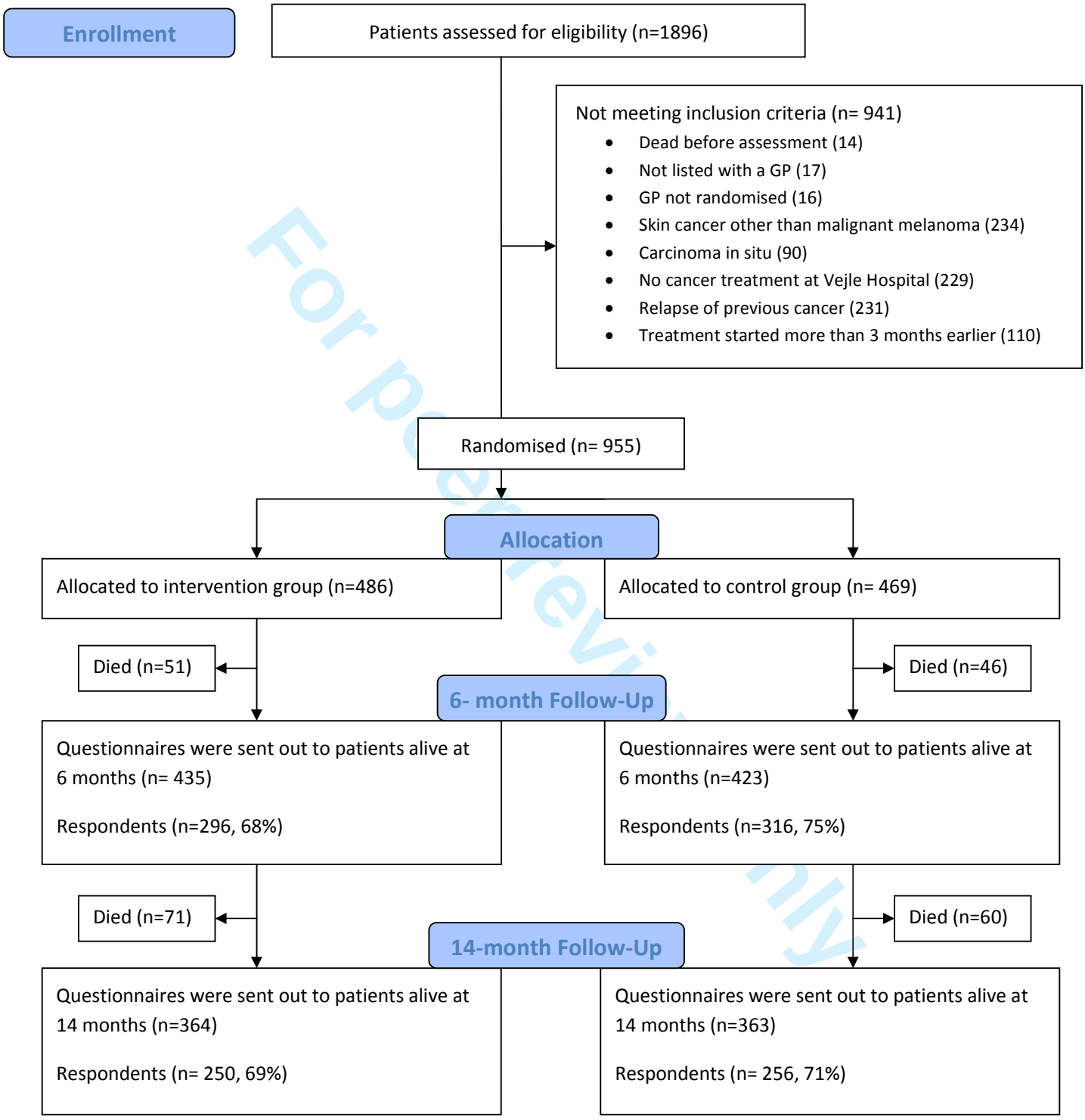

Figure 2. General needs and problems among cancer patients.

Psychological level	• Fear of death or recurrence • Guilt feelings about being sick • Anger at general practitioner or "system" for not having taken action soon enough • Troubles adjusting to new self-image • Sense of being left in limbo after discharge from the hospital • Risk of developing depression • Reconsiderations about priorities in life and how one wants to live life with or after a cancer disease • Sexual problems
Social level	• Concerns about the well-being of spouse, children and other relatives • Changed body image or sexuality • Changed position/status in marriage, in family, at work, etc. • Concerns about possible infertility caused by treatment • Information about patient associations and similar groups for patients and relatives
Physical level	• Physical capacity according to daily activities, need for special facilities, homecare, conversions of the home, etc. • Need for dietary advice, e.g. to prevent undue weight loss • Support in order to accept physical changes and late complications like tiredness, amputation, infertility, pain, etc.
Work-related level	• Concerns about losing one's job • Concerns about having to give up one's former responsibilities or change field of work due to reduced ability to work • Opportunities for financial support during sick-leave, flexible job, etc. • Support to keep in contact with workplace during sick-leave
Financial level	• Social rights like mileage allowances, reimbursement of assistive technology, etc. • Concerns about a decrease in income and consequences hereof in relation to housing, spouse, children, etc. • Conditions regarding pension or incapacity benefit

Table 1. Baseline demographic and medical characteristics for all included patients (n=955).

Demographic characteristics	Control group (n=469)	Intervention group (n=486)
Age, years		
Mean (CI)	63.6 (62.5 to 64.6)	63.2 (62.2 to 64.3)
Median	64	64
Range	21 to 98	28 to 92
Sex		
Male (%)	134 (28.6)	133 (27.4)
Female (%)	335 (71.4)	353 (72.6)
Cancer type	Numbers (%)	Numbers (%)
Cancer of breast	206 (43.9)	201 (41.4)
Cancer of lung	69 (14.7)	75 (15.4)
Malignant melanoma	44 (9.4)	35 (7.2)
Cancer of rectum/anus	33 (7.0)	45 (9.3)
Cancer of colon	29 (6.2)	39 (8.0)
Cancer of ovaries	12 (2.6)	9 (1.9)
Cancer of bilary system	7 (1.5)	8 (1.6)
Cancer of brain	6 (1.3)	8 (1.6)
Cancer of prostate	8 (1.7)	3 (0.6)
Cancer of corpus uteri	6 (1.3)	5 (1.0)
Myelomatosis	6 (1.3)	5 (1.0)
Lymphoma	3 (0.6)	4 (0.8)
Unspecified location	16 (3.4)	16 (3.3)
Other diagnoses	24 (5.1)	33 (6.8)

Table 2. Health-Related Quality of Life (EORTC QLQ-C30) outcome variables and mean differences at 6 and 14 months (95% confidence intervals).

	6 months				14 months			
Outcome variable	n	Mean (CI)	Mean difference (95% CI)	P	n	Mean (CI)	Mean difference (95% CI)	P
Global Health Status/qol								
Control group	297	68,0 (65.5 to 70.5)			246	72.8 (70.3 to 75.3)		
Intervention group	281	69,3 (66.7 to 71.9)	1.25 (-2.4 to 4.9)	0.50	240	72.1 (69.6 to 74.7)	-0.71 (-4.3 to 2.8)	0.69
Physical functioning								
Control group	294	79.0 (76.4 to 81.5)			240	81.9 (79.3 to 84-5)		
Intervention group	280	79.7(77.1 to 82.4)	0.77 (-2.9 to 4.4)	0.68	234	82.0 (79.4 to 84.6)	-0.08 (-3.6 to 3.8)	0.97
Role functioning								
Control group	291	71.3 (67.7 to 74.9)			239	78.0 (74.4 to 81.7)		
Intervention group	277	72.5 (68.8 to 76.1)	1.18 (-3.9 to 6.3)	0.65	235	78.8 (75.0 to 82.5)	0.70 (-4.5 to 5.9)	0.79
Emotional functioning								
Control group	293	80.5 (78.1 to 83.0)			240	80.7 (77.9 to 83.4)		
Intervention group	278	81.6 (79.1 to 84.1)	1.02 (-2.5 to 4.5)	0.57	238	80.8 (78.0 to 83.6)	0.12 (-3.8 to 4.1)	0.95
Cognitive functioning								
Control group	290	83.0 (80.5 to 85.5)			245	82.6 (79.7 to 85.5)		
Intervention group	278	83.9 (81.3 to 86.4)	0.88 (-2.7 to 4.5)	0.63	238	85.1 (82.1 to 88.2)	2.53 (-1.7 to 6.7)	0.24
Social functioning								
Control group	295	85.7 (83.0 to 88.4)			242	88.2 (85.4 to 91.0)		
Intervention group	280	86.0 (83.2 to 88.8)	0.28 (-3.6 to 4.2)	0.89	238	87.4 (84.6 to 90.3)	-0.77 (-4.8 to 3.2)	0.71
Fatigue								
Control group	292	37.4 (34.3 to 40.6)			244	32.1 (28.8 to 35.3)		
Intervention group	279	34.2 (30.9 to 37.4)	-3.27 (-7.8 to 1.3)	0.16	234	32.3 (28.9 to 35.6)	0.23 (-4.5 to 4.9)	0.92
Nausea and vomiting								
Control group	300	8.1 (6.1 to 10.0)			244	5.5 (3.9 to 7.2)		
Intervention group	284	8.0 (6.0 to 10.0)	-0.11 (-2.9 to 2.7)	0.94	236	5.6 (3.9 to 7.3)	0.05 (-2.3 to 2.4)	0.97
Pain								
Control group	283	23.0 (19.8 to 26.2)			241	21.9 (18.5 to 25.4)		
Intervention group	274	22.0 (18.8 to 25.3)	-0.95 (-5.5 to 3.6)	0.68	234	21.4 (17.8 to 24.9)	-0.56 (-5.5 to 4.4)	0.83
Dyspnoea								
Control group	297	17.0 (13.9 to 20.2)			245	13.2 (10.0 to 16.5)		
Intervention group	286	17.9 (14.7 to 21.2)	0.87 (-3.6 to 5.4)	0.71	233	15.4 (11.9 to 18.8)	2.11 (-2.6 to 6.8)	0.38
Insomnia								
Control group	302	27.5 (24.0 to 31.0)			248	29.6 (25.6 to 33.6)		
Intervention group	285	27.3 (23.6 to 30.9)	-0.23 (-5.3 to 4.8)	0.93	240	28.5 (24.4 to 32.6)	-1.08 (-6.8 to 4.6)	0.71
Appetite loss								
Control group	301	14.1 (11.0 to 17.2)			246	9.6 (7.1 to 12.2)		
Intervention group	288	15.9 (12.7 to 19.0)	1.79 (-2.7 to 6.2)	0.43	239	7.9 (5.4 to 10.5)	-1.67 (-5.3 to 2.0)	0.37
Constipation								
Control group	299	12.6 (9.7 to 15.5)			248	11.9 (9.0 to 14.9)		
Intervention group	284	11.3 (8.3 to 14.2)	-1.33 (-5.4 to 2.8)	0.53	236	8.9 (5.9 to 11.9)	-3.03 (-7.4 to 1.1)	0.16
Diarrhoea								
Control group	299	11.3 (8.8 to 13.9)			250	11.4 (8.5 to 14.2)		
Intervention group	284	11.4 (8.8 to 14.1)	0.08 (-3.6 to 3.8)	0.97	238	10.0 (7.0 to 13.0)	-1.38 (-5.5 to 2.8)	0.51
Financial difficulties								
Control group	297	7.6 (5.4 to 9.8)			242	6.5 (3.9 to 9.0)		
Intervention group	284	8.0 (5.7 to 10.2)	0.34 (-2.8 to 3.5)	0.83	236	6.7 (4.1 to 9.4)	0.27 (-3.4 to 4.0)	0.89
Mean values from 0 to 100. A score of 100 indicates optimal function or maximum symptom intensity (i.e. for functional measures, an increase indicates improvement, while for symptoms, an increase indicates worsening)								

Table 3. Psychological distress (POMS) at 14 months and mean differences between groups (95 confidence intervals).

Outcome variable	n	Mean range	Mean (95% CI)	Mean difference (95% CI)	P
Anger/hostility		0 to 28			
Control group	223		2.03 (1.59 to 2.48)		
Intervention group	230		1.88 (1.43 to 2.33)	-0.15 (-0.79 to 0.48)	0.64
Confusion/bewilderment		0 to 20			
Control group	229		2.45 (2.04 to 2.86)		
Intervention group	231		2.11 (1.69 to 2.53)	-0.34 (-0.92 to 0.25)	0.26
Depression/dejection		0 to 32			
Control group	223		3.85 (3.20 to 4.51)		
Intervention group	229		3.26 (2.61 to 3.92)	-0.59 (-1.52 to 0.34)	0.21
Fatigue/inertia		0 to 20			
Control group	226		4.65 (4.08 to 5.22)		
Intervention group	234		4.14 (3.02 to 4.10)	-0.51 (-1.32 to 0.29)	0.21
Tension/anxiety		0 to 24			
Control group	226		3.82 (3.28 to 4.36)		
Intervention group	233		3.56 (3.02 to 4.10)	-0.26 (-1.02 to 0.50)	0.50
Vigour/activity		0 to 24			
Control group	218		10.28 (9.51 to 11.05)		
Intervention group	228		10.09 (9.31 to 10.86)	-0.20 (-1.29 to 0.89)	0.72
Total mood disturbance		0 to 124			
Control group	200		4.87 (2.29 to 7.45)		
Intervention group	210		4.19 (1.62 to 6.76)	-0.68 (-4.32 to 2.97)	0.72

Mean values of each subscale depends on the number of items related to the individual subscale which varies from 5 to 8, each item ranging from 0 to 4. Total mood disturbance is calculated by summing up the scores on the five negative symptom subscales and subtracting the score on the one positively scored subscale, vigour/activity. A higher score indicates a higher degree of symptoms/feelings within the related subscale.

Contributors

SHB, JK, JS and DGH contributed to conception and study design. SHB, DGH, JK and JS obtained the funding. SHB, JK, JS and DGH wrote the protocol. SHB and DGH were responsible for recruitment of patients. SHB collected and managed the data. PVL was the study statistician. SHB and PVL performed the statistical analysis. SHB, PVL, JK, JS and DGH contributed to the interpretation of data. SHB drafted the first version of the manuscript. SHB, JK, JS, PVL and DGH critically reviewed, revised, and supplemented the manuscript. All authors approved the final version. SHB is the guarantor.

Licence for publication

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted

work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The study was approved by the Danish Data Protection Agency. The Regional Committee on Biomedical Research Ethics evaluated the project and concluded that the intervention did not need an approval from the Danish National Committee on Biomedical Research Ethics according to Danish law (Project-ID: S-20082000-7).

Data

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing

No additional data available.

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Enhanced involvement of general practitioners in cancer rehabilitation: a randomised controlled trial.

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Abstract

Objective: To test the hypothesis that a multimodal intervention giving the general practitioner (GP) an enhanced role in cancer rehabilitation improves patients' health-related quality of life and psychological distress.

Design: Cluster randomised controlled trial. All general practices in Denmark were randomised to an intervention group or to a control group. Patients were subsequently allocated to intervention or control (usual procedures) based on the randomisation status of their GP.

Setting: All clinical departments at a public regional hospital treating cancer patients and all general practices in Denmark.

Participants: Adult patients treated for incident cancer at Vejle Hospital, Denmark, between 12 May 2008 and 28 February 2009. A total of 955 patients (486 to intervention, 469 to control group) registered with 323 general practices were included.

Intervention: The intervention included an interview about rehabilitation needs with a rehabilitation coordinator at the regional hospital, information from the hospital to the GP about individual needs for rehabilitation and an encouragement of the GP to contact the patient to offer his support with rehabilitation.

Main outcome measures: The primary outcome was health-related quality of life measured 6 months after inclusion using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Secondary outcomes included quality of life at 14 months and additional subscales of the EORTC QLQ-C30 at 6 and 14 months, and psychological distress at 14 months using the Profile of Mood States (POMS) scale.

Results: No effect of the intervention was observed on primary and/or secondary outcomes after 6 and 14 months.

Conclusion: A multimodal intervention aiming to give the GP an enhanced role in cancer patients' rehabilitation did not improve quality of life or psychological distress.

Trial registration: ClinicalTrials.gov, registration ID number NCT01021371.

Background

Addressing the unmet needs of individual rehabilitation of cancer patients is paramount (1-4). The underlying problems are often psychological or social and many persist after treatment or emerge late in the illness continuum (5-8). Rehabilitation is defined by WHO as "a process intended to enable people with disabilities to reach and maintain optimal physical, sensory, intellectual, psychological and/or social function" (9) which is the conceptual frame for this study. Hence, rehabilitation is a complex and long-lasting process, but evidence on how and when to identify the patients' needs, what initiatives to offer, and how to manage the efforts is sparse (2;10-13).

General practice is characterised by continuity with frequent encounters with each patient, covering wide-ranging issues (14). Hence, general practitioners (GPs) generally have profound knowledge about the patients' prior health status, mental vulnerability and social network. General practice may, therefore, be able to initiate the rehabilitation process and take on the task of coordinating or providing the rehabilitation services needed, but currently the role of GPs is not well-defined (15-23). Studies do, however, show that GPs are willing to undertake these tasks and that the patients wish that their GPs were more proactive in doing so (24-25).

The objective of this trial was to investigate the effect of a multimodal intervention giving the GP an enhanced role in improving patients' health-related quality of life and psychological distress following cancer. To validate our results we conducted subgroup analyses of the large and homogeneous group of breast cancer patients.

Material and methods

We conducted a cluster randomised, controlled trial where all general practices in Denmark were randomised to an intervention group or to a control group by means of the unique provider number of each practice. Patients were subsequently allocated according to the randomisation of their GP. Feasibility of the intervention and the study details have previously been published (26).

Participants

All adult patients (≥18 years) newly diagnosed with cancer and admitted to Vejle Hospital between 12 May 2008 and 28 February 2009 were assessed for eligibility. Patients were included if treated at Vejle Hospital for a cancer diagnosed within the last 3 months and if listed with a general practice. Patients with carcinoma in situ or non-melanoma skin cancers were not included (Figure 1).

Two rehabilitation coordinators, both nurses with oncological experience, assessed all patients for eligibility and managed the intervention. The patients were sampled across departments, type of cancer, stage, and potential rehabilitation needs by use of the electronic patient files (26).

Setting

The study was conducted at Vejle Hospital, a public general hospital in the region of Southern Denmark (1.2 million inhabitants) (27). Cancer patients were allocated from all of Denmark.

The Danish publicly funded healthcare system ensures free access to general practice which is responsible for primary care needs, and GPs function as gatekeepers to

the rest of the healthcare system. More than 98% of all Danish residents are registered with a general practice. On average each GP meets 9 incident cancer patients during one year (28).

GPs' opportunities to refer patients to relevant rehabilitation services vary between the different municipalities, just as the availability of private patient associations and other relief organisations. These conditions might influence the quality of the rehabilitation interventions offered.

The intervention

The intervention comprised a patient interview about rehabilitation needs performed by the rehabilitation coordinators, followed by information to the GP about the patient's individual rehabilitation needs and cancer patients' rehabilitation needs in general. The core of the information was that the GP was encouraged to contact the patient to facilitate a rehabilitation process (Figure 2).

The patient interviews were conducted according to an interview guide (29) and based on a checklist of general needs and problems among cancer patients (Figure 2). Interviews were most often conducted at the hospital, but in some cases by phone. During the interview, the concept of rehabilitation was explained and the individual needs for physical, psychological, sexual, social, work- and economy-related rehabilitation were identified. It was explained that physical, psychological, sexual, social, work-related and financial issues (1-4;30) might occur at any time and change during the disease trajectory (7-8). In order to address these problems, patients were advised to consult their GP during treatment and after discharge.

Following each interview, the patient's GP was informed about the patient's actual problems and needs for rehabilitation and encouraged to be proactive, i.e. the GP was encouraged to contact the patient personally to offer support and guidance in order to identify and address actual and future needs for rehabilitation. Subsequently, the GP received an e-mail summarising the information, supplemented by general information about cancer patients' needs and problems (Figure 3). The information was personally conveyed by phone, if possible, and always sent electronically along with the more general information. Patients and GPs in the control group received the usual care and were not contacted by the rehabilitation coordinators (26).

Outcomes and sampling of data

The primary outcome was health-related quality of life measured 6 months after inclusion using the Global Health Status of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (31;32). The secondary outcomes were psychological distress at 14 months assessed by the 6 scales of the Profile of Mood States (POMS) (33) (depression/dejection, anger/hostility, tension/anxiety, vigour/activity, fatigue/inertia and confusion/bewilderment), and the Global Health Status at 6 months and functional (physical, emotional, role, cognitive or social functioning) and symptom scales (fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea or financial difficulties) of the EORTC QLQ-C30 at 6 and 14 months.

Data were sampled in identical ways irrespective of allocation status by use of patient questionnaires administered to patients alive at 6 and 14 months after inclusion. Non-responders were sent one reminder after 3 weeks (26).

Sample size

The sample size was estimated based on the primary outcome measure. According to the EORTC Tables of Reference Values (34) for all cancer patients, all stages, the Global Health Status is normally distributed with a mean of 61.3 and an SD of 24.2. A change of at least 8 units was assumed to be clinically relevant (34;35).

If the lowest acceptable statistical power was 80%, then, based on the two-sample t-test with a type 1 error alpha=0.05, the sample size was calculated to be 144 patients per group. The study was subject to clustering because the unit of randomisation was at the level of the GP, whereas the primary outcome measure was at the level of the patient. A strong effect on outcome of the individual practice was expected, but no data supported estimation of cluster effect. To allow maximum clustering it was attempted to include patients to each group from a minimum of 144 practices.

Randomisation

Prior to study start, all 2181 general practices in Denmark were randomly allocated to the intervention or control group by the unique provider number of each practice using a computerised random-number generator in the statistical program Stata version 10.0 (StataCorp, College Station, TX, USA). Hence, randomisation was performed at practice level meaning that all GPs working under the same provider number were allocated to the same group. Consequently, spill-over effect between GPs and patients from the same practice was minimised.

Blinding

The study was not blinded. The list of randomisation was available to the RCs during assessment of patient eligibility. Allocation status was obvious during intervention.

Statistical analysis

Baseline patient characteristics were described using descriptive statistics in order to present the distribution of age, sex and cancer type. We conducted intention to treat analyses and numerical outcomes of the RCT were analysed using a multi-level linear model, accounting for possible cluster effects caused by the cluster randomisation. All secondary outcomes were adjusted for confounding effect of age and sex. Missing values were regarded as missing at random.

The statistical analyses were performed using Stata version 11.0 (StataCorp, College Station, TX, USA).

Development and piloting of questionnaires and intervention

Before designing the intervention we established a theoretical basis through review of papers, reports and textbooks about the problems faced by cancer patients and GPs with respect to individual rehabilitation and continuity across healthcare sectors (1-3;16-24;36).

The questionnaires and the procedures of identification, assessment and inclusion of patients were pilot tested prior to study start. The procedures have been described in detail (26).

Results

In total 955 patients fulfilled the criteria for inclusion and 486 patients were allocated to the intervention group and 469 to the control group (Figure 1). The patients were registered with 323 general practices. Patients were on average aged 63 years at baseline and 72% were female. The most frequent cancer localisations were breast (43%) and lung (15%). The intervention and control groups showed similar baseline characteristics (Table 1). For the primary outcome, Global Health Status at 6 months, we obtained data from 281 patients from 131 practices in the intervention group and 297 patients from 125 practices in the control group, in total 612 of 858 (71%) patients (95%-confidence interval for ICC 0.000 - 0.103) (Figure 1).

The intervention had no statistically significant impact on the primary or on the secondary outcomes (Tables 2 and 3). Adjustment for age and sex of the secondary outcomes showed results similar to the unadjusted analysis. Intention to treat analyses on all outcomes of the group of breast cancer patients showed no statistical differences between patients in the intervention and control group (mean difference in primary outcome of 1.77 (-3.2 to 6.8)). Per protocol analyses on all outcomes were used to analyse if the personal telephone contact to the GP was crucial. The patients receiving all elements of the intervention showed no statistically significant difference when compared to the control group (mean difference in primary outcome of -4.43 (-9.7 to 0.8)).

Discussion

Principal findings

This intervention including a hospital-based patient interview about rehabilitation, individual and general information to the GP and an encouragement to contact the patient and

facilitate a process of rehabilitation did not improve quality of life or relieve psychological distress of patients newly diagnosed with cancer.

Strengths and weaknesses of the study

The study included 955 patients and the pre-study power calculation and the precision of the statistical estimates indicate that the study could have detected relevant effects of the intervention. The confidence interval of the difference in global health status after 6 months ranged between -2.4 and 4.9 units. Clinically relevant differences have been suggested to correspond to at least 8 units (34;35).

An important question is whether any spill-over effects may have improved care for the patients in the control group, leading to an apparently smaller impact of the intervention. Information about the study and the concept of rehabilitation was given to the staff at the involved departments at Vejle Hospital during the inclusion period, but the intervention was managed by the two rehabilitation coordinators without influence on the care provided for the patients in the control group. The cluster randomisation was performed to ensure that GPs only cared for patients in either the intervention or the control group. GPs in the control group were not informed about the study and we have no reason to believe that information about the study was disseminated between GPs in the two groups.

Another question is whether we used the most relevant outcome measures. Process measures are often used to evaluate interventions. However, despite successful implementation of interventions, the impact on patients' wellbeing is often sparse. Hence, we deliberately chose patients' quality of life as the primary outcome. Further, the EORTC

QLQ-C30 and the POMS questionnaires are both well-validated instruments to evaluate change of quality of life in cancer patients and psychological distress in general (31-35).

The intervention was designed to support rehabilitation irrespective of the character of the problem, cancer type, age and sex. We included patients with various cancer types, different prognosis, health problems and needs of supportive care. The inhomogeneity of the study population might have diluted effects in groups of patients with specific problems or diagnoses. It cannot be ruled out that a similar intervention might have effect on subgroups of patients with specific cancers or special needs. However, no effect was observed when analysing the large and rather homogeneous group of breast cancer patients.

The intervention included a personal telephone contact to the patients' GP but some GPs were not reachable (26). A priori we assumed that this personal contact could be of major importance, but per protocol analysis showed no differences in outcomes for patients where the rehabilitation coordinators managed to reach the GP by phone.

Relations to other studies

To our knowledge, only three papers have specifically evaluated the impact of GP involvement in cancer rehabilitation in a randomised design (17;36-37). A shared care programme (n=250) conducted in Denmark in 2003 included transfer of knowledge from oncologists to GPs, improved communication between parties, and active patient involvement (17). This intervention had a positive impact on patient evaluation of cooperation between primary and secondary healthcare sectors, but not on quality of life. A Norwegian study from 2005 (n=91) evaluated the effect of an invitation to a 30-minute consultation with the patient's GP, aiming at creating a closer and more frequent contact

between patients and GPs (36). No increase in number of consultations or improvement of quality of life was observed. The latest study was conducted in Sweden in 2008 (n=481) and tested the effectiveness of individual support, group rehabilitation and a combination of the two compared to standard care (37). The individual support included individual psychological and nutritional support along with intensified primary health care, including extended information about the diagnosis, education in cancer care, and supervision of the patient's home care nurse and GP by a multi-professional oncology team. The Swedish study did not show an improvement either in quality of life or psychological well-being when compared to standard care. Further, a systematic review (38) including the three studies concluded that none of the interventions improved quality of life or patient wellbeing, but due to possible methodological problems further studies on the topic are needed.

Meaning

Interventions aiming to give the GP an enhanced role in cancer rehabilitation seem to have difficulties improving quality of life. Furthermore, a number of papers evaluating the effect of various other types of interventions aiming to improve quality of life of cancer patients (39-44) have demonstrated that this may be difficult in general. To better understand the intervention and the impact on GP and patient behaviour further studies will include evaluation of process measures like GP proactivity, patient participation in different rehabilitation activities, and GP and patient satisfaction.

Future studies should evaluate the importance of the organisation of cancer treatment and rehabilitation. Is an unclear organisation with many partners (hospital departments, GPs, municipalities and private organisations) an impediment to effective

rehabilitation? A well-organised system with defined roles and easy referral to various elements of rehabilitation (specialised physiotherapy, social counselling, psychological advice etc.) may be of importance for the effect of a GP intervention. To improve rehabilitation it may also be important to develop screening tools that support identification of patients with special needs. Initiatives supporting the GPs in undertaking a proactive role for patients with special needs should be considered. The effect of interventions should, however, be carefully evaluated in order to ensure efficient use of resources before implementation.

Figure 1. Study flow.

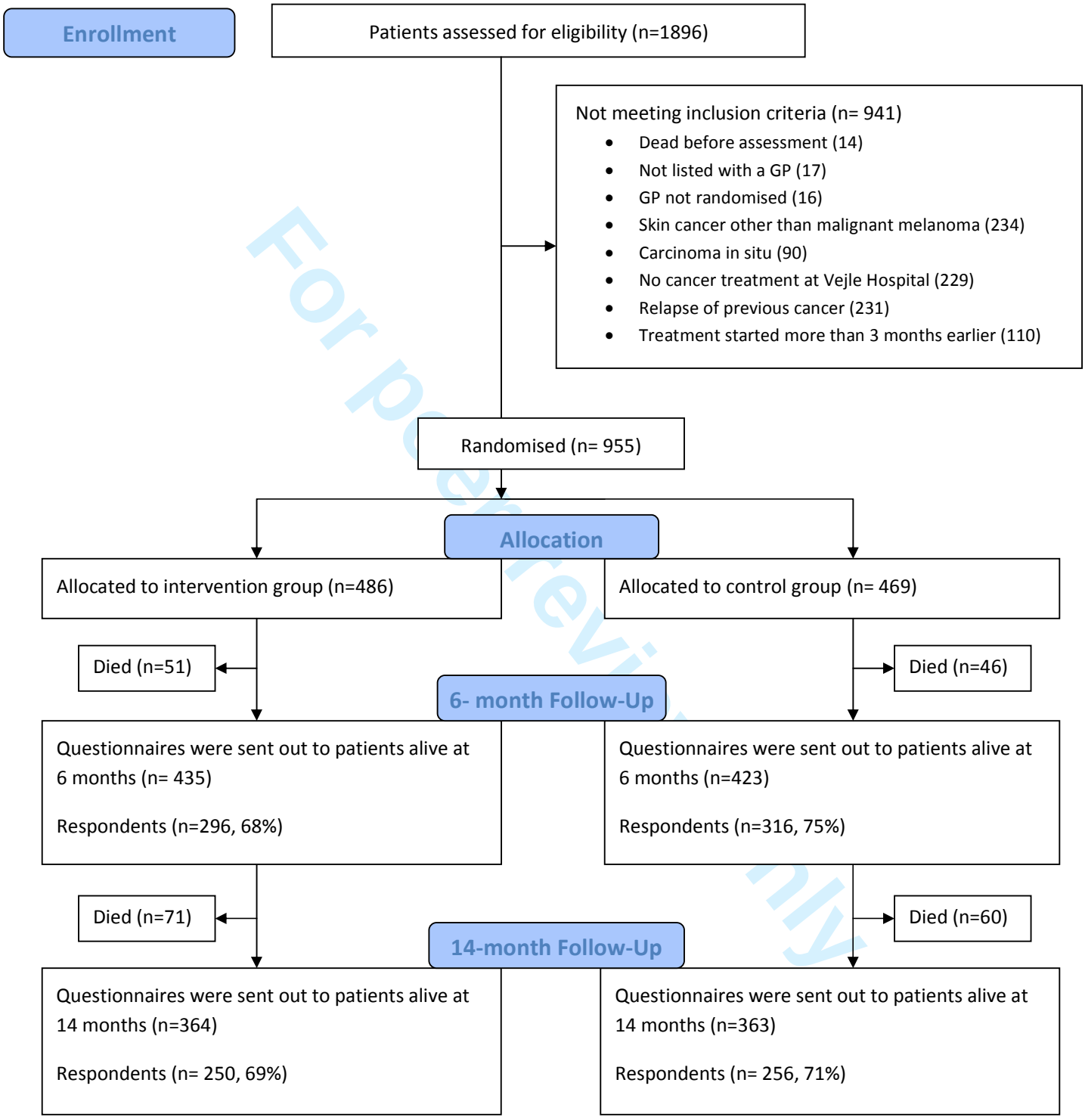

Figure 2. General needs and problems among cancer patients.

Psychological level	• Fear of death or recurrence • Guilt feelings about being sick • Anger at general practitioner or "system" for not having taken action soon enough • Troubles adjusting to new self-image • Sense of being left in limbo after discharge from the hospital • Risk of developing depression • Reconsiderations about priorities in life and how one wants to live life with or after a cancer disease • Sexual problems
Social level	• Concerns about the well-being of spouse, children and other relatives • Changed body image or sexuality • Changed position/status in marriage, in family, at work, etc. • Concerns about possible infertility caused by treatment • Information about patient associations and similar groups for patients and relatives
Physical level	• Physical capacity according to daily activities, need for special facilities, homecare, conversions of the home, etc. • Need for dietary advice, e.g. to prevent undue weight loss • Support in order to accept physical changes and late complications like tiredness, amputation, infertility, pain, etc.
Work-related level	• Concerns about losing one's job • Concerns about having to give up one's former responsibilities or change field of work due to reduced ability to work • Opportunities for financial support during sick-leave, flexible job, etc. • Support to keep in contact with workplace during sick-leave
Financial level	• Social rights like mileage allowances, reimbursement of assistive technology, etc. • Concerns about a decrease in income and consequences hereof in relation to housing, spouse, children, etc. • Conditions regarding pension or incapacity benefit

Table 1. Baseline demographic and medical characteristics for all included patients (n=955).

Demographic characteristics	Control group (n=469)	Intervention group (n=486)
Age, years		
Mean (CI)	63.6 (62.5 to 64.6)	63.2 (62.2 to 64.3)
Median	64	64
Range	21 to 98	28 to 92
Sex		
Male (%)	134 (28.6)	133 (27.4)
Female (%)	335 (71.4)	353 (72.6)
Cancer type	Numbers (%)	Numbers (%)
Cancer of breast	206 (43.9)	201 (41.4)
Cancer of lung	69 (14.7)	75 (15.4)
Malignant melanoma	44 (9.4)	35 (7.2)
Cancer of rectum/anus	33 (7.0)	45 (9.3)
Cancer of colon	29 (6.2)	39 (8.0)
Cancer of ovaries	12 (2.6)	9 (1.9)
Cancer of bilary system	7 (1.5)	8 (1.6)
Cancer of brain	6 (1.3)	8 (1.6)
Cancer of prostate	8 (1.7)	3 (0.6)
Cancer of corpus uteri	6 (1.3)	5 (1.0)
Myelomatosis	6 (1.3)	5 (1.0)
Lymphoma	3 (0.6)	4 (0.8)
Unspecified location	16 (3.4)	16 (3.3)
Other diagnoses	24 (5.1)	33 (6.8)

Table 2. Health-Related Quality of Life (EORTC QLQ-C30) outcome variables and mean differences at 6 and 14 months (95% confidence intervals).

	6 months				14 months			
Outcome variable	n	Mean (CI)	Mean difference (95% CI)	P	n	Mean (CI)	Mean difference (95% CI)	P
Global Health Status/qol								
Control group	297	68,0 (65.5 to 70.5)			246	72.8 (70.3 to 75.3)		
Intervention group	281	69,3 (66.7 to 71.9)	1.25 (-2.4 to 4.9)	0.50	240	72.1 (69.6 to 74.7)	-0.71 (-4.3 to 2.8)	0.69
Physical functioning								
Control group	294	79.0 (76.4 to 81.5)			240	81.9 (79.3 to 84-5)		
Intervention group	280	79.7(77.1 to 82.4)	0.77 (-2.9 to 4.4)	0.68	234	82.0 (79.4 to 84.6)	-0.08 (-3.6 to 3.8)	0.97
Role functioning								
Control group	291	71.3 (67.7 to 74.9)			239	78.0 (74.4 to 81.7)		
Intervention group	277	72.5 (68.8 to 76.1)	1.18 (-3.9 to 6.3)	0.65	235	78.8 (75.0 to 82.5)	0.70 (-4.5 to 5.9)	0.79
Emotional functioning								
Control group	293	80.5 (78.1 to 83.0)			240	80.7 (77.9 to 83.4)		
Intervention group	278	81.6 (79.1 to 84.1)	1.02 (-2.5 to 4.5)	0.57	238	80.8 (78.0 to 83.6)	0.12 (-3.8 to 4.1)	0.95
Cognitive functioning								
Control group	290	83.0 (80.5 to 85.5)			245	82.6 (79.7 to 85.5)		
Intervention group	278	83.9 (81.3 to 86.4)	0.88 (-2.7 to 4.5)	0.63	238	85.1 (82.1 to 88.2)	2.53 (-1.7 to 6.7)	0.24
Social functioning								
Control group	295	85.7 (83.0 to 88.4)			242	88.2 (85.4 to 91.0)		
Intervention group	280	86.0 (83.2 to 88.8)	0.28 (-3.6 to 4.2)	0.89	238	87.4 (84.6 to 90.3)	-0.77 (-4.8 to 3.2)	0.71
Fatigue								
Control group	292	37.4 (34.3 to 40.6)			244	32.1 (28.8 to 35.3)		
Intervention group	279	34.2 (30.9 to 37.4)	-3.27 (-7.8 to 1.3)	0.16	234	32.3 (28.9 to 35.6)	0.23 (-4.5 to 4.9)	0.92
Nausea and vomiting								
Control group	300	8.1 (6.1 to 10.0)			244	5.5 (3.9 to 7.2)		
Intervention group	284	8.0 (6.0 to 10.0)	-0.11 (-2.9 to 2.7)	0.94	236	5.6 (3.9 to 7.3)	0.05 (-2.3 to 2.4)	0.97
Pain								
Control group	283	23.0 (19.8 to 26.2)			241	21.9 (18.5 to 25.4)		
Intervention group	274	22.0 (18.8 to 25.3)	-0.95 (-5.5 to 3.6)	0.68	234	21.4 (17.8 to 24.9)	-0.56 (-5.5 to 4.4)	0.83
Dyspnoea								
Control group	297	17.0 (13.9 to 20.2)			245	13.2 (10.0 to 16.5)		
Intervention group	286	17.9 (14.7 to 21.2)	0.87 (-3.6 to 5.4)	0.71	233	15.4 (11.9 to 18.8)	2.11 (-2.6 to 6.8)	0.38
Insomnia								
Control group	302	27.5 (24.0 to 31.0)			248	29.6 (25.6 to 33.6)		
Intervention group	285	27.3 (23.6 to 30.9)	-0.23 (-5.3 to 4.8)	0.93	240	28.5 (24.4 to 32.6)	-1.08 (-6.8 to 4.6)	0.71
Appetite loss								
Control group	301	14.1 (11.0 to 17.2)			246	9.6 (7.1 to 12.2)		
Intervention group	288	15.9 (12.7 to 19.0)	1.79 (-2.7 to 6.2)	0.43	239	7.9 (5.4 to 10.5)	-1.67 (-5.3 to 2.0)	0.37
Constipation								
Control group	299	12.6 (9.7 to 15.5)			248	11.9 (9.0 to 14.9)		
Intervention group	284	11.3 (8.3 to 14.2)	-1.33 (-5.4 to 2.8)	0.53	236	8.9 (5.9 to 11.9)	-3.03 (-7.4 to 1.1)	0.16
Diarrhoea								
Control group	299	11.3 (8.8 to 13.9)			250	11.4 (8.5 to 14.2)		
Intervention group	284	11.4 (8.8 to 14.1)	0.08 (-3.6 to 3.8)	0.97	238	10.0 (7.0 to 13.0)	-1.38 (-5.5 to 2.8)	0.51
Financial difficulties								
Control group	297	7.6 (5.4 to 9.8)			242	6.5 (3.9 to 9.0)		
Intervention group	284	8.0 (5.7 to 10.2)	0.34 (-2.8 to 3.5)	0.83	236	6.7 (4.1 to 9.4)	0.27 (-3.4 to 4.0)	0.89
Mean values from 0 to 100. A score of 100 indicates optimal function or maximum symptom intensity (i.e. for functional measures, an increase indicates improvement, while for symptoms, an increase indicates worsening)								

Table 3. Psychological distress (POMS) at 14 months and mean differences between groups (95 confidence intervals).

Outcome variable	n	Mean range	Mean (95% CI)	Mean difference (95% CI)	P
Anger/hostility		0 to 28			
Control group	223		2.03 (1.59 to 2.48)		
Intervention group	230		1.88 (1.43 to 2.33)	-0.15 (-0.79 to 0.48)	0.64
Confusion/bewilderment		0 to 20			
Control group	229		2.45 (2.04 to 2.86)		
Intervention group	231		2.11 (1.69 to 2.53)	-0.34 (-0.92 to 0.25)	0.26
Depression/dejection		0 to 32			
Control group	223		3.85 (3.20 to 4.51)		
Intervention group	229		3.26 (2.61 to 3.92)	-0.59 (-1.52 to 0.34)	0.21
Fatigue/inertia		0 to 20			
Control group	226		4.65 (4.08 to 5.22)		
Intervention group	234		4.14 (3.02 to 4.10)	-0.51 (-1.32 to 0.29)	0.21
Tension/anxiety		0 to 24			
Control group	226		3.82 (3.28 to 4.36)		
Intervention group	233		3.56 (3.02 to 4.10)	-0.26 (-1.02 to 0.50)	0.50
Vigour/activity		0 to 24			
Control group	218		10.28 (9.51 to 11.05)		
Intervention group	228		10.09 (9.31 to 10.86)	-0.20 (-1.29 to 0.89)	0.72
Total mood disturbance		0 to 124			
Control group	200		4.87 (2.29 to 7.45)		
Intervention group	210		4.19 (1.62 to 6.76)	-0.68 (-4.32 to 2.97)	0.72

Mean values of each subscale depends on the number of items related to the individual subscale which varies from 5 to 8, each item ranging from 0 to 4. Total mood disturbance is calculated by summing up the scores on the five negative symptom subscales and subtracting the score on the one positively scored subscale, vigour/activity. A higher score indicates a higher degree of symptoms/feelings within the related subscale.

Contributors

SHB, JK, JS and DGH contributed to conception and study design. SHB, DGH, JK and JS obtained the funding. SHB, JK, JS and DGH wrote the protocol. SHB and DGH were responsible for recruitment of patients. SHB collected and managed the data. PVL was the study statistician. SHB and PVL performed the statistical analysis. SHB, PVL, JK, JS and DGH contributed to the interpretation of data. SHB drafted the first version of the manuscript. SHB, JK, JS, PVL and DGH critically reviewed, revised, and supplemented the manuscript. All authors approved the final version. SHB is the guarantor.

Licence for publication

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted

work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The study was approved by the Danish Data Protection Agency. The Regional Committee on Biomedical Research Ethics evaluated the project and concluded that the intervention did not need an approval from the Danish National Committee on Biomedical Research Ethics according to Danish law (Project-ID: S-20082000-7).

Data

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing

No additional data available.

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Checklist of items to include when reporting a cluster randomised trial

* = addition to CONSORT *Modifications to checklist in italics*			
PAPER SECTION and topic	Item	Descriptor	Reported on Page No.
TITLE & ABSTRACT	1*	How participants were allocated to interventions (e.g., "random allocation", "randomised", or "randomly assigned"), *specifying that allocation was based on clusters*	2
INTRODUCTION Background	2*	Scientific background and explanation of rationale, *including the rationale for using a cluster design.*	4+8
METHODS Participants	3*	Eligibility criteria for participants *and clusters* and the settings and locations where the data were collected.	5
Interventions	4*	Precise details of the interventions intended for each group, *whether they pertain to the individual level, the cluster level or both,* and how and when they were actually administered.	6-7
Objectives	5*	Specific objectives and hypotheses, *and whether they pertain to the individual level, the cluster level or both*.	4
Outcomes	6*	Report clearly defined primary and secondary outcome measures, *whether they pertain to the individual level, the cluster level or both*, and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	7
Sample size	7*	How *total* sample size was determined *(including method of calculation, number of clusters, cluster size, a coefficient of intracluster correlation (ICC or k), and an indication of its uncertainty*) and, when applicable, explanation of any interim analyses and stopping rules.	8
Randomisation.			5+8
Sequence generation	8*	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification, *matching*).	
Allocation concealment	9*	Method used to implement the random allocation sequence, *specifying that allocation was based on clusters rather than individuals and* clarifying whether the sequence was concealed until interventions were assigned.	
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (Masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	8-9
Statistical methods	12*	Statistical methods used to compare groups for primary outcome(s) *indicating how clustering was taken into account*; methods for additional analyses, such as subgroup analyses and adjusted analyses.	9
RESULTS Participant flow	13*	Flow of *clusters and* individual participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of *clusters and* participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	10+15 (Figure 1)
Recruitment	14	Dates defining the periods of recruitment and follow-up.	5+15 (Figure 1)
Baseline data	15*	Baseline information for each group *for the individual and cluster levels as applicable*	17 (Table 1)
Numbers analyzed	16*	Number of *clusters and* participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	10
Outcomes and Estimation	17*	For each primary and secondary outcome, a summary of results for each group measures *for the individual or cluster level as applicable*, and the estimated effect size and its precision (e.g., 95% confidence interval) *and a coefficient of intracluster correlation (ICC or k) for each primary outcome.*	10+18-19 (Table 2+3)
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed,	10

		including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	None
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	10-12
Generalisability	21*	Generalisability (external validity) *to individuals and/or clusters (as relevant)* of the trial findings.	12-13
Overall evidence	22	General interpretation of the results in the context of current evidence.	13-14

Figure 1

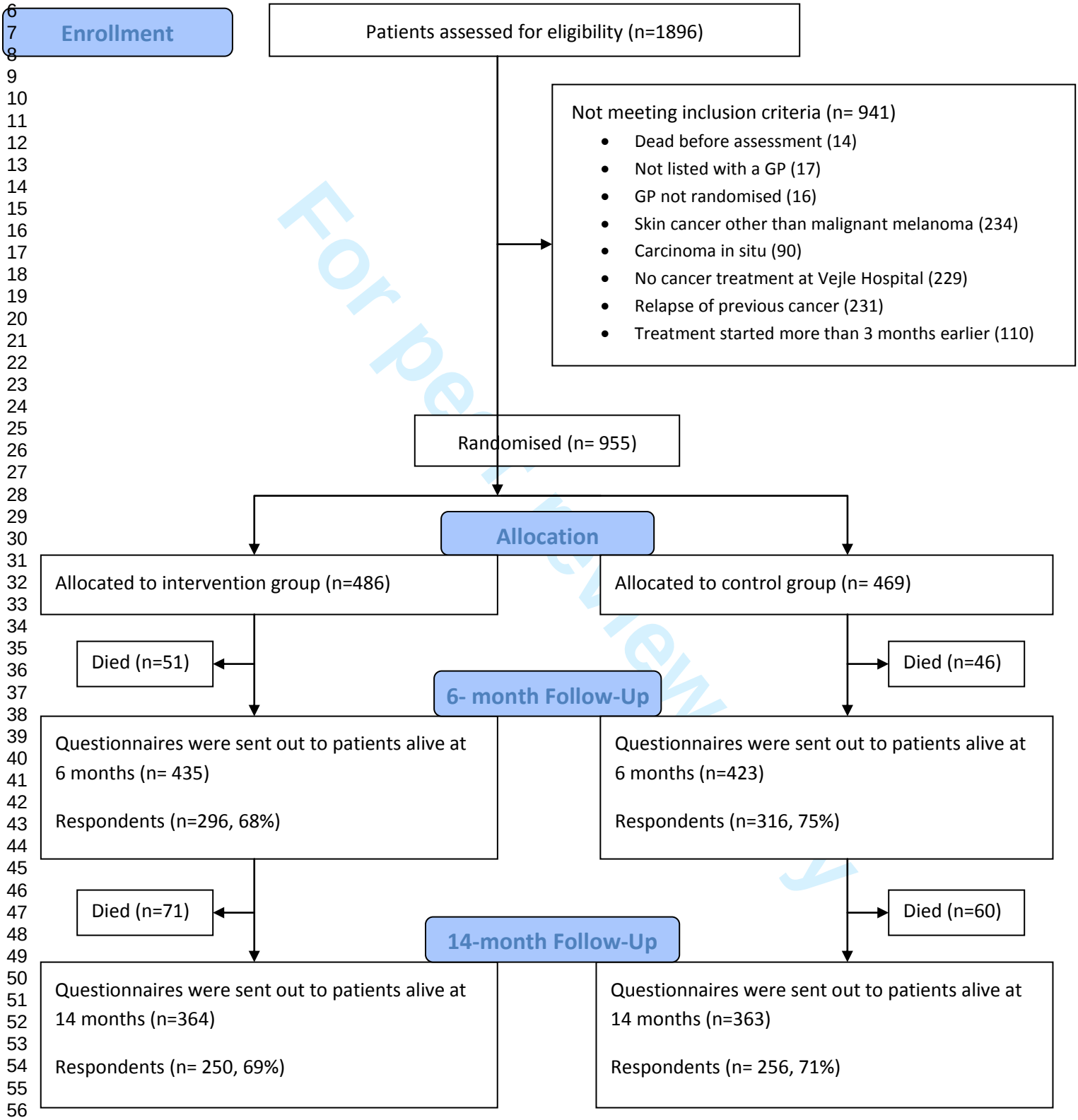

Figure 2. General needs and problems among cancer patients.

Psychological level	• Fear of death or recurrence • Guilt feelings about being sick • Anger at general practitioner or "system" for not having taken action soon enough • Troubles adjusting to new self-image • Sense of being left in limbo after discharge from the hospital • Risk of developing depression • Reconsiderations about priorities in life and how one wants to live life with or after a cancer disease • Sexual problems
Social level	• Concerns about the well-being of spouse, children and other relatives • Changed body image or sexuality • Changed position/status in marriage, in family, at work, etc. • Concerns about possible infertility caused by treatment • Information about patient associations and similar groups for patients and relatives
Physical level	• Physical capacity according to daily activities, need for special facilities, homecare, conversions of the home, etc. • Need for dietary advice, e.g. to prevent undue weight loss • Support in order to accept physical changes and late complications like tiredness, amputation, infertility, pain, etc.
Work-related level	• Concerns about losing one's job • Concerns about having to give up one's former responsibilities or change field of work due to reduced ability to work • Opportunities for financial support during sick-leave, flexible job, etc. • Support to keep in contact with workplace during sick-leave
Financial level	• Social rights like mileage allowances, reimbursement of assistive technology, etc. • Concerns about a decrease in income and consequences hereof in relation to housing, spouse, children, etc. • Conditions regarding pension or incapacity benefit