A multidimensional cancer rehabilitation program for cancer survivors

Effectiveness on health-related quality of life

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Abstract

Objective: A multidimensional rehabilitation program for cancer survivors was developed to overcome cancer-related problems and to improve quality of life. The two purposes of the study were to describe the effectiveness of the program and to obtain information about patient preferences for multi or mono dimensional rehabilitation programs.

Methods: Subjects: cancer survivors with different diagnoses, and cancer-related physical and psychosocial problems. Intervention: a 15-week rehabilitation program including individual exercise, sports, psycho-education, and information. Group-wise randomization was implemented by assigning one half of the patients to the complete program while the other half were allowed to choose which program components they considered relevant. Measures: Health-Related Quality of Life [RAND-36 and Rotterdam Symptom Check List (RSCL)], exercise capacity (symptom limited bicycle ergometry), muscle force (hand-held dynamometry), and patient preferences. Measurements were performed before (T0) and after the rehabilitation program (T1), and at a 3-month follow-up (T2).

Results: After the rehabilitation program, cancer survivors (n=63) displayed statistically significant improvements on health-related quality of life with effect sizes (ES) varying from 0.38 to 0.99 (RAND-36) and from −0.34 to −0.57 (RSCL), most persistent at 3-month follow-up. Furthermore, statistically significant improvements in exercise capacity and muscle force of upper and lower extremities were displayed after rehabilitation. If offered a choice, 80% of the patients prior to start and 58% of the patients after completion of the program indicated that they preferred the entire multidimensional program.

Conclusion: A multidimensional rehabilitation program has statistically and clinically relevant beneficial effects on health-related quality of life, exercise capacity, and muscle force in cancer patients with different diagnoses. Furthermore, if offered the choice, the majority of cancer survivors seem to prefer multidimensional programs to programs with only one component.
Introduction

Cancer patients can suffer from serious physical and psychosocial side effects due to cancer and cancer treatment [1–5]. Both physical and psychosocial side effects can occur in the short term but have also been described as persisting over the years after completion of treatment [6] and have the potential to diminish quality of life in cancer survivors.

Physical side effects like fatigue, reduced muscle strength, and impaired physical capacity [7] can be explained by cancer-related, such as tumor activity and anemia, and treatment-related factors. The treatment of cancer, including surgery, chemotherapy, and radiation, may induce initial cardio-respiratory and muscular skeletal deconditioning. After these initial physical impairments, a vicious cycle of fatigue, reduced activity, and an even further impaired physical capacity may appear and contribute to the persistence of physical problems, even years after the completion of cancer treatment.

A major psychological side effect is the elevated level of depressive feelings reported by patients during the first months after diagnosis. Approximately one quarter of cancer patients report depressive symptoms during the initial period after diagnosis. A significant percentage of cancer patients, ranging from 15% to 30%, seem to continue to experience depressive symptoms 1 year after diagnosis [8,9]. Moreover, cancer patients report other psychosocial problems such as anxiety, mood disturbances, stress, insecurity, grief, low self-esteem, social isolation, and problems with job reintegration [1,2,10–16].

Several mono- or multidimensional rehabilitation programs have been developed to overcome cancer-related physical and psychosocial side effects and to improve the quality of life of cancer survivors. Monodimensional rehabilitation programs consist of either psychosocial or physical interventions. The focus of psychosocial interventions [17–19] is primarily on improving psychological functioning. They are therefore described as less likely to address the physical and functional problems that survivors may encounter [20]. Nevertheless, several different psychosocial interventions have been described to facilitate coping with the disease and to improve quality of life [21,22].

The effectiveness of physical training, i.e., exercise training, has recently been described in several publications [23–27]. Exercise training is reported to be beneficial for cancer patients because it is aimed at improving functional capacity, muscle strength, and cancer-related fatigue which may, in turn, contribute to a better overall quality of life [7,16,27–35].

A multidimensional approach including both physical and psychological interventions is recognized as an effective intervention for patients with heart or lung disease to improve quality of life. There are indications that a multidimensional rehabilitation program is also beneficial to breast cancer patients [36,37]. However, it is, as yet, unclear whether multidimensional rehabilitation programs are feasible and effective for cancer survivors irrespective of their diagnosis type.

Rehabilitation participants appear to have more physical and psychological problems at entry than do patients who chose not to participate in a rehabilitation program [38]. Furthermore, it has been demonstrated that 26% of cancer survivors expressed a need for rehabilitation [39]. These survivors showed a significantly lower quality of life when compared with those expressing no need for professional help. Because healthcare providers now recognize patients as experts with unique knowledge of their own health and treatment preferences, health states, and outcomes, it might be of considerable interest to obtain information about cancer patients’ preferences for mono or multidimensional rehabilitation programs.
For the present, we developed a multidimensional rehabilitation program based on Engel’s bio-psychosocial model [40]. This model acknowledges that physical problems may induce psychological and social problems and vice versa. Furthermore, the model implies that physical interventions might influence physical problems as well as psychological and social problems, and that psychosocial interventions have the potential to influence physical problems. A further implication of the model may be that well-matched interventions may enhance the effects of the entire intervention program. Therefore, we developed a multidimensional rehabilitation program including four types of interventions to reduce a wide range of problems in cancer survivors.

The purpose of this study was twofold. First, we were interested in the effects of the multidimensional rehabilitation program for cancer survivors with different types of cancer on (1) health-related quality of life including physical, psychological, and social functioning, (2) exercise capacity, and (3) patient appreciation. We hypothesized that the multidimensional program would result in immediate beneficial and clinically relevant effects on health-related quality of life that would be sustained at a 3-month follow-up. Second, we were interested in obtaining information about patient preferences for mono- or multidimensional rehabilitation programs by offering half of the patients the entire multidimensional rehabilitation program and the other half of the patients a choice. We expected the majority of cancer patients to choose a multidimensional rehabilitation program due to the wide range of problems that they might experience.

Methods

Patients
Patients were eligible for the study if they met the following criteria: age ≥18 years; referred by hospital specialists or general practitioners; last cancer-related treatment >3 months ago; estimated life expectancy ≥1 year; and an indication for rehabilitation. The latter meant a minimum of three positive findings on the following questions, as judged by a physician:
1. Physical complaints like aching muscles, problems with coordination, headache, nausea, heart palpitations, shortness of breath
2. Reduced physical capacity compared with before the illness, e.g., less able to walk or cycle
3. Psychological problems like increased anxiety level, depression, uncertainty, lack of energy or nervousness
4. Increased levels of fatigue
5. Sleep disturbances
6. Problems in coping with reduced physical and psychosocial functioning due to cancer

Patients were not included if they met one of the following criteria:
- A very low level of activity, e.g., less than 50% of their daytime ambulant, rapid fatigue appearance on performance of low physical activity, and activity of daily living (ADL) dependency
- Inability to travel independently to the rehabilitation centre
- Cognitive disturbances that may interfere with participation in the rehabilitation program (e.g., participants who are unable to be instructed, to think three-dimensionally, to complete questionnaires)
- Serious psychopathology and emotional instability that may impede participation in the rehabilitation program (e.g., being in the process of a divorce or the death of a loved one).

**Procedures**

After being referred to the study, patients were consecutively enrolled in groups of 8-12 patients. Then, an information session including a video session was organized to inform patients about the content of the four components (individual exercise, sports, information, and psycho-education) of the multidimensional rehabilitation program. During the information session, patients were informed about the group-wise randomization. Groups were randomly assigned the entire rehabilitation program condition or the choice-rehabilitation program condition. The entire rehabilitation program condition implied that patients would receive all four components, and the choice condition meant that patients could compose their own program from the four components, as judged beneficial to them. Randomization took place subsequent to patient intake by a physician and cancer nurse. If randomized into the choice condition, patients had 1 week to compose their own program. During the period of the study (1999–2001), 81 patients were referred to and appeared eligible for the program. The randomization procedure resulted in the provision of the entire rehabilitation program to 41 patients, while 40 patients were offered the choice to compose a program of the components they considered relevant.

All patients gave informed written consent to participating in the study and for the acquisition of medical information from their hospital charts. Medical data were verified by record linkage with the population-based cancer registry of the Comprehensive Cancer Centre North-Netherlands (cccN). The Medical Ethics Committee of University Hospital Groningen approved the study. Measurements were performed before (T0) and after the rehabilitation program (T1) and at a 3-month follow-up (T2).

**Rehabilitation program**

The 15-week program consisted of four components and took place in a rehabilitation centre in groups of 8-12 cancer patients. The choice of a group-oriented program was based on studies that showed that peer contact may facilitate processes of social support, social comparison, and modeling in the participants of rehabilitation programs [41]. The entire rehabilitation program consisted of the following components: (a) individual exercise, (b) sports, (c) psycho-education, and (d) information (Fig. 1).

**Figure 1**

The content and frequency of the program components

<table>
<thead>
<tr>
<th>Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>11</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>I.E. (1.5 hours)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sp (1 hour)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PE (2 hours)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Inf (1 hour)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Abbreviation: I.E, Individual Exercise; Sp, Sports; PE, Psycho-education; Inf, Information.
Individual exercise
The exercise program consisted of 15 sessions of 1.5 h each and was supervised by a physical therapist. It was aimed at improving exercise capacity and muscle force. Accordingly, the exercise program was divided into a bicycle training and a muscle force training program.

Bicycle training program. Prior to the start of the exercise training, a symptom limited bicycle ergometry test was performed. This test was used as the basis for the development of an individual exercise training schedule. This training schedule was based on the training heart rate (THR), computed by using the Karvonen formulae [42,43]. The exercise training was performed at a THR of HRrest+50 to 60% (HRmax–HRrest) during Weeks 1-3 and at a THR of HRrest+70 to 80% (HRmax–HRrest) during Weeks 4-9. This aerobic exercise training was performed over 15–20 min, with a warm-up before and a cooling down after the training.

Muscle force training. General muscle force training of trunk and lower and upper extremities was performed and based on the individual 1-Repetiton Maximum (1-RM), which was defined before the training. Individual intensity of muscle force training started at 50% of the 1-RM during the first week and was increased by 5-10% during the following weeks, with a frequency of 12 repetitions over three series.

In the individual exercise program, patients were also advised to perform walking exercise at home, lasting 10-20 min once a week.

Sports
The sports program consisted of 17 sessions of 1 h each. The sessions were supervised by a physical therapist and were directed towards “enjoying sports”, “self-confidence”, and “body knowledge”. To increase the chance that patients would continue sport activities in their leisure time after the end of the rehabilitation program, patients were provided with and encouraged to perform a variety of sports and games activities such as badminton, soccer, mini-golf, swimming, curling, and balancing games. During the performance of certain sport activities, the patients were instructed to become aware of physical sensations or limitations, so that they would recognize and respect limitations when performing sports or recreational activities at home.

Psycho-education
The psycho-educational program consisted of nine sessions of 2 h each. The aims of the psycho-educational program were to reduce negative emotions and to improve coping with the disease. A psychosocial specialist with several years of experience in conducting group sessions with cancer survivors led the psycho-educational program. This course leader discussed the following psychologically oriented topics with respect to cancer: “confrontation with cancer”, “anxiety”, “stress”, “depression”, “asking professional help”, and social support”. Over several sessions, expressive-supportive techniques were used to explore negative emotions and to provide the opportunity to receive support from other cancer survivors. In addition, breathing exercises, relaxation exercises, and exercises from the Rational-Emotive Therapy were used to provide patients with stress-management techniques. Patients were instructed to practice the exercises and to prepare every session at home. All sessions were described in a course book that was used by the course leader and participants.
Information
The information program consisted of 10 sessions of 1 h each. The aim of this program was to reduce uncertainty due to lack of knowledge of the disease by providing information with respect to cancer-related subjects. The information sessions were conducted in group sessions by several professional healthcare providers who had specific knowledge of the following cancer-related subjects: “medical aspects of cancer”, “cancer-related fatigue”, “food”, “sexuality”, “sport”, “body image”, “work and insurance”, “complementary medicine”, “pain” and “daily activities”. During the sessions, patients were provided with information but also had the opportunity to raise questions and to share experiences with other cancer survivors.

Outcome measures
Quality of life
General health-related quality of life was measured using the RAND-36, a multidimensional self-report questionnaire assessing the following nine domains of global health-related quality of life: physical functioning (10 items), social functioning (2 items), role impairment due to physical problems (4 items), role impairment due to emotional problems (3 items), mental health (5 items), vitality (4 items), pain (2 items), general health appraisal (5 items), and overall quality of life (1 item). After recoding and transformation, scores range from 0 to 100, and a higher score represents better health. The psychometric characteristics of the instrument are described as follows: internal consistency ranges from $\alpha=.71$ to .92; test–retest is sufficient; the instrument has high convergent validity and low divergent validity [44]. The RAND-36 manual provides the scores of a normative group of the Dutch population, which was a randomly selected community group of a midsize town in the north of the Netherlands. The mean age of this population was 44.1 years, with range 18-89, and 65% were women. Furthermore, the rehabilitation program participants’ RAND-36 scores were compared with a reference group of cancer patients not referred to a rehabilitation program. The reference group consisted of a sample of 2783 cancer patients entered into the registry of the CCCN during the same period as the rehabilitation program took place. Three references were matched based on gender, age, diagnosis, and time since diagnosis for every patient in the rehabilitation group (n=81). This match was successful for 73 patients, and for the remaining eight patients, we found seven matches, resulting in a total of 226 reference patients.

Disease specific health-related quality of life was measured with the Rotterdam Symptom Check List (RSCl). This self-report measure contains 39 items that differentiate between disease and treatment states, and treatment processes. It consists of the following domains: physical symptom distress (23 items), psychological distress (7 items), activity level (8 items), and overall valuation of quality of life (1 item). Responses are presented on four-point Likert-type scale for most items. A higher score reflects a greater level of burden of impairment. Norm scores for the general population are available in the manual. The psychometric characteristics of the instrument are described as follows: internal consistency is good; construct validity and clinical validity are sufficient [45]. A cut-off score of 15 for the psychological distress scale can be used to indicate the presence of “disease” [45,46].

Physical variables
Exercise capacity
A symptom-limited bicycle ergometry test was performed using a ramp 10, 15, or 20 protocol, depending on the patient’s fitness. This implied that the load was increased every minute by
10, 15, or 20 W, respectively, in such a way that patients could reach their maximal workload within 10 min. The test was terminated on the basis of patient’s symptoms or at the physician’s discretion [47]. Maximal workload in Watts at maximal performance was taken for analysis.

Muscle force
The maximal voluntary isometric muscle force of the right and left extremities of the following muscle groups was measured: extension of the knee, flexion of the elbow, and extension of the elbow using a hand-held dynamometer [Force Evaluating & Testing (microFET), Hoggan Health Industries, USA]. The “break method” was used for all measurements. To employ this technique, the examiner gradually overcomes the force produced by the patient until the extremity gives way [48]. All measurements were performed at least three times, with recovery intervals of at least 10 s. Peak forces (in Newtons) were recorded, and the mean values of three technically correct measurements were taken for analysis and expressed as percentages of predicted normal muscle strength accounting for age and gender.

Patient appreciation
A program evaluation form was used to obtain information about patient satisfaction with the various components of the program and the program as a whole. Patients were asked to express their satisfaction with each component and the entire program on a scale from 0 (no satisfaction) to 10 (high satisfaction) immediately after the completion of the program. They were also asked if they would recommend the program to others (yes or no).

Patient preferences
Before the rehabilitation program, patients randomized into the choice condition were asked to indicate which components of the program they wished to participate in. Furthermore, after completing the rehabilitation program, all patients were asked to indicate the components considered relevant to themselves and those that would be chosen if the choice were offered.

Statistical analyses
Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 11.0). Confidence interval analyses (CIA) were performed for comparison of the reference group and patients at T0. Chi-square tests, Mann–Whitney tests, and independent t tests were used to compare participants who completed the program (stay-ins) with those who did not (dropouts). Repeated measures ANOVA performed for time were used to assess change over time. Nonparametric Wilcoxon tests were used to examine differences before and after the program and at 3-month follow-up. Mann–Whitney tests were used to examine differences in outcome between those who participated in all four components of the program and those who followed the program of fewer components. Effect sizes (ES) and thresholds at the 5% level were calculated according to Cohen [49] as indices measuring the magnitude of a treatment effect. Middel et al. [50] showed that ES also reflects clinical relevance. An ES <0.20 indicates “no change”, ES ≥0.20, <0.50 as “a small change”, ES ≥0.50, <0.80 as “a moderate change”, and ES ≥0.80 as “a considerable change”. Frequencies and mean scores were used to examine patient preferences and their subjective evaluation of the program.
Results

Patient characteristics
Sixteen percent of the 81 participants were male. The mean (sd) age of the participants was 51.6 (9.3) years.

Table 1
Patient characteristics at time of inclusion (T0), n=81

<table>
<thead>
<tr>
<th>Mean age (SD), years</th>
<th>51.6 (9.3)</th>
</tr>
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<tbody>
<tr>
<td>Gender, male : female (n (%))</td>
<td>13 (16): 68 (84)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physician reported indication criteria for rehabilitation (yes)</th>
<th>n</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Physical complaints</td>
<td>53</td>
<td>65.4</td>
</tr>
<tr>
<td>Reduced physical capacity</td>
<td>64</td>
<td>79.0</td>
</tr>
<tr>
<td>Psychological problems</td>
<td>56</td>
<td>69.1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>68</td>
<td>84.0</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>49</td>
<td>60.5</td>
</tr>
<tr>
<td>Coping/acceptance problems</td>
<td>36</td>
<td>44.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>48</td>
<td>59.3</td>
</tr>
<tr>
<td>Non Hodgkin Lymphoma /M.Hodgkin</td>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>Gynaecological cancer</td>
<td>6</td>
<td>7.3</td>
</tr>
<tr>
<td>Head and neck cancer</td>
<td>5</td>
<td>6.2</td>
</tr>
<tr>
<td>Rest category &lt; 5%</td>
<td>15</td>
<td>18.6</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Stage of disease</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Stage I</td>
<td>14</td>
<td>17.3</td>
</tr>
<tr>
<td>Stage II</td>
<td>40</td>
<td>49.9</td>
</tr>
<tr>
<td>Stage III</td>
<td>16</td>
<td>19.8</td>
</tr>
<tr>
<td>Stage IV</td>
<td>4</td>
<td>4.9</td>
</tr>
<tr>
<td>Not applicable</td>
<td>5</td>
<td>6.2</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>1.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer treatment before rehabilitation</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical treatment</td>
<td>62</td>
<td>76.5</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>51</td>
<td>63.3</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>54</td>
<td>68.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time between treatment and rehabilitation program</th>
<th>n</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>≤ 6 months</td>
<td>31</td>
<td>38.3</td>
</tr>
<tr>
<td>&gt;6-12 months</td>
<td>22</td>
<td>27.2</td>
</tr>
<tr>
<td>&gt;12-18 months</td>
<td>14</td>
<td>17.3</td>
</tr>
<tr>
<td>&gt;18 months</td>
<td>12</td>
<td>14.8</td>
</tr>
<tr>
<td>Missing</td>
<td>2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Mean (SD) in months: 11.3 (13.2)
Fifty-nine percent of the patients were women with breast cancer and 41% had other cancer diagnoses. Two-thirds of the patients had Stage I or II disease. Two-thirds of the participants had completed treatment during the preceding year (Table 1). The most frequently-reported indication for rehabilitation was fatigue, followed by reduced physical capacity and psychological problems (Table 1).

**Preliminary analyses**

**Dropouts versus stay-ins**

Eighteen patients did not complete the program: 12 patients developed a cancer recurrence and dropped out of the program of their own volition. A further six patients left the program for personal reasons (two), because of claustrophobia (one), severe nausea (one), and for unknown reasons (one). The remaining 63 patients completed the rehabilitation program and the questionnaires at To, T1, and T2. Dropout was therefore 22.2%.

The $\chi^2$ and $t$ tests revealed no significant differences between dropouts and stay-ins with respect to gender, age, cancer diagnosis, time since completion of treatment, and time since diagnosis. $\chi^2$ tests revealed significantly more cancer recurrences in the dropout than in the stay-in group ($p<.001$).

At baseline, no significant differences were found between dropouts and stay-ins with respect to the RAND-36 domains, except for the general health appraisal domain. The dropout group (mean=43.3, SD=12.2) appraised their health lower than did the stay-ins (mean=55.4, SD=15.1; $p=.002$). Furthermore, with respect to the RSCL, dropouts (mean=44.7, SD=12.2) displayed statistically significant greater psychological distress than did the stay-ins (mean=32.7, SD=21.2; $p=.025$). Dropouts (mean=51.0, SD=19.7) had a lower overall valuation of quality of life (RSCL) when compared with the stay-ins (mean=35.5, SD=15.5; $p<.001$).

Fisher’s Exact Test showed that the percentage of those who dropped out of the study was similar in the entire program condition (7/41=17.1%) and in the choice condition (11/40=27.5%; $p=.30$).

**Participants versus reference groups**

Baseline scores on the questionnaires of the referred patients were compared with the normative Dutch population group [44] and to the matched sample of cancer patients from the CCCN (Table 2). At time of inclusion (To), the referred group of patients had lower mean scores on every RAND-36 domain compared with the general population. The referred patients also showed significantly lower scores on all RAND-36 domains than did the matched sample of cancer patients. A striking result was the extremely low score of the referred patients on the role limitations due to physical problems domain. Furthermore, at baseline, the referred patients reported higher mean scores on the RSCL domains of physical symptom distress, psychological distress, and overall valuation of quality of life compared with the general population (Table 3).
### Table 2
RAND-36 scores for a Dutch normative population [44], a reference group of cancer patients, and patients at T0, T1 and T2

<table>
<thead>
<tr>
<th></th>
<th>General population n=1063</th>
<th>Reference group of cancer patients n=226</th>
<th>Patients at T0 n=81</th>
<th>Patients at T1 n=63</th>
<th>Effect sizes T0-T1</th>
<th>95% Confidence Interval (ES)</th>
<th>Patients at T2 n=63</th>
<th>Repeated measures analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>81.9 (23.9)</td>
<td>74.3 (22.2)</td>
<td>62.4 (20.3) †††</td>
<td>70.3 (21.1) ***</td>
<td>.38</td>
<td>.05 to .71</td>
<td>73.2 (18.8) †††</td>
<td>15.1 ***</td>
</tr>
<tr>
<td>Social functioning</td>
<td>86.9 (20.5)</td>
<td>79.0 (24.4)</td>
<td>59.0 (33.3) †††</td>
<td>70.4 (21.5) ***</td>
<td>.50</td>
<td>.17 to .84</td>
<td>67.7 (24.6) ††</td>
<td>7.7 †††</td>
</tr>
<tr>
<td>Role limitation</td>
<td>79.4 (35.5)</td>
<td>57.2 (42.1)</td>
<td>21.5 (34.1) †††</td>
<td>59.0 (42.0) ***</td>
<td>.75</td>
<td>.41 to 1.1</td>
<td>46.6 (20.2) ††</td>
<td>14.8 †††</td>
</tr>
<tr>
<td>Role limitation</td>
<td>84.1 (32.3)</td>
<td>74.0 (39.0)</td>
<td>39.3 (42.9) †††</td>
<td>62.9 (43.0) ‡‡‡</td>
<td>.54</td>
<td>.21 to .88</td>
<td>65.1 (42.6) †‡</td>
<td>5.6 ‡‡</td>
</tr>
<tr>
<td>Mental health</td>
<td>76.8 (18.4)</td>
<td>74.8 (15.1)</td>
<td>61.7 (17.1) †††</td>
<td>69.1 (16.5) ‡‡‡</td>
<td>.44</td>
<td>.10 to .77</td>
<td>69.4 (16.9) ††</td>
<td>4.8 ‡‡</td>
</tr>
<tr>
<td>Vitality</td>
<td>67.4 (19.9)</td>
<td>62.9 (19.8)</td>
<td>46.1 (20.3) ††</td>
<td>56.7 (19.7) ***</td>
<td>.53</td>
<td>.19 to .86</td>
<td>56.7 (20.8) ††</td>
<td>13.3 †††</td>
</tr>
<tr>
<td>Pain</td>
<td>79.5 (25.6)</td>
<td>80.4 (24.4)</td>
<td>68.7 (21.8) ††</td>
<td>77.5 (21.2) †</td>
<td>.41</td>
<td>.07 to .74</td>
<td>71.0 (23.0) †</td>
<td>3.6 ‡</td>
</tr>
<tr>
<td>General health appraisal</td>
<td>72.7 (22.7)</td>
<td>66.9 (23.2)</td>
<td>52.6 (15.4) †††</td>
<td>59.9 (16.7) ‡‡</td>
<td>.45</td>
<td>.12 to .79</td>
<td>56.0 (17.0) †</td>
<td>2.4</td>
</tr>
<tr>
<td>Change in health</td>
<td>52.4 (19.4)</td>
<td>59.3 (30.4)</td>
<td>45.1 (36.7) †</td>
<td>77.8 (26.8) †††</td>
<td>.99</td>
<td>.64 to 1.3</td>
<td>76.2 (26.7) †††</td>
<td>20.4 †††</td>
</tr>
</tbody>
</table>

CIA for comparisons between a reference group and patients at T0 (†). Wilcoxon tests between patients at T0 and T1 (*), calculated ES (T0-T1) with 95% Confidence Interval (CI).
Wilcoxon tests between patients at T0 and T2 (‡), and between patients at T1 and T2 (§). Repeated measures ANOVA for change over time (#). A higher score reflects better health.

* p < .05, § p < .05, † p < .05, ‡ p < .05, †† p < .01, ‡‡ p < .01, ††† p < .001, ‡‡‡ p < .001, †††† p < .001.
### Table 3

<table>
<thead>
<tr>
<th></th>
<th>General population n=102</th>
<th>Patients at T0 n=81</th>
<th>Patients at T1 n=63</th>
<th>Effect sizes T0-T1</th>
<th>95 % Confidence Interval (ES)</th>
<th>Patients at T2 n=63</th>
<th>Repeated measures analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall valuation of life</td>
<td>21.1 (8.3)</td>
<td>39.2 (17.5)</td>
<td>30.7 (22.0)</td>
<td>-4.3</td>
<td>-7.6 to -1.0</td>
<td>30.5 (17.1)</td>
<td>1.7</td>
</tr>
<tr>
<td>Psychological distress</td>
<td>17.0 (18.1)</td>
<td>35.4 (20.1)</td>
<td>24.2 (18.8)</td>
<td><strong>-5.7</strong></td>
<td>-9.1 to -2.3</td>
<td>23.8 (19.8)</td>
<td>7.1***</td>
</tr>
<tr>
<td>Physical symptom distress</td>
<td>9.9 (9.0)</td>
<td>25.2 (12.1)</td>
<td>18.5 (11.5)</td>
<td><strong>-5.6</strong></td>
<td>-9.0 to -2.3</td>
<td>18.7 (10.7)</td>
<td>17.7***</td>
</tr>
<tr>
<td>Activity level</td>
<td>Not available</td>
<td>15.9 (12.9)</td>
<td>10.5 (11.3)</td>
<td><strong>-4.4</strong></td>
<td>-7.7 to -1.1</td>
<td>14.8 (31.3)</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Wilcoxon test of comparisons of (a) patients at T0 and at T1(*) and calculated ES with 95% Confidence Interval, (b) patients at T0 and T2(‡), and (c) patients at T1 and T2. Repeated measures ANOVA for change over time (#). A higher score represents more burden of distress.

‡ p<.05, ‡‡ p<.01, *** p<.001, ‡‡‡ p<.001.

Seventy-nine percent of the patients had scores on the domain of psychological distress of the RSCL above the cut-off score of 15. The baseline scores of muscle force as a percentage of predicted normal (Table 4) showed that the muscle force of the upper extremities was slightly diminished whereas the muscle force of the lower extremities was severely diminished.

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>To Mean (SD)</th>
<th>T1 Mean (SD)</th>
<th>T2 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>W</strong> max (W)</td>
<td>128.7 (44.8)</td>
<td>141.1 (36.4)</td>
<td>Not available</td>
</tr>
<tr>
<td>Muscle strength biceps Brachii (% pred)</td>
<td>93.5 (23.4)</td>
<td>106.2 (27.7)</td>
<td>106.8 (25.0)</td>
</tr>
<tr>
<td>Muscle strength triceps Brachii (% pred)</td>
<td>98.7 (47.3)</td>
<td>106.1 (33.1)</td>
<td>110.3 (34.0)</td>
</tr>
<tr>
<td>Muscle strength Quadriceps Femoris (% pred)</td>
<td>70.8 (22.0)</td>
<td>80.9 (25.1)</td>
<td>84.8 (24.0)</td>
</tr>
</tbody>
</table>

Muscle strength is expressed as a percentage of predicted normal considering gender and age.

** p<.01, *** p<.001, ‡‡‡ p<.001.

Hypothesis 1: Effects of the multidimensional rehabilitation program

Quality of life questionnaires

Repeated measures ANOVA of those patients who completed all three measurements (n=63), performed for time, indicated a significant effect for time in every domain of the Rand-36 and RSCL (Tables 2 and 3), except in the domain of general health appraisal, activity level, and overall valuation.

Wilcoxon tests revealed significant short-term (T0–T1) improvements in every domain of the Rand-36 (Table 2) and in the RSCL domains, except for overall valuation of quality of life (Table 3). Wilcoxon tests showed that most improvements in general health-related quality of life were sustained at the 3-month follow-up (T0–T2), except for the domains of...
pain and general health appraisal (Table 2). Wilcoxon tests (T0–T2) showed improvements in all domains of the RSCL at the 3-month follow-up, including in the domain of overall valuation of life (Table 3). Although a slightly lower score was found at T2 than at T1 on some of the subscales, the only significant difference found (Wilcoxon test) was a positive one, namely, a further improvement of physical functioning (p=.03). ES (T0–T1), expressing the magnitude of the changes, varied from 0.38 to 0.99 (RAND-36) and from −0.57 to −0.43 (RSCL), as is shown in Tables 2 and 3. ES showed clinical relevant changes in all domains of the questionnaires, varying from “small” changes (six domains), to “moderate” changes (six domains) and “large” changes (one domain; Fig. 2).

Post hoc, we performed power analyses for the ES (5% level, two tailed), based on the smallest and largest ES, according to the tables of Kreamer [51]. The smallest ES (.38, n=63) revealed a power between 80% and 90%; the largest ES (.99, n=63) revealed a power >90%.

Gender differences. Mann–Whitney tests revealed no differences in outcome between men and women.

Disease related variables. Mann–Whitney tests revealed no differences between patients having Stages I–II disease and patients having Stages III–IV disease, except in the domain change of health (Z=−2.8, p<.01), indicating more positive change in patients having Stages I+II disease. Of the patients, 59.3% suffered from breast cancer. The percentages of patients with a different diagnosis were very small. It was therefore decided to make a dichotomous variable of having breast cancer (1) or having a different cancer diagnosis (0). Mann–Whitney tests revealed no differences between patients treated for breast cancer or for another type of cancer, except in the domain change of health (Z=−2.2, p=.03), indicating more positive change in patients treated for breast cancer. Pearson correlational analyses revealed no association of time since completion of treatment with quality of life after the program, except in the domain of change of health (r =−.38, p<.01) and pain (r =.26, p=.43).

Figure 2
ES of RAND-36 and RSCL after the program (To-T1, n=63)
Choice versus entire program. Mann–Whitney tests to compare the patients who followed the entire rehabilitation program with the eight patients who followed a program of less components at T1 revealed no significant differences in outcome between the two groups.

Physical variables
The measurement of $W_{\text{max}}$ and muscle force was not possible in all cases, due to mechanical breakdown of the apparatus and some patients experiencing claustrophobia and nausea. In addition, a few patients did not want the test because they thought it was irrelevant, painful, uncomfortable, or too strenuous. Paired $t$ tests revealed statistically significant short-term improvements of maximal workload. Furthermore, statistically significant improvements in muscle force were found immediately after the rehabilitation program, which were sustained at the 3-month follow-up (Table 4).

Patient appreciation
The mean program evaluation scores given to the different components of the program were individual exercise: 8.1 (0.5); sports: 8.1 (0.9); psycho-education 8.0 (0.9); and information: 7.2 (1.1). The mean evaluation score of the entire program was 8.2 (0.9). Eighty-one and a half percent of the patients would recommend the program to others.

Hypothesis 2: Patient preferences
Of the 40 patients who were offered a choice condition, 32 (80%) chose the entire multidimensional rehabilitation program with four components. Eight (20%) patients preferred a program with fewer than four components. One patient rejected the individual exercise component, two patients rejected the sports component, two patients rejected the psycho-education component, and two patients rejected the information component. These seven patients still followed a multidimensional program, including physical and psychological components. The eighth patient rejected two psychosocial components, namely, psycho-education and information. All patients who completed the program were asked at T1 what kind of program they would have composed themselves based on their experiences with the program they were following. Thirty (48%) patients chose a multidimensional program with all four components, 23 (36%) patients chose a three-component program, 5 (8%) patients chose two components, and 5 (8%) patients choose only one component. Fisher’s Exact Test showed that 58% ($n=19/33$) of the patients who were offered a choice at the start of the program and 37% ($n=11/30$) of the patients who did not have the opportunity to choose indicated that they would have chosen all four components of the program ($p=.13$).

Discussion
One of the two aims of this study was to describe the effects of a multidimensional rehabilitation program on (1) health-related quality of life, (2) exercise capacity, and (3) patient appreciation. The hypothesis that the multidimensional rehabilitation program would result in beneficial and clinically relevant improvements in health-related quality of life, including physical, psychological, and social functioning, was confirmed by the study. Furthermore, most improvements found in the short term were sustained in the longer term.
The study results are in line with earlier studies showing that multidimensional oncology rehabilitation programs have beneficial effects on psychological distress, general physical complaints, physical capacity, and the quality of life of breast cancer patients [36,37,52,53]. This study also revealed that dropout was low and unrelated to diagnosis. Furthermore, no effects of gender or type of cancer were found, nor of stage of disease or time since completion of treatment with the exception of change of health. These results suggest that the program is feasible and equally effective for men and women and for patients diagnosed with different types or stages of disease, and that it is effective regardless of time since completion of treatment.

This study not only showed that there were statistically significant improvements in health-related quality of life after the multidimensional rehabilitation program, but, moreover, ES showed that changes appeared to be also clinically relevant. A meta-analysis of psychological interventions showed weighted ES for quality of life measures varying from 0.17 to 0.28 [54]. In another study in which a combined intervention of group psychotherapy and home-based, unsupervised physical exercise was evaluated, ES were reported ranging from 0.16 to 0.34 [55]. The ES of this multidimensional rehabilitation program, ranging from 0.38 to 0.99, are considerably higher than those of the studies mentioned above. This underlines the clinical effectiveness of this multidimensional program, including supervised individual exercise, sports, psycho-education, and information.

In addition to the results described above, physiological improvements in physical functioning were found, i.e., improvement in maximal exercise capacity and improvement in muscle force of the upper and lower extremities. These results are in keeping with the findings of other researchers [20,27,28,35,56-59]. The results may indicate that the individual exercise and sports components account for the reduction of physical problems found, because genuine physiological improvements only occur due to the presence of physical training principles.

Patient appreciation scores indicated that patients were satisfied with the components of the program and with the program as a whole. Patients were least satisfied with the information component. This accords with the literature over the past three decades, which has consistently identified that many patients and family members are dissatisfied with cancer education [60]. Therefore, future research should pay serious attention to this component.

The second aim of this study was to obtain information about patient preferences for mono- or multidimensional rehabilitation programs, as healthcare professionals are now increasingly encouraged to consider patient preferences for treatments. An interesting finding of this study was that, if offered the choice before the start of the rehabilitation program, most cancer survivors preferred to follow the entire program rather than a program with fewer components. After the completion of the program, the majority of the participants would again have chosen multidimensional programs, although the percentage of participants that chose multidimensional programs after the completion of the program was lower than the percentage found prior to the start of the program. These results may indicate that cancer survivors have an a priori general preference for multidimensional programs, possibly based on the presence of complaints that are physical, psychological, and/or social in nature. Patients possibly consider multidimensional programs most appropriate and effective for their wide range
of problems. Participants who were given the choice were more likely to choose the entire program again after the completion of their program than were the participants who did not receive this choice. No additional pattern in choice preference was found in these groups. However, it was obvious that most participants preferred a program that combined a physical and psychological component, and that only a small percentage of the participants chose only one component.

This study confirms that cancer patients perceive themselves as having poor health-related quality of life persisting after the completion of initial treatment. This is also reported in other studies of patients with gastric, esophageal [11], breast [61], head and neck [10], lung, colon, and prostate cancer [62]. However, the patients participating in our study might not be representative of cancer patients in general, as they displayed lower quality of life than did the matched control group of cancer patients not referred to a cancer rehabilitation program. As expected, the latter had a lower quality of life than did the general population but a higher quality of life than did the referred cancer patients. The poor quality of life in our group of patients may be the result of selection, because only patients who met three of the six rehabilitation criteria were referred to our program. Simultaneously, these patients form exactly the target population for cancer rehabilitation programs that focus on improvement and recovery, indicating that the referral procedure was appropriate.

Due to the design of the study and the small number of patients who chose a program of fewer components, it was not possible to determine the effects of the various components. Nevertheless, the Engel Bio-Psychosocial model states that physical interventions support the effects of psychosocial interventions and vice versa. For example, a reduction of psychological distress may be due to psycho-educational intervention or to the “attention” patients receive from healthcare providers and/or the social support of peers. It may also be that improvements due to physical exercise lead to an improvement in quality of life. These “transfer effects” have been described by other researchers [24,25,27,63].

The measurement of muscle force in cancer patients brings to light an additional finding. Muscle force of the upper extremities appeared not to be extremely low at baseline, although a large number of breast cancer patients who have a potential risk of lymphoedema participated. However, the muscle force of the lower extremities showed considerable reduction. This latter phenomenon has also been described in other studies with chronic disease patients, e.g., COPD patients [64]. This finding can be explained by the fact that under conditions of disuse, such as hospitalization and during treatment, most patients tend to receive bed rest and adopt a prolonged sedentary lifestyle [7] that seems to mainly affect the muscles of the lower extremities. Under conditions of disuse, a rapid breakdown and excretion of muscle enzymes that normally produce energy for activity occur, leading to decreased energetic potential. Because physical activity or exercise is the normal mechanism for stimulating or maintaining the biochemical basis for energy, this study may offer the therapeutic implication that muscle exercise training is most appropriate for muscles of the lower extremities. Another implication may be that, during hospitalization, patients should be encouraged to perform physical exercises to prevent muscular problems due to disuse.
Study limitations
A limitation of our study was the lack of a control group, implying that improvements as a result of natural recovery could not entirely be excluded. However, the majority of patients had received their last cancer treatment more than 6 months prior to study entry – the mean time between completion of treatment and rehabilitation program was 11.3 months and the median time since diagnoses was 16.1 months. Therefore, on the basis of this timeline, it may be assumed that most natural recovery had already occurred before the commencement of the program. The finding that rehabilitation participants in the study experienced more problems than did the cancer controls not referred to a rehabilitation program suggests that natural recovery was unsuccessful. As a result, the changes described in our study concerning health-related quality of life probably reflect the genuine effects of the multidimensional program.

Conclusion
Cancer patients referred to a multidimensional rehabilitation program experienced serious physical and psychosocial problems and perceived themselves to have decreased quality of life in comparison with the general population and matched cancer controls not referred to a rehabilitation program. The multidimensional rehabilitation program under study here has beneficial clinically relevant short- and long-term effects on health-related quality of life, including physical, psychological, and social functioning. In addition, the results indicated that a multidimensional program is feasible for cancer survivors with different cancer diagnoses. Finally, if offered the choice, the majority of cancer survivors seem to prefer multidimensional programs to monodimensional programs.

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A multidimensional cancer rehabilitation program for cancer survivors

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A multidimensional cancer rehabilitation program for cancer survivors


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A multidimensional cancer rehabilitation program for cancer survivors


