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**Journal of Occupational Rehabilitation**

ISSN 1053-0487

J Occup Rehabil  
DOI 10.1007/s10926-011-9341-1

Journal of  
Occupational  
Rehabilitation

Available  
online  
[www.springerlink.com](http://www.springerlink.com)

 Springer

Volume 18, Number 1  
March 2008  
10926 • ISSN 1053-0487  
18(1) 1-XXX (2008)

 Springer

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# Rehabilitation Using High-Intensity Physical Training and Long-Term Return-to-Work in Cancer Survivors

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**Abstract** *Introduction* Due to large and increasing numbers of cancer survivors, long-term cancer-related health issues have become a major focus of attention. This study examined the relation between a high-intensity physical rehabilitation program and return-to-work in cancer survivors who had received chemotherapy. *Methods* The intervention group, consisting of 72 cancer survivors from one hospital (8 men and 64 women, mean age 49 years), followed an 18-weeks rehabilitation program including strength and interval training, and home-based activities. An age-matched control group, consisting of 38 cancer survivors (9 men and 29 women), was recruited from two other hospitals. They received only standard medical care. All subjects were evaluated during a telephone interview on employment issues, conducted at  $\pm 3$  years after diagnosis. The main outcomes were change

in working hours per week and time until return-to-work. *Results* Patients in the intervention group showed significant less reduction in working hours per week [ $-5.0$  h/week vs.  $-10.8$  h/week ( $P = .03$ )]. Multivariate analyses showed that the training intervention, the age of patients, and the number of working hours pre-diagnosis could explain the improvement in long-term participation at work. Time until (partial) return-to-work was 11.5 weeks for the intervention group versus 13.2 weeks for the control group ( $P = .40$ ). On long-term follow-up, 78% of the participants from the intervention group versus 66% from the control group had returned to work on the pre-diagnosis level of working hours ( $P = .18$ ). *Conclusion* Rehabilitation using high-intensity physical training is useful for working patients to minimize the decreased ability to work resulting from cancer and its treatment.

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**Keywords** Cancer · Rehabilitation · Exercise · Sports ·  
Employment · Work · Sick leave

## Introduction

Cancer treatment has made substantial progress in the last few decades, resulting in an average 5-year survival rate that approaches 60% for female and 46% for male patients [1]. Together with a relatively high incidence rate, this leads to a large number of cancer survivors. However, in spite of the progress in terms of survival, scientific evidence exists that long-term adverse effects are more prevalent, serious and persistent than expected [2]. Therefore, long-term cancer-related health issues have become a major focus of attention in oncology research and clinical practice. Systematic reviews and meta-analyses assessing the effectiveness of exercise interventions in cancer survivors showed that

physical training is an effective and favorable intervention to improve quality of life, cardio respiratory fitness, physical functioning, and symptoms of fatigue [3–6].

The ability to work and to retain employment are important components of a rehabilitation process due to the increased risk of unemployment in cancer survivors [7]. From a societal point of view, it is important to reduce avoidable work incapacity, and from an individual point of view, a decreased ability to work frequently results in financial loss, social isolation and reduction of self-esteem [8]. Additionally, being employed is significantly related to a higher quality of life in cancer survivors than being unemployed, and thus returning to work is highly desirable for these patients [8, 9]. Cancer-related fatigue appeared to predict the rate of return-to-work [10, 11].

In this study, the relation between a physical rehabilitation program and the rate of return-to-work on long-term will be examined. We are aware of the fact that cancer rehabilitation is a complex phenomenon that needs a multifactorial approach. In the past, we were able to show that an 18-weeks high-intensity resistance and endurance training program induces persistent long-term improvements in physical capacity, health-related quality of life (HRQoL) and fatigue [12, 13]. We assume that by improving fatigue levels in cancer survivors, it may also be possible to improve return-to-work rates in patients who have received chemotherapy.

## Materials and Methods

### Patients

The study was conducted between July 2001 and June 2005 in three district teaching hospitals: Máxima Medical Centre (MMC) Veldhoven (NL), MMC Eindhoven (NL) and VieCuri MC Venlo (NL). From 2001 onwards, the MMC Veldhoven used a high-intensity physical training program of 18 weeks as part of a standard medical care for all cancer survivors after chemotherapy. Patients from this hospital were assigned to the intervention group if they met the eligibility criteria for the study. They were followed from the start of the rehabilitation program up to 12 months after completing the program. The age-matched control patients were retrospectively recruited from a group of cancer patients in two other hospitals. They received chemotherapy in the same period as the intervention group. However, they did not receive a physical rehabilitation program as part of their medical care. Baseline data concerning disease and treatment were identified from the medical records, and retrospectively the same inclusion and exclusion criteria as used for the intervention group (see later) were applied.

All patients (both groups) provided informed consent, and the study was approved by the Research Ethics Committee of the MMC Veldhoven. Eligibility criteria included patients: (1) with histological confirmed cancer with no indication of recurrence or progression, (2) treated with curative intention with primary or adjuvant chemotherapy, (3) aged 18–65 years (since one is considered adult at the age of 18 and the retirement age is set at 65 years, because the *Dutch General Old Age Pensions Act (AOW)* provides for basic state pensions for people aged 65 and older) and (4) in paid employment at the time of diagnosis. Exclusion criteria included patients, who: (1) suffered from newly diagnosed cancer, (2) were not capable of performing basic skills, (3) suffered from cognitive disorders or severe emotional instability, (4) had other serious diseases that might hamper physical performance capacity (e.g., heart failure, chronic obstructive pulmonary disease) and (5) were self-employed (since legislation and sick leave reimbursement of these subjects in the Netherlands is substantially different from individuals engaged in paid employment).

### Physical Training and Assessment of Muscle Strength and Peak VO<sub>2</sub> Exercise Performance

Training started a minimum of 6 weeks after completing chemotherapy to counteract bias resulting from spontaneous recovery after chemotherapy. The 18-weeks training program consisted of high-intensity resistance and endurance training, supervised by an experienced physiotherapist. At first, strength exercises were performed at 65% to 80% of the one-repetition maximum (1-RM), consisting of two sets of 10 repetitions. After the twelfth week, the emphasis shifted from muscle strength to muscle endurance involving training consisting of two sets of 20 repetitions but at less resistance (35–40% of 1-RM). Every 4 weeks the training progress was evaluated, and the training result was adjusted by means of indirectly determined 1-RM values. The strength training consisted of six exercises targeting the large muscle groups: (1) vertical row (focusing on mc longissimus, mc biceps brachii, mc rhomboideus); (2) leg press (mc quadriceps, mc glutei, mc gastrocnemius); (3) bench press (mc pectoralis major, mc triceps); (4) pull over (mc pectoralis, mc triceps brachii, mc deltoideus, mc trapezius); (5) abdominal crunch (mc rectus abdominis); (6) lunge (mc quadriceps, mc glutei, hamstrings).

Along with this supervised training program, patients were instructed to undertake endurance activities at home, such as walking and cycling. A more detailed description of the training program and the assessment of muscle strength and peak VO<sub>2</sub> exercise performance can be found in the study of De Backer et al. [12].

To identify and exclude patients with medical contraindications to exercise, cardiopulmonary and muscular limitations were assessed by physical examination and by cardiopulmonary exercise testing before the start of the training program. Muscle strength and peak  $\text{VO}_2$  exercise performance was also tested after 18 weeks of training to assess training-related changes. A sports physician supervised not only the training protocol, but also encouraged patients to continue their training activities at home after the end of the training program.

## Outcome Measures

### Questionnaire

A telephonic job resumption questionnaire was used. To allow enough time for patients to return to work, the questionnaire was conducted at least 2 years after diagnosis and at least 1 year after cessation of oncologic treatment. This questionnaire was validated in research on chronic diseases and work [14]. The following variables of patients were sampled: gender, age, living situation, highest education level, main wage-earner, work situation and working hours before diagnosis, during treatment, and after treatment both in the short and in the long-term, and compliance to and specification of any oncologic rehabilitation.

Return-to-work was divided as follows:

Change in working hours, measured as the difference between the working hours per week 2 years after diagnosis of the disease and before the disease was diagnosed. A time period of 2 years was chosen since in Dutch legislation concerning sick leave after 2 years an independent occupational insurance physicians makes a definite assessment;

Time-to-return-to-work (often partial), measured as number of weeks from cessation of treatment with chemotherapy or radiotherapy until the first day of (partial) return-to-work;

Time-to-full-return-to-work, measured as number of weeks from cessation of treatment with chemotherapy or radiotherapy until the first day of full return-to-work. Full return is attained when a patient works actually the hours stated in their work contract.

## Statistical Analyses

Statistical analyses were carried out using SPSS for Windows Release version 14.0. Normality of distribution was tested by calculation of the coefficients of skewness (asymmetry) and kurtosis (flatness).

Differences in baseline characteristics between the intervention and control group were analyzed by Student's  $t$  test or Mann–Whitney test. For categorical data we used  $\chi^2$ -tests.

Group differences between the time until initial (partially) and full return-to-work were analyzed using Kaplan–Meier survival analyses. We used the log-rank test to determine the level of significance.

In order to remove possible confounders for the main outcome variables, univariate and multivariate regression analyses were used. We first used a univariate analysis to obtain potential explanatory variables, including group, gender, age, highest education level, main wage-earner, weekly working hours pre-diagnosis, year of diagnosis, type of tumor, treatment methods, the time between treatment and completing the questionnaire, and duration of treatment. We only included variables that were significantly related ( $P \leq .10$ ) to the outcome variable in a multivariate regression model with backward stepwise regression and removal criteria of  $P > .05$ . We assumed that multicollinearity is not an issue when the Variance Inflation Factor (VIF) values were lower than 5 and tolerance values were larger than 0.2. The level of significance in all analyses was set at  $P \leq .05$ .

## Results

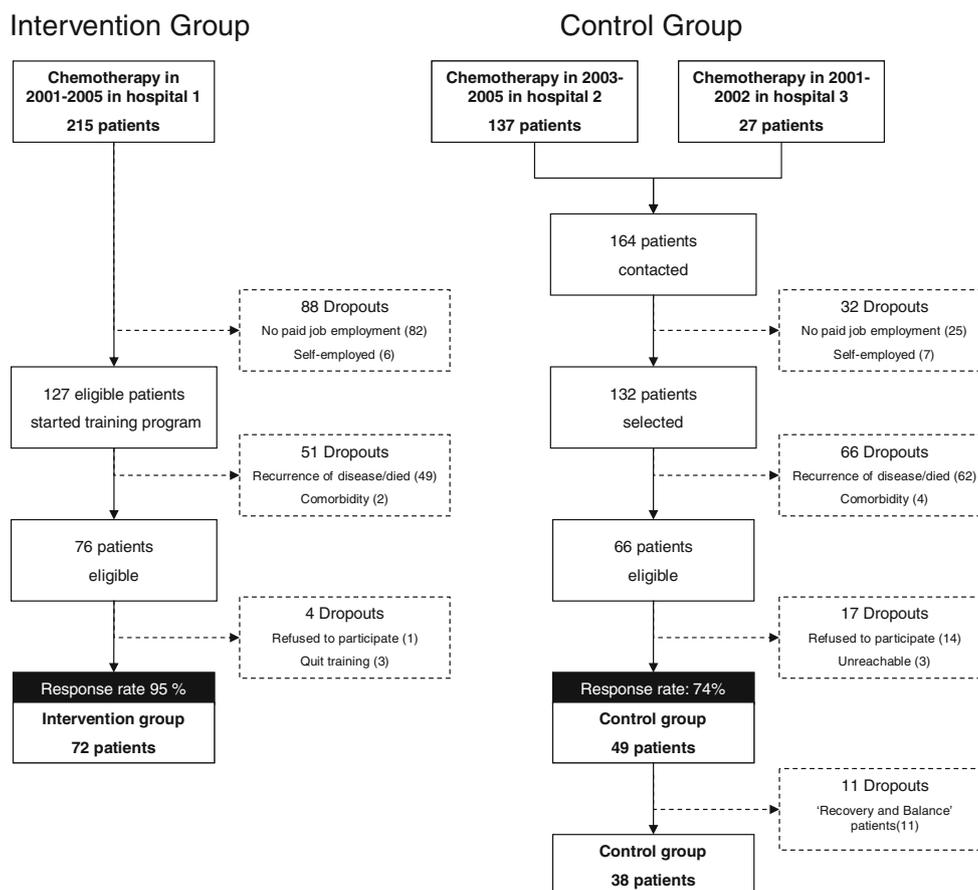
### Study Population

#### Intervention Group

From July 2001 until June 2005, 215 patients were curatively treated with chemotherapy and adjuvant therapy and underwent the training program in the MMC Veldhoven (hospital 1). As shown in the flow chart in Fig. 1, 82 patients, who did not have paid employment at the time of diagnosis, and 6 patients, who were self-employed, were excluded. During the study period, 49 patients died or suffered from a recurrence of the disease, and 2 patients quit the training program because of rheumatic disease and intervertebral disc hernia. As a result 76 patients were eligible. Four patients had not been able to complete the training program (two had resumed work and were not able to combine training and work, one person stopped the training for personal reasons, and one patient refused to answer the job resumption questionnaire). This finally resulted in an intervention group of 72 patients with a response rate of 95% (see Fig. 1).

#### Control Group

As shown in the flow chart of Fig. 1, the control group consisted of patients from two different hospitals. Twenty-seven eligible patients treated between 2001 and 2002 were identified by oncologists in the MMC Eindhoven (hospital 3), and 137 potentially eligible patients treated between



**Fig. 1** Flowchart of the study population. Hospital 1 = Máxima Medical Centre (MMC) Veldhoven (NL); hospital 2 = VieCuri MC Venlo (NL); hospital 3 = MMC Eindhoven (NL)

2003 and June 2005 were identified by oncologists of VieCuri MC Venlo (hospital 2). Twenty-five patients, who did not have paid employment at the time of diagnosis, and seven patients, who were self-employed, were excluded. Four patients had severe co morbidity that influenced employment and were therefore excluded and 62 patients died or suffered from recurrence of the disease.

Consequently, 66 patients were found eligible for recruitment in the study. Fourteen cancer survivors refused to participate, and three patients could not be reached, either by telephone or by mail. The response rate was therefore 74%.

Although we assumed that in the control group no patient would have followed any physical rehabilitation program, it appeared that 11 patients followed a rehabilitation program called 'Recovery and Balance'. This includes a physical training of more moderate intensity. Apart from its training effect this program is also aimed at improvement of coping skills and reduction of kinesiophobia [15]. These 11 patients were excluded from the main analysis since we wanted to compare our intervention with no physical intervention. As a result, the control group consisted of 38 patients. Nevertheless, to consider a possible selection bias, we also

repeated all analyses after including the above-mentioned 11 patients.

### Baseline Characteristics of the Study Population

All baseline characteristics of patients in both groups did not differ significantly (see Table 1).

### Return-to-Work

#### Change in Working Hours

Long-term follow-up showed that the decrease in working hours per week as compared to the pre-diagnosis status was significantly less in the intervention group with a mean difference of -5.0 h/week for the intervention group compared to -10.8 in the control group ( $P = .03$ ) as shown in Table 2.

#### Time-to-(full)-Return-to-Work

Table 2 also shows the results of time to (full) return-to-work. Time to return to work was 11.5 versus 13.2 weeks

**Table 1** Patient characteristics at baseline

|  | Intervention group<br>N (%) | Control group<br>N (%) | <i>P</i> -value |
|--|-----------------------------|------------------------|-----------------|
| Gender   |                             |                        |                 |
| Men  | 8 (11.1%)                   | 9 (23.7%)              | 0.08            |
| Woman  | 64 (88.9%)                  | 29 (76.3%)             |                 |
| Age (years)  |                             |                        |                 |
| Mean ( $\pm$ SD)   | 49 yrs ( $\pm$ 8.3)         | 49 yrs ( $\pm$ 9.2)    | 0.84            |
| Range  | Range 26–62 yrs             | Range 28–63 yrs        |                 |
| Tumour type  |                             |                        |                 |
| Breast   | 51 (70.8%)                  | 26 (68.4%)             | 0.49            |
| Ovarian  | 2 (2.8%)                    | 0                      |                 |
| Hodgkin lymphoma   | 5 (6.9%)                    | 5 (13.2%)              |                 |
| Non-Hodgkin lymphoma   | 5 (6.9%)                    | 2 (5.3%)               |                 |
| Colorectal   | 5 (6.9%)                    | 5 (13.2%)              |                 |
| Lung   | 1 (1.4%)                    | 0                      |                 |
| Testis   | 3 (4.2%)                    | 0                      |                 |
| Treatment  |                             |                        |                 |
| Chemotherapy   | 72 (100%)                   | 38 (100%)              | 0.77            |
| + Radiotherapy   | 4 (5.6%)                    | 3 (7.9%)               |                 |
| + Surgery  | 18 (25.0)                   | 10 (26.3%)             |                 |
| + Radiotherapy + Surgery   | 44 (61.1%)                  | 20 (52.6%)             |                 |
| Treatment period in weeks ( $\pm$ SD)                              | 19.8 ( $\pm$ 6.7)           | 20.6 ( $\pm$ 4.6)      | 0.46            |
| Time between diagnosis and questionnaire in weeks ( $\pm$ SD)      | 168.5 ( $\pm$ 48.9)         | 170.6 ( $\pm$ 31.8)    | 0.78            |
|  | Range 96–306                | Range 110–236          |                 |
| Time between last treatment and questionnaire in weeks ( $\pm$ SD) | 139.5 ( $\pm$ 48.9)         | 142.7 ( $\pm$ 30.0)    | 0.68            |
|  | Range 70–280                | Range 81–203           |                 |
| Work   |                             |                        |                 |
| Weekly working hours pre-diagnosis ( $\pm$ SD)                     | 27.2 ( $\pm$ 9.6)           | 29.5 ( $\pm$ 12.0)     | 0.29            |
| Highest education level  |                             |                        |                 |
| Primary school   | 0                           | 2 (2.8%)               | 0.73            |
| Junior secondary vocational education                              | 4 (10.5%)                   | 9 (12.5%)              |                 |
| Senior secondary vocational education                              | 7 (18.4)                    | 9 (12.5)               |                 |
| Intermediate vocational training                                   | 13 (34.2)                   | 18 (25.0%)             |                 |
| Higher professional education                                      | 3 (7.9%)                    | 7 (9.7%)               |                 |
| Higher vocational education  | 9 (23.7%)                   | 19 (26.4%)             |                 |
| University education   | 2 (5.3%)                    | 8 (11.1%)              |                 |
| Wage earner  |                             |                        |                 |
| Main wage earner   | 27 (37.5%)                  | 15 (39.5%)             | 0.84            |
| Living situation   |                             |                        |                 |
| Alone  | 12 (16.7%)                  | 5 (13.2%)              | 0.48            |
| With partner   | 30 (41.7%)                  | 16 (42.1%)             |                 |
| With partner and kids  | 25 (34.7%)                  | 17 (44.7%)             |                 |
| With kids  | 3 (4.2%)                    | 0                      |                 |
| With others  | 2 (2.8%)                    | 0                      |                 |
| Chemotherapy   |                             |                        |                 |
| AC, breast   | 13 (18.1%)                  | 4 (10.5%)              | 0.12            |
| CMF, breast  | 4 (5.6%)                    | 9 (23.7%)              |                 |
| FEC, breast  | 31 (43.1%)                  | 13 (34.2%)             |                 |
| TAC, breast  | 2 (2.8%)                    | 0                      |                 |

**Table 1** continued

|  | Intervention group<br>N (%) | Control group<br>N (%) | <i>P</i> -value |
|--|-----------------------------|------------------------|-----------------|
| Adriamycin-Docetaxel, <i>breast</i>                  | 1 (1.4%)                    | 0                      |                 |
| Carboplatin-paclitaxel, <i>ovarian</i>               | 2 (2.8%)                    | 0                      |                 |
| ABVD/MOPP/EBVP/BEACOPP/DHAP, <i>Hodgkin lymphoma</i> | 5 (6.9%)                    | 5 (13.2%)              |                 |
| CHOP/CVP/CHVmP/BV, <i>Non-Hodgkin lymphoma</i>       | 5 (6.9%)                    | 2 (5.2%)               |                 |
| 5-FU Leucovorin, <i>colorectal</i>                   | 5 (6.9%)                    | 5 (13.2%)              |                 |
| BEP, <i>testis</i>                                   | 3 (4.2%)                    | 0                      |                 |
| Cisplatinum/Gemcitabine, <i>lung</i>                 | 1 (1.4%)                    | 0                      |                 |

AC = adriamycin + cyclophosphamide, CMF = cyclophosphamide + methotrexate + fluorouracil, FEC = fluorouracil + epirubicin + cyclophosphamide, TAC = docetaxel + doxorubicin + cyclophosphamide, ABVD = doxorubicin + bleomycin + vinblastine + dacarbazine, MOPP = mustargen + vincristine + procarbazine + prednisone, EBVP = epirubicin + bleomycin + vincristine + prednisone, BEACOPP = bleomycin + etoposide + doxorubicin + cyclophosphamide + vincristine + procarbazine + prednisone, DHAP = cytarabine + cisplatin, CHOP = cyclophosphamide + doxorubicin + vincristine + prednisone, CVP = cyclophosphamide + vincristine + prednisone, CHVmP/BV = cyclophosphamide doxorubicin + teniposide + prednisone + bleomycin + vincristine, BEP = bleomycin + etoposide + cisplatin  
*P*-values were analyzed by Student's *t* test or Mann–Whitney test (continuous data) or  $\chi^2$  tests (categorical data)

**Table 2** First and full return-to-work and change in working hours per week

|   | Intervention Group<br>(n = 72)   | Control Group<br>(n = 38)        | <i>P</i> value |
|---|----------------------------------|----------------------------------|----------------|
| Returned-to-work (% and number of patients)                 | 94% (n = 68)                     | 89% (n = 34)                     | 0.34           |
| Full-return-to-work (% and number of patients)              | 78% (n = 56)                     | 66% (n = 25)                     | 0.18           |
| Change in working hours (hours)                             | −5.0 (±10.9)<br>Range −41/+22    | −10.8 (±14.7)<br>Range −55/+8    | 0.03*          |
| Rate of full-return-to-work as % of hours pre-diagnosis (%) | 83.1 (±44.0)<br>Range 0.0/+237.5 | 66.1 (±44.3)<br>Range 0.0/+166.7 | 0.05*          |
| Time-to-return-to-work (weeks)                              | 11.5 (±11.1)<br>Range 0–52       | 13.2 (±16.7)<br>Range 0–78       | 0.40**         |
| Time-to-full-return-to-work (weeks)                         | 34.8 (±21.3)<br>Range 0–112      | 29.3 (±23.2)<br>Range 4–104      | 0.49**         |

Values are presented as mean (±SD)

\* Significant difference with *P* ≤ .05

\*\* *P*-value determined by the log-rank test

(*P* = .40). After an average of 3 years post-diagnosis, 56 patients (78%) in the physical activity group compared to 25 patients in the control group (66%) had returned to work on the pre-diagnosis level of working hours (*P* = .18) (see Kaplan–Meier curves in Figs. 2, 3). Inclusion of the previously mentioned 11 patients from the control group did not change the results of the analyses.

### Univariate and Multivariate Analyses

Table 3 shows the results of the univariate regression analysis. Explanatory variables that were related to the outcome variable (*P* < 0.10) were tested in a multivariate model. As shown in Table 4, only group, age, and the number of weekly working hours pre-diagnosis contributed

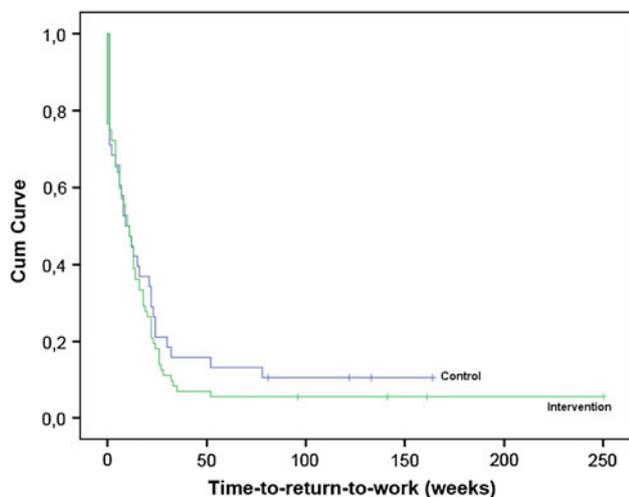
to the model, with an explained variance of 29%. These results indicate that the older a survivor the least changes in working hours. The same trend holds true for survivors with the highest weekly working hours pre-diagnosis. The data of VIF and tolerance indicate no multicollinearity problem.

Inclusion of the excluded 11 patients from the control group did not change the results of these analyses.

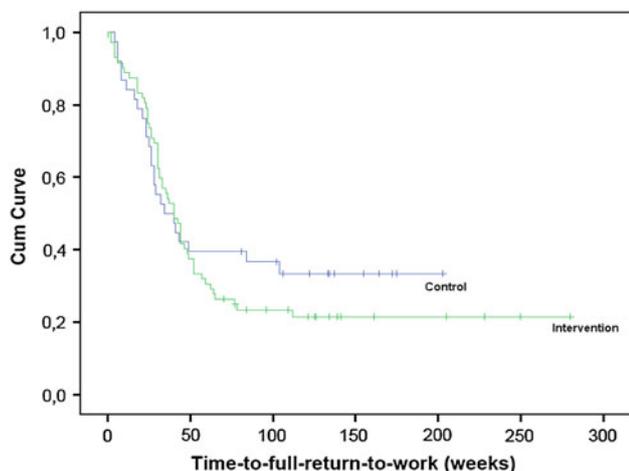
### Discussion

#### Main Findings and Interpretation of Outcomes

This study investigated the long-term effects of a high-intensity physical training program, which was embedded



**Fig. 2** Kaplan–Meier curve of time-to-return-to-work in cancer survivors. The difference in time-to-return-to-work between the groups determined by the log rank test is not significant ( $P = .40$ )



**Fig. 3** Kaplan–Meier curve of time-to-full-return-to-work in cancer survivors. The difference in time-to-full-return-to-work between the groups determined by the log rank test is not significant ( $P = .49$ )

in a rehabilitation program, on the rate of return-to-work in cancer patients treated with chemotherapy. In addition to earlier published improvements in levels of fatigue, physical performance, and quality of life both immediately post-rehabilitation as well as at the long term [13], such a high-intensity training also substantially improved the number of working hours on long-term participation in paid labor.

Multivariate regression analyses showed that, besides physical support, the age of patients, and the weekly working hours pre-diagnosis also influenced the long-term participation at work. In literature, evidence regarding age and the relation to return-to-work is inconsistent. Some

**Table 3** Univariate linear regression analysis of the change in weekly working hours on a number of explanatory variables

| Explanatory variables                         | Outcome variable: change in weekly working hours |                 |
|---|--|-----------------|
|   | Regression coefficient                           | <i>P</i> -value |
| Group (Physical training intervention)        | 0.218  | 0.02            |
| Gender  | −0.230   | 0.02            |
| Age   | −0.331   | 0.00            |
| Highest education level                       | −0.163   | 0.83            |
| Living situation                              | 0.230  | 0.22            |
| Main wage-earner                              | −0.115   | 0.23            |
| Weekly working hours pre-diagnosis            | −0.356   | 0.00            |
| Year of diagnosis                             | 0.257  | 0.12            |
| Type of tumour                                | −0.341   | 0.04            |
| Treatment methods                             | 0.232  | 0.02            |
| Time between last treatment and questionnaire | −0.059   | 0.54            |
| Duration of treatment                         | −0.019   | 0.85            |

studies found that older cancer survivors were less likely to be employed than their (cancer-free) referents [16–19], others did not find an increased risk of unemployment with increasing age [7, 20]. Besides these observations, it is well known that employers would rather hire younger employees compared with older ones. This may also have a negative influence on the (return-to) work-rates of older unemployed cancer survivors. In this study age ranged from 26 to 63 years, with a mean of 49 ( $\pm$ SD 8.3) years. In the total study population 49% are aged > 50 years (20 survivors [53%] in the control group and 34 [47%] in the intervention group). Hypothetically, this percentage of cancer survivors is at increased risk for early retirement based on above referenced literature. Our results, however, do not confirm this hypothesis because age was not a factor associated with the number of cancer survivors that actually returned to work ( $P = .31$ , unpublished data). This is in line with the findings of one prospective study in 2011 [20] and the meta-analysis and meta-regression of 36 studies, performed by De Boer et al. in 2009 [7]. Moreover, we observed a significant association between age and the amount of working hours on long-term. Older survivors seem to have less reduction in working hours on long term than young ones. No other previous studies documented this outcome. It is difficult to come up with a good explanation for this finding. It could be that the values, beliefs and norms of older people are more based on working ethos. Therefore, they are more likely to return to work after their disease.

Also the number of weekly working hours pre-diagnosis contributed to the improvement of the long-term

**Table 4** Backward stepwise regression model to predict the change in weekly working hours

| Variable                           | Standardized $\beta$ coefficient | <i>t</i> value | <i>P</i> value | CI               | Tolerance | VIF  | Total R <sup>2</sup> |
|------------------------------------|----------------------------------|----------------|----------------|------------------|-----------|------|----------------------|
| Physical training intervention     | 0.173                            | 2.107          | 0.04           | 0.269–8.868      | 0.99      | 1.01 | 0.290                |
| Age                                | −0.362                           | −4.404         | 0.00           | −0.798 to −0.302 | 0.99      | 1.01 |                      |
| Weekly working hours pre-diagnosis | −0.372                           | −4.506         | 0.00           | −0.643 to −0.250 | 0.98      | 1.02 |                      |

CI Confidence interval, VIF Variance inflation factor

participation at work. This may be related to the fact that the persons with high weekly hours are often the main wage earners in the family. The relatively higher drop in working hours in the patients with a lower number of working hours pre-diagnosis may underline the need for special attention also for these patients.

There is no significant difference in time to (full) return-to-work. This is likely due to the fact that timing to (partially) return-to-work coincided with training. The effort and time that the patients needed to perform an 18 weeks high-intensity physical training program most probably interfered with capacity for performing work in short-term.

To our knowledge, there is only one study that examined the effect of a physical intervention program on resumption of work. Berglund et al. prospectively examined the effects of a 7-weeks rehabilitation program in 60 cancer patients [21]. In contrast to our results, no significant difference was found in the rate of return-to-work between cancer survivors with and without their rehabilitation program [21]. These different results might be explained by the fact that their program with an emphasis on information and physical and coping skills training was distinctly different from our program concerning duration and the intensity at which the patients were trained and supervised.

The percentage of survivors, who full returned to work in our study, was 78% for the intervention group and 66% for the controls. This is favorable compared to data from the literature, in which the percentage of job resumption of cancer survivors varied from 30 to 93%, with a mean rate of 62% across all studies [8]. Since our intervention group still had a decrease to 78%, it is tempting to search for further optimization and additional interventions that might be beneficial. Literature showed that the rate of returning to work after treatment also depends on the advices of consulted physicians [17, 22, 23]. In a pilot study on return-to-work, cancer patients were provided with an educational leaflet about job resumption and enhanced communication with their physicians [23]. The patients of that study showed favorable return-to-work outcomes when compared to the findings of a prospective study about work return without counseling of patients [10]. In our study the cancer rehabilitation program of the intervention group was focused mainly on physical aspects and encompassed high intensity training and coaching/counseling to continue at

long term. Nowadays it becomes more accepted that, apart from physical and medical aspects, cancer rehabilitation programs also need to include psychological and social support (i.e., a multidisciplinary intervention). It is likely that active counseling of cancer patients on employment issues in such a clinical and rehabilitation setting additionally improves the return-to-work rates. In cardiac rehabilitation Dumont et al. [24] already reported substantial benefits of a cardiac rehabilitation program, in which participation at work was also addressed on a structural basis.

An important social aspect influencing return-to-work is the support by the employer and/or a nation's health system. In the Netherlands, cancer patients who are unable to work still receive income. During the first 2 years of sick-leave, income is often paid by the insurance of the employer and after 2 years by the state (disability pension). In many cases employer and company or insurance physicians follow the patient's wishes about resuming work [25]. In countries with other regulations concerning sick leave and income reimbursement there may be a different general situation concerning the return-to-work rates.

#### Limitations of the Study

A high proportion of the participants in our study were survivors of breast cancer (70%). This is mainly due to the high incidence of breast cancer in our society. It is an open question whether the observed results are generalizable to patient groups with other cancer types. Comparing cancer survivors from different hospitals is not an ideal situation and a randomized controlled trial (RCT) would be a more optimal study design than we used in this study. However, as nowadays the short- and long-term benefits of exercise are recognized more widely in research and clinical practice [12, 26–28], it can be considered unethical to keep patients away from an exercise-containing rehabilitation program, making RCT-designed studies in patients from one hospital unwanted. In our study, we were able to demonstrate that both groups had similar baseline characteristics and analyses for potential confounders did not affect the result.

A limitation of the study is the lack of knowledge about the physical characteristics (muscle strength, peak oxygen uptake) and fatigue in the controls. Consequently, a

relationship between these parameters and the time and rate of return-to-work cannot be evaluated properly. Nevertheless, we assume that training effects were responsible for the difference in working hours from diagnosis to 2 years post-diagnosis between intervention and control group, since other studies showed a stable situation in a control group over time [29].

Another limitation of the study may be the lower rate of respondents in the control group (=74%) as compared with the intervention group (=95%). Based upon the information available from the patient files of some non-responders in the control group, we got the impression that a considerable number of these patients were in poor physical condition, and therefore, did not want to participate. However, we do not expect that this lower response rate contributed to our favorable results on work return. On the contrary, inclusion of these patients would have probably led to more favorable results on return-to-work by comparing both groups.

A last limitation could be the fact that patients were not able to exactly recall the details and times of return-to-work.

## Conclusion

We conclude that in cancer survivors, apart from favorable effects on physical fitness, an oncologic rehabilitation program including high-intensity physical training also results in substantial economic benefits by significantly improving job resumption. As cancer rehabilitation needs to include medical, physical, psychological, and social support in the return to work effort, the importance of a multidisciplinary intervention cannot be stressed enough.

**Acknowledgments** The authors would like to thank the Rabobank, Foundation Roparun, and the Research Foundation of the MMC Veldhoven for financial support of this study.

**Conflict of interest** No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the author(s) or upon any organization with which the author(s) is/are associated.

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