

## Changes in fatigue, health-related quality of life and physical activity after a one-week educational program for cancer survivors

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### ABSTRACT

**Background:** Rehabilitation aims to improve function, but the effects of different programs are not clear. The aims of the present study were to: (1) compare the level of fatigue and health-related quality of life (HRQOL) of cancer survivors admitted to a one-week inpatient educational program (IEP) to the general population (NORMS), (2) examine changes in fatigue, HRQOL and physical activity after the IEP and (3) examine the proportions of survivors for female and male separately with clinically relevant improvement (>10% of maximum scale).

**Methods:** Cancer survivors  $\geq 18$  years, diagnosed with breast-, prostate- or gastrointestinal cancer within the last 10 years, about to attend a one-week IEP were invited to an observational study with a pre-post design. The IEP included lectures, group discussions and physical activity. The participants completed a questionnaire on the arrival day (T0) and three months after the stay (T1). Fatigue was assessed by the Fatigue Questionnaire and HRQOL by Short Form-36.

**Results:** Compared to NORMS, both female and male participants had significantly higher mean levels of fatigue and poorer HRQOL at T0 and T1. From T0 to T1, among all participants physical fatigue was reduced from 12.6 (SD 3.9) to 11.8 (SD 3.8;  $p < .001$ ), mental fatigue from 6.3 (SD 2.2) to 6.0 (SD 2.2;  $p = .044$ ) and total fatigue from 19.0 (SD 5.3) to 17.8 (SD 5.4;  $p = .001$ ). Among female participants, 30% experienced clinically relevant improvement in physical fatigue, 28% in total fatigue and 36% in general health. Of male participants, 31% displayed a clinically relevant improvement in role limitations physical.

**Conclusion:** Participants in the IEP reduced their levels of fatigue and improved aspects of HRQOL, more often observed among female participants than among males. Because of the lack of a control group it is not possible to conclude whether the changes were due to the IEP.

### ARTICLE HISTORY



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## Introduction

Cancer survivors often experience physical and psychosocial adverse effects, such as fatigue and deconditioning, from the disease and its treatment affecting their health-related quality of life (HRQOL) [1–5]. These adverse health effects can become clinically apparent during treatment or emerge months or even years after end of treatment [6]. The severity and frequency of the adverse effects will vary across cancer types and negatively affect upon HRQOL differently, in part due to individual variability such of personality traits, coping strategies and health literacy [7,8]. Many cancer survivors are able to return to a normal everyday life without support, but

about 20–60% report need for health professional assistance [9,10].

Existing rehabilitation programs for cancer patients and survivors differ in terms of aims, content and structure. Knowledge of the effects of such programs and of information about the optimal delivery in terms of intensity, volume and components is still lacking. Further, characteristics of those who attend the programs and those who gain a potential clinically relevant improvement are also of importance. Scott et al. [11] concluded that multidisciplinary interventions, consisting of a physical component and a psychosocial component, had positive effects on physical aspects of HRQOL function among cancer survivors.

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 Supplemental data for this article can be accessed [here](#).

Programs focusing on a specific outcome such as diet, physical activity or stress management appeared to be more effective than those with multiple aims. Further, interventions with longer duration (range 6–12 months) showed no additional improvement than interventions conducted over a period of up to 12 weeks (range 4–12 weeks) [11]. The effects of rehabilitation programs for cancer survivors have mainly been studied within an outpatient setting and most of the inpatient settings have lasted for 3–4 weeks. To our knowledge, only a few studies have investigated the effects of a short one-week inpatients educational program (IEP) on fatigue, HRQOL and level of physical activity (LPA) [12,13]. In addition, as far as we know studies have not observed gender-related differences of change during such short programs on fatigue, HRQOL and LPA or which factors are associated to a clinically relevant change. Such knowledge is important for future planning of relevant rehabilitation programs.

The aims of the present study were therefore to: (1) compare the level of fatigue and HRQOL at admission to a one-week IEP for cancer survivors to the general population (NORMS), (2) examine changes in fatigue, HRQOL and LPA following the IEP for all participants combined and for female and male separately and (3) examine the proportions of survivors for female and male separately with clinically relevant improvement (>10% of maximum scale) for the outcomes that statistically significantly improve after the IEP and factors associated with clinically relevant improvement.

## Material and methods

### Participants

The study was an observational study with a pre-post design. Participants about to attend a one-week cancer diagnosis specific IEP (breast-, prostate- or gastrointestinal cancer) at The Norwegian Resource Center for Coping with Cancer (Montebello-Center, MBC), between September 2011 and February 2013, were invited to participate. All participants were referred to MBC by a medical doctor confirming the 'need for participation in the program' and that the participant managed daily routines without assistance.

Inclusion criteria for the current study were age  $\geq 18$  years and a diagnosis of breast-, prostate- or gastrointestinal cancer within the last 10 years. Participants who between the assessment at admittance to the IEP and follow-up: (1) had experienced progression of their cancer and/or; (2) had undergone surgery, radiotherapy and/or chemotherapy and/or; (3) had experienced a severe health condition such as myocardial infarction were not eligible for the present study and were excluded ( $n = 39$ ).

### The general population

Normative data from Norwegian general population (NORMS) on fatigue ( $n = 2323$ , age range 19–80 years, mean age 44.9 (SD 16.5)) [14] and HRQOL ( $(n = 2118$ , mean age 55.7 (SD 14.1)) [15] were used for comparison to our sample.

### Inpatient educational program (IEP)

Since 1990 the MBC has offered IEP for cancer patients and survivors and their partners/relatives. The overall goals of all programs at the MBC are to improve participants coping with cancer-specific health problems and motivate the participants to adopt a healthy lifestyle by information and activities. Approximately 20–30 participants attend each course and their partners/relatives are invited to take part. An oncologist, a nurse, a social worker, a psychologist, a nutritionist and a physiotherapist/sports instructor lead the different parts of the program. Parts of the IEP are specific for each cancer diagnosis while most of the content is common across the courses. The scheduled program of the one-week IEP consisted of approximately 30h. The lectures amounted to about 50–55% of total planned hours, the physical activities to approximately 20–25% and the group sessions to roughly 25%.

During the six-day program the participants attend standardized lectures on cancer-related topics, such as cancer and its treatment, risk of adverse effects, work, social resources and support, sexuality, psychological reactions and lifestyle. The lectures on cancer, its treatment and risk of adverse effects (e.g., challenges with stoma after gastrointestinal cancer and lymphedema after breast cancer) were specific for each of the three types of cancer, while the lectures on the other themes were quite similar for all three types of diagnosis.

Further, the participants attend group sessions which were led by a group leader and the themes were related to the lectures.

Physical activity was performed in groups of 6–9 participants and all participants were invited and encouraged to take part in the activity sessions. Physical activities included outdoor walking (with and without poles), water gymnastics, resistance training or physical exercises in the gym. A practical session on nutrition and cooking was also offered.

### Procedure

On the day of arrival at MBS, written information about the study, a written consent form and a questionnaire were delivered to the eligible participants. Consenting participants signed the consent form and completed the questionnaire before the program started the next day (T0). Those who completed the questionnaire at T0 received a follow-up questionnaire by mail with a pre-paid return envelope enclosed three months after the IEP (T1). A reminder was sent to those who did not return the questionnaire delivered at T1 within approximately three weeks.

### Measurements

All data were based on the participants responses to a questionnaire including instruments on fatigue, HRQOL, LPA and questions on demographic and medical variables.

## Fatigue

Fatigue was measured by the Fatigue Questionnaire (FQ) [16]. FQ consists of seven questions covering physical fatigue and four questions covering mental fatigue. Each question has four response alternatives scored from 0–3 (Likert scores), with higher scores indicating higher levels of fatigue. Summarized scores for physical fatigue range from 0 to 0–21 and from 0–12 for mental fatigue. Total fatigue is the sum of physical fatigue and mental fatigue and range from 0–33 [16]. The FQ has good to very good psychometric properties [17]. A clinically relevant change was defined as a change corresponding to 10% or more of the maximum score in each scale ( $\geq 3.3$  point-change in total fatigue,  $\geq 2.1$  point-change in physical fatigue and  $\geq 1.2$  point-change in mental fatigue) [18].

## HRQOL

HRQOL was assessed by the Medical Outcomes Study Short Form 36 (SF-36) version 1 [19]. SF-36 consists of eight scales; physical function, role limitations due to physical problems, bodily pain, general health, vitality, social function, role limitations due to emotional problems and mental health. The responses on each item within each scale were summed and transformed to 0–100 scales (0 = worst health state and 100 = best health state) [19]. SF-36 has shown to be a valid and reliable measure of self-reported health [20]. A change corresponding to 10% or more of the maximum score ( $\geq 10$  point-change) in each scale of SF-36 was defined as a clinically relevant change [21,22].

## LPA

LPA was assessed by the Nord-Trøndelag Health Study Physical Activity Questionnaire (HUNT 1 PA-Q) [23]. HUNT 1 PA-Q consists of three questions regarding frequency, duration and intensity in specific activities, e.g., outdoor walking, skiing, swimming or training. An index score was calculated based on the product of frequency, duration and intensity, giving a score from 0 (lowest LPA) to 15 (highest LPA). The HUNT 1 PA-Q has shown acceptable test-retest reliability in a Norwegian adult male population [23].

## Demographic and medical variables

Demographic variables included gender, age, partnership (living alone/living with a partner [married or cohabitant]), education ( $\leq 12$  y/ $>12$  y) and work status (full-time/part-time/retired/disability or social support).

Medical variables included type of cancer (prostate-, breast- or gastrointestinal cancer), time since diagnosis (months), type of treatment (non-systemic [surgery and/or radiotherapy]/systemic [chemotherapy and/or hormone therapy  $\pm$  surgery and/or radiotherapy]), relapse or progression of cancer before T0 (no/yes), comorbidity (no/yes) (defined as any long-lasting [ $>12$  months] physical and/or psychiatric condition which had led to reduced daily functioning).

Lifestyle variables included daily smoking (no/yes) and LPA (index score).

## Statistical analysis

Missing responses for Fatigue Questionnaire and SF-36 were substituted by the mean of those items present if at least half of the items from the scale were filled in. Differences in demographical, medical and lifestyle variables between completers and dropouts were analyzed by chi-square tests and independent sample *t*-tests. One-sample *t*-tests were used to analyze for differences in levels of fatigue and HRQOL between participants at the IEP and the NORMS (within females and males separately) [14,15]. Mean changes in fatigue, HRQOL and LPA from T0 to T1 were analyzed with paired sample *t*-test. For the outcomes that statistically significantly improved from T0 to T1, the proportions of participants with clinically relevant improvements were calculated. Univariate logistic regression analyses were used to evaluate demographic (age, partnership and education), medical variables (time since diagnosis, treatment, relapse/progression of cancer before T0 and comorbidity) and lifestyle variables (smoking and LPA) significantly associated with the clinically relevant improvements (versus no clinically relevant improvement). A *p* value less than .05 was considered statistical significant. Variables statistically associated with the outcome variables in the univariate analysis and the different baseline scores of the scales under examination were included as explanatory variables in the multivariate logistic regression analyses. Adjusted odds ratios (aOR) were presented with 95% confidence intervals (95% CI). The analyses were performed using SPSS version 21.0 for Windows (SPSS, Chicago, IL). Due to content wise overlap between the fatigue questionnaire and the vitality scale of the SF-36, only results from the fatigue questionnaire were used as outcome related to aim 3.

## Ethics

The study was approved by the South-East Regional Committee for Medical and Health Research Ethics (2010/1132a/REK South-East A) and the Institutional Review Board of Oslo University Hospital. Written consent forms were provided from all participants.

## Results

### Participants flow and characteristics at T0

Of all 482 invited individuals, 332 participants agreed to participate at T0, giving a study participation rate at baseline of 69%. A response rate at T1 of 235 of 332 evaluable participants completed the questionnaire at both T0 and T1, resulting in an overall participation rate at T1 of 49% (235 of 482). There was no difference in gender, age or time since diagnosis between those who completed both questionnaires and those who only completed at T0. A significantly higher portion of those who completed at both time points were

**Table 1.** Baseline characteristics of the participants.<sup>a</sup>

Variables	All participants	Females	Males	<i>p</i> Value
No. of participants	235	148	87	
<i>Demographical characteristics</i>				
Age (years)				
Median (range)	59.4 (30–83)	54.3 (30–74)	65.4 (43–83)	<.001 <sup>b</sup>
Living with a partner (married or cohabitant), <i>n</i> (%)	175 (75)	110 (75)	65 (76)	.9 <sup>c</sup>
Education >12 years, <i>n</i> (%)	133 (57)	89 (61)	44 (51)	.12 <sup>c</sup>
Work status, <i>n</i> (%)				
Full-time	37 (16)	20 (14)	17 (20)	<.001 <sup>c</sup>
Part-time	29 (13)	24 (17)	5 (6)	
Retired	60 (26)	19 (13)	41 (48)	
Disability benefit/social support	103 (45)	80 (56)	23 (27)	
<i>Medical characteristics</i>				
Cancer diagnosis, <i>n</i> (%)				
Breast cancer	133 (57)	133 (90)	0 (0)	
Prostate cancer	75 (32)	0 (0)	75 (86)	
Gastrointestinal cancer	27 (11)	15 (10)	12 (14)	
Months since diagnosis				
Median (range)	12.4 (2–119)	12.4 (4–91)	12.4 (2–119)	.48 <sup>b</sup>
Treatment, <i>n</i> (%)				
Non-systemic (surgery and/or radiotherapy)	61 (26)	17 (12)	44 (52)	<.001 <sup>c</sup>
Systemic (chemotherapy and/or hormone therapy +/- surgery and/or radiotherapy)	170 (74)	129 (88)	41 (48)	
Relapse/progression of cancer before T0, <i>n</i> (%)	25 (11)	10 (7)	15 (17)	.01 <sup>c</sup>
Comorbidity, <i>n</i> (%)	73 (31)	45 (31)	28 (33)	.71 <sup>c</sup>
<i>Lifestyle characteristics</i>				
Smoking, <i>n</i> (%)	28 (12)	14 (10)	14 (16)	.12 <sup>b</sup>
Physical activity score, mean (SD)	3.8 (2.8)	3.9 (2.8)	3.7 (3.0)	.65 <sup>d</sup>

<sup>a</sup>Numbers may be less than 235 because of missing data (range 229–235).

<sup>b</sup>Mann-Whitney test.

<sup>c</sup>Chi-square test.

<sup>d</sup>Independent *t*-test.

highly educated (57 vs. 44%,  $p = .03$ ), nonsmokers (12 vs. 21%,  $p = .03$ ) and the LPA was higher (3.8 vs. 2.8,  $p = .004$ ; data not shown). For all participants, median age at survey was 59.4 y (range 30–83), 75% were living with a partner, 57% had been diagnosed with breast-, 32% with prostate- and 11% with gastrointestinal cancer, respectively. Median time since diagnosis was 12.4 months (range 2–119) and 11% had experienced a relapse or progression of cancer before T0 (Table 1). Compared to the female participants, the males were older (65.4 vs. 54.3 y,  $p < .001$ ), a higher proportion had retired and had experienced a relapse or progression of cancer before T0 (48 vs. 13%,  $p < .001$  and 17 vs. 7%,  $p = .01$ , respectively). Female participants had more often received systemic treatment compared to male participants (88 vs. 48%,  $p < .001$ ; Table 1).

### Fatigue and health-related quality of life compared to NORMS

Compared to the NORMS, both the female and male participants reported significantly higher mean levels of physical-, mental- and total fatigue (Figure 1(a,b)) and lower levels on all SF-36 scales (Figure 1(c,d)) at T0 and T1,  $p < .05$  for all.

### Mean changes in fatigue, HRQOL and LPA from T0 to T1 among all participants and females and males separately

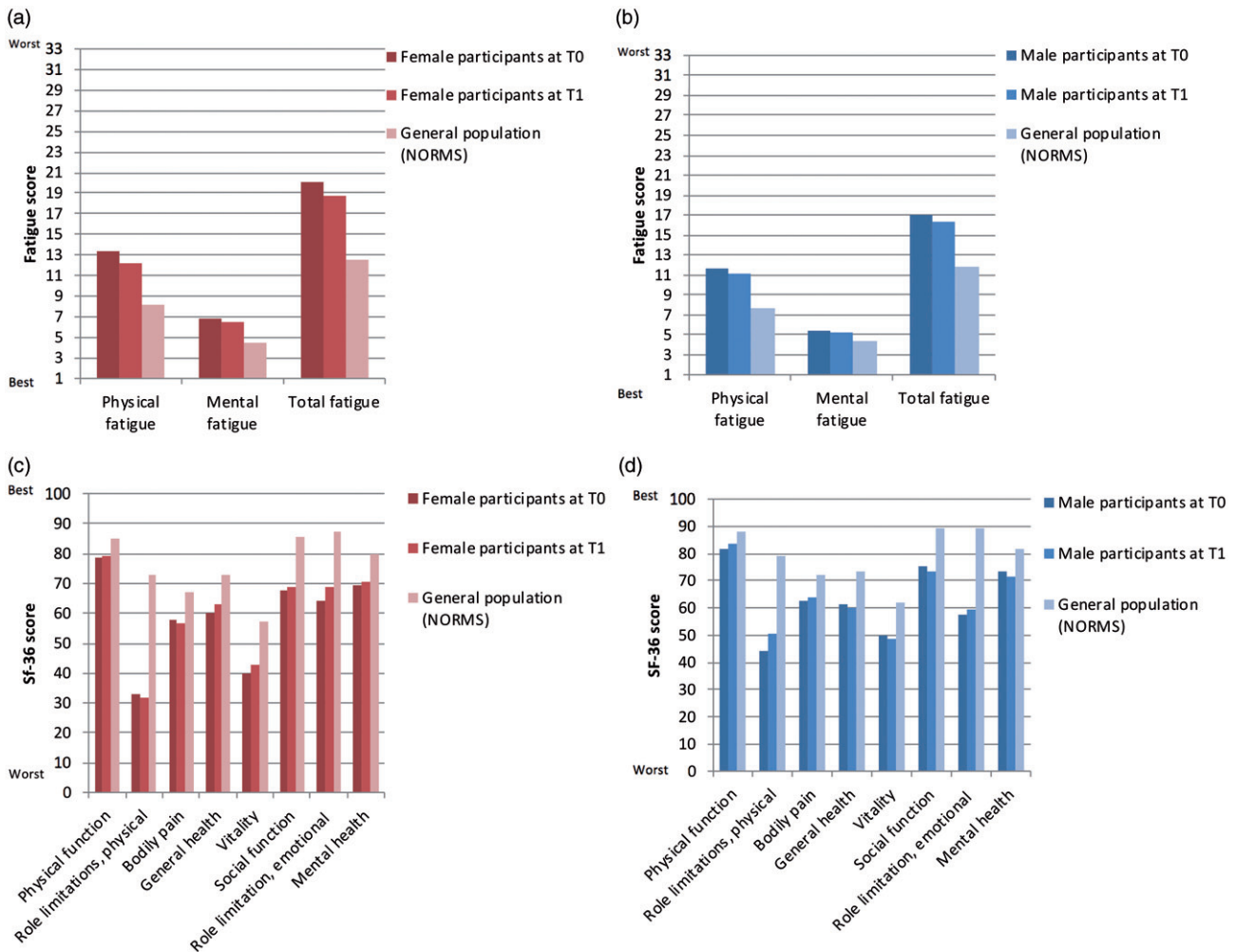
Among all participants combined, the mean physical fatigue score was reduced from 12.6 (SD 3.9) to 11.8 (SD 3.8;  $p < .001$ ), the mean mental fatigue score reduced from 6.3 (SD 2.2) to 6.0 (SD 2.2;  $p = .044$ ) and the total fatigue score

reduced from 19.0 (SD 5.3) to 17.8 (SD 5.4;  $p = .001$ ; Table 2). For the females separately statistically significant reductions from T0 to T1 were found for physical fatigue (–1.1 SD 3.8) and total fatigue (–1.4 SD 5.3), whereas no statistically significant changes were found in the levels of fatigue among the males (–0.4 SD 3.4 and –0.6 SD 4.4 for physical and total fatigue, respectively; Table 2).

No statistically significant changes in mean scores were found from T0 to T1 for any of the eight SF-36 scales or in self-reported LPA for both genders combined (Table 2). For the females separately, significant improvements of mean scores were found of the general health (3.4 SD 18.3) and vitality (3.1 SD 17.7) scales. Among the males, the mean score of the scale on role limitations due to physical problems, improved from T0 to T1 (7.4 SD 33.9; Table 2).

### Clinically relevant improvements in females and males separately and associated factors

Clinically relevant improvements were analyzed only for the outcomes which improved statistically significant from T0 to T1 in females and males separately (Table 2). Among female participants, 30% reported a clinically relevant improvement in physical fatigue, 28% in total fatigue and 36% in GH (Figure 2). In the univariate analyses among the female participants, high education [aOR 2.56; 95% CI (1.13–5.75),  $p = .023$ ] and relapse or progression of cancer before T0 [aOR 4.46; 95% CI (1.19–16.7),  $p = .027$ ] were associated with increased odds for clinically relevant improvement in total fatigue (Supplementary File 1). In multivariate analysis, adjusted for the total fatigue baseline score, none of these variables were associated with a clinically relevant



**Figure 1.** (a) Physical, mental and total fatigue score in female participants at T0 and T1 compared to the general population (NORMS). (b) Physical, mental and total fatigue score in male participants at T0 and T1 compared to the general population (NORMS). (c) SF-36 scale scores in female participants at T0 and T1 compared to the general population (NORMS). (d) SF-36 scale scores in male participants at T0 and T1 compared to the general population (NORMS). \*Significant differences between NORMS and female and male participants at T0 and at T1 (one sample t-tests),  $p < .05$ .

improvement in total fatigue. No sociodemographic- or medical variables were significantly associated with clinically relevant improvements in physical fatigue and GH in the univariate analysis (Supplementary Files 2 and 3).

In male participants, 31% had a clinically relevant improvement in role limitations due to physical problems (Figure 2). No sociodemographic or medical variables were significantly associated with clinically relevant improvement in the univariate analysis (Supplementary File 4).

## Discussion

In the present study we showed that both female and male cancer survivors admitted in the IEP reported significantly higher mean levels of fatigue and poorer HRQOL at T0 and T1 compared to their NORMS [14,15]. For both genders combined physical-, mental- and total fatigue significantly improved from T0 to T1. Among female participants separately statistically significant improvements were found in physical and total fatigue, and the SF-36 scales general health and vitality. Male participants only improved in the

SF-36 scale on role limitations due to physical problems. Overall, more female participants had clinically relevant improvements than male participants after the IEP.

In line with a previous study we observed higher levels of fatigue and lower HRQOL at admission to an IEP compared to NORMS for both gender [24]. However, the levels of fatigue and HRQOL of male participants of the one-week IEP were closer to the level among NORMS than was the case for the female participants. These results indicate that the MBS has attracted participants who might experience a need for rehabilitation. Three months after end of the IEP the levels of fatigue were still higher and HRQOL poorer compared to the NORMS. These findings are in line with other recent findings in larger samples of cancer patients and cancer survivors and the most noticeable differences were found for role functioning, social functioning, fatigue and sleep loss [25].

Our results showed improvements in total fatigue including physical fatigue and mental fatigue among all participants. In line with our results, Bertheussen et al. [24] found improvements in fatigue after 3–4 week of inpatient rehabilitation. Contrary to our findings, Rottman et al. [13] and

**Table 2.** Changes in fatigue, health-related quality of life (HRQOL) and physical activity among all participants and among females and males separately.<sup>a</sup>

Variables	All participants (n = 235)				Females (n = 148)				Males (n = 87)										
	T0		T1		Change in score T0 to T1		T0		T1		Change in score T0 to T1		T0		T1		Change in score T0 to T1		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p Value*	
<b>Fatigue (FQ)</b>																			
Physical fatigue	12.6 (3.9)	11.8 (3.8)	-0.86 (3.7)	<.001	13.3 (3.7)	12.2 (3.6)	-1.1 (3.8)	<.001	11.5 (4.0)	11.1 (4.1)	-0.4 (3.4)	.25	11.5 (4.0)	11.1 (4.1)	-0.4 (3.4)	.25			
Mental fatigue	6.3 (2.2)	6.0 (2.2)	-0.26 (2.0)	.044	6.8 (2.3)	6.5 (2.4)	-0.3 (2.2)	.08	5.4 (1.6)	5.2 (1.7)	-0.2 (1.5)	.31	5.4 (1.6)	5.2 (1.7)	-0.2 (1.5)	.31			
Total fatigue	19.0 (5.3)	17.8 (5.4)	-1.1 (5.0)	.001	20.1 (5.2)	18.7 (5.3)	-1.4 (5.3)	.001	16.9 (4.9)	16.3 (5.3)	-0.6 (4.4)	.2	16.9 (4.9)	16.3 (5.3)	-0.6 (4.4)	.2			
<b>HRQOL (SF-36)</b>																			
Physical function	79.9 (19.0)	81.1 (17.8)	1.2 (12.3)	.13	78.5 (18.0)	79.3 (16.5)	0.8 (12.9)	.47	82.5 (20.7)	84.5 (19.6)	2.0 (11.2)	.10	82.5 (20.7)	84.5 (19.6)	2.0 (11.2)	.10			
Role limitations: physical	36.9 (40.8)	38.9 (40.8)	2.0 (37.8)	.41	32.9 (40.0)	31.8 (38.8)	-1.1 (39.7)	.74	43.9 (41.3)	51.3 (41.4)	7.4 (33.9)	.046	43.9 (41.3)	51.3 (41.4)	7.4 (33.9)	.046			
Bodily pain	59.8 (25.9)	59.4 (24.8)	-0.4 (21.6)	.78	58.0 (25.5)	56.9 (23.1)	-1.1 (21.9)	.55	62.9 (26.5)	63.7 (27.0)	0.8 (21.1)	.74	62.9 (26.5)	63.7 (27.0)	0.8 (21.1)	.74			
General health	60.3 (21.7)	62.0 (22.9)	1.7 (17.8)	.14	59.8 (21.3)	63.2 (22.6)	3.4 (18.3)	.026	61.0 (22.3)	59.9 (23.2)	-1.1 (16.5)	.54	61.0 (22.3)	59.9 (23.2)	-1.1 (16.5)	.54			
Vitality	43.5 (21.0)	44.9 (20.8)	1.4 (17.1)	.21	39.5 (20.2)	42.6 (19.0)	3.1 (17.7)	.037	50.3 (20.7)	48.9 (23.1)	-1.4 (15.8)	.41	50.3 (20.7)	48.9 (23.1)	-1.4 (15.8)	.41			
Social function	70.5 (22.4)	70.6 (23.6)	0.1 (19.6)	.93	67.6 (21.2)	68.8 (21.8)	1.3 (19.5)	.43	75.4 (23.7)	73.6 (26.3)	-1.8 (19.9)	.38	75.4 (23.7)	73.6 (26.3)	-1.8 (19.9)	.38			
Role limitations: emotional	61.6 (41.7)	65.3 (41.6)	3.8 (44.8)	.21	63.9 (42.1)	69.0 (40.3)	5.1 (48.0)	.20	57.5 (40.9)	58.9 (43.3)	1.4 (38.7)	.74	57.5 (40.9)	58.9 (43.3)	1.4 (38.7)	.74			
Mental health	71.1 (17.1)	70.9 (16.8)	-0.2 (13.6)	.84	69.5 (16.3)	70.6 (14.1)	1.2 (13.7)	.30	73.9 (18.1)	71.4 (20.7)	-2.5 (13.1)	.08	73.9 (18.1)	71.4 (20.7)	-2.5 (13.1)	.08			
<b>Physical activity (HUNTI PA-Q)</b>																			
Index score	3.7 (2.8)	3.7 (2.7)	0.04 (2.2)	.79	3.8 (2.7)	3.6 (2.4)	-0.2 (2.1)	.29	3.5 (2.8)	4.0 (3.0)	-0.5 (2.3)	.09	3.5 (2.8)	4.0 (3.0)	-0.5 (2.3)	.09			

<sup>a</sup>Numbers may be less than 235 (range 223–235), 148 for females (range 143–148) and less than 87 for males (range 80–87) because of missing data.  
 FQ: The Fatigue Questionnaire; SF-36: The Medical Outcomes Study Short Form 36; HUNTI PA-Q: Nord-Trøndelag Health Study Physical Activity Questionnaire.  
 \*Paired sample t-test were used for continuous variables.

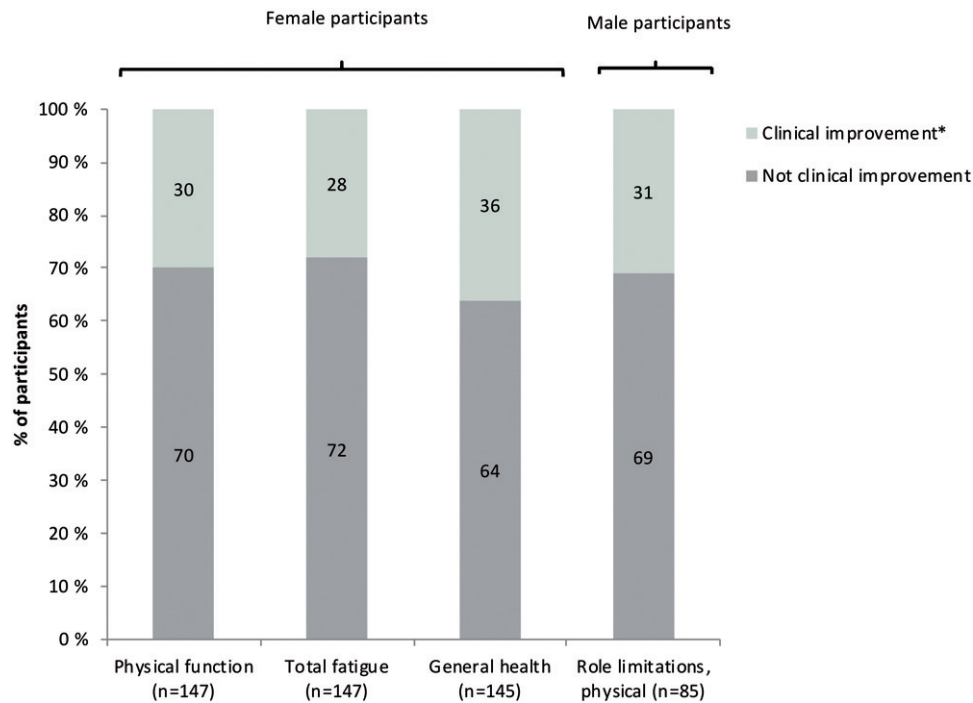
Ross et al. [26] found no positive effects on distress or well-being (including fatigue-related dimensions) after a comparable one-week IEP at 1-, 6- and 12-month follow-up compared to a control group. However, Rottman et al. [13] did not evaluate whether the changes over time within each group were significant. Their finding might be explained by the baseline scores were almost similar to the general the Danish population limiting the potential for improvement. The baseline scores of our population were significantly poorer than similar scores in the general Norwegian population thus allowing for potential effects of the IEP.

In analyses of each gender separately, the female participants experienced reductions in both physical and total fatigue, whereas among the male participants no significant changes were found. HRQOL among the female participants significantly improved in the general health and vitality scales, and the male participants improved in the role limitations due to physical problems scale. This might indicate that female participants are more prone to benefit from this specific IEP than male participants. Other possible explanations might be the skewed gender distribution of our sample (more females) or that the male participants had lower levels of fatigue and better HRQOL at admission to the IEP and therefore less potential to improve. Small improvement after rehabilitation found in some groups emphasizes the importance of screening for rehabilitation needs prior to admission to specialized rehabilitation programs. However, no recommendation which could guide evaluation of individual rehabilitation needs exist today.

Our findings indicate that around one third of the female participants experienced a clinically relevant improvement in physical and total fatigue as well as in general health. Further around one third of the male participants experienced a clinically relevant improvement in role limitations due to physical problems. Given the potential explanations for these findings stated previously, we still think this finding warrants further investigations. It might be that the content of the program is more in line with rehabilitation needs experienced by females.

Also to mention, given that HRQOL among cancer survivors may increase the longer it is since they were successfully treated, an increase observed during our study period could be partly due to this underlying trend. Hence, the effect of our intervention may be smaller than what we observed.

The results point to more focus to a gender-related adjustment of the content of the IEP and the content being more oriented towards the participants specific needs. For example, for female participants it might be useful to focus more on understanding fatigue and coping strategies for fatigue including psychological intervention (for e.g., cognitive behavioral, psychoeducational and mindfulness) and physical activity interventions (e.g. aerobic and resistance training) [27]. Perhaps a more physical approach to the male participants would be helpful, including 'walk-and-talk' instead of group sessions sitting in a room. We have previously found that prostate cancer patients were less likely to report need for supportive group sessions compared to



**Figure 2.** Proportion of female participants with a clinical improvement from T0 to T1 in physical and total fatigue as well as general health and proportion of male participants with a clinical improvement from T0 to T1 in role limitations and physical. \*Clinical improvement:  $\geq -2.1$  point on physical fatigue,  $\geq -3.3$  point on total fatigue,  $\geq 10$  point on general health, vitality and in role limitations, physical ( $>10\%$  of maximum scale).

breast cancer patients [10]. Wessels et al. [28] state that female cancer patients found support, counseling and rehabilitation more important than the male cancer patients did.

Lamprecht et al. [29] point out that at the start of a rehabilitation program prostate cancer patients report the greatest impairments in role physical function while for breast cancer patients the greatest impairment are in emotional functioning. It is also pertinent to remind about general rule of thumb that rehabilitation should be individualized which is not possible within the present organization of the IEP at the MBC. Also the importance of follow-up should be discussed in terms of conditions that can enhance the effect of the IEP. Scott et al summarize that at least one booster telephone call in addition to the intervention showed a positive significant difference regarding outcomes [11]. Practically, the latter could be organized as individual plans following the one-week IEP at MBC focused towards each participant's certain needs.

The cut-point used (a change of at least 10% or more of the maximum score of each scale) to calculate a clinically relevant change in our study is one option suggested in the literature [22]. According to Osoba et al. [21] several various approaches, using different HRQOL measures among different types of cancer, have resulted in similar answers. A change from 5–10% of the scale breadth is noticeable to patients as a meaningful change. We could also have used change directly without dividing into two groups, which are analyses that would use more of the information gathered on change. Given our intention of directly studying what impacted a clinically relevant change, we chose to dichotomize change to be able to conclude on this specific research question.

Limitations to this study include lack of a control group, a limited number of males participating and the modest participation rate of 49% at T1. The differences in terms of time since diagnosis, extent of cancer, treatment received and health status is a limitation, but due to the referral patterns of the MBC this could not be changed up front to the present study. The majority of the participants were women treated for breast cancer and with high education and the generalization of the results is somewhat restricted to that. We are aware that the heterogeneity of the sample limits generalizability of our results to the broader population. The results of the study findings are valid for participants at the MBC and probably to a certain degree for other cancer patients/survivors with a self-reported need for rehabilitation. A limitation affecting the potential generalizability of our study is the lack of standardized NORMS data according to the age distribution of our sample. Strengths of the study are the use of validated and well-established instruments FQ and SF-36, a robust design and a well described population with a reduced subjective health (fatigue and HRQOL).

In conclusion, the participants in the IEP reduced their levels of fatigue and improved aspects of HRQOL, more often observed among female participants than among males. The results might point to a need for a gender-related adjustment of the content of the IEP and the content being more oriented towards the participant's specific needs. Because of the lack of a control group it is not possible to conclude whether the changes were due to the IEP or occurred by chance. Rehabilitation institutions should develop guidelines for referral of patients of needs which have the chance to improve. Furthermore, such institutions should have evaluation of the effects.

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