

**Quality of Life in Cancer Survivors After Participating in a Multidisciplinary
Rehabilitation Program: A Pre-Post study**

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202001489 Master thesis

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July 9, 2021

Abstract

Background: Cancer survivors struggle with many physiological and psychological complaints, such as fatigue, depression, and anxiety. These complaints strongly affect cancer survivors' quality of life (QOL). For this client base, the Roessingh clinic in Enschede offers a multidisciplinary rehabilitation program based on Acceptance and Commitment Therapy (ACT). The main goal was to determine whether QOL increased and whether depression, anxiety, and fatigue decreased over time for cancer survivors recruited over three years. In addition, the study explored whether depression, anxiety, and fatigue moderate QOL.

Methods: Forty-eight cancer survivors were allocated to the rehabilitation program by Roessingh. The study used a pre-posttest design with four assessments. Wilcoxon rank tests determined whether QOL, depression, anxiety and fatigue changed over time. In addition, a moderation analysis via *Process* provided information on whether depression, anxiety, and fatigue function as moderators. **Results:** Results showed that QOL scores improved significantly, and depression, anxiety and fatigue reduced significantly over time.

Furthermore, neither different levels of depression, anxiety, nor fatigue moderated QOL.

Limitations: The study lacks a control group and has high levels of fluctuations. Thus, results do not determine whether the treatment program effectively increases survivors' QOL.

Conclusions: Clinicians are encouraged to use a multidisciplinary treatment setting with

Acceptance and Commitment therapy components to improve cancer survivors' QOL.

However, the study design warrants further research, for example, by implementing a waitlist control group or comparing the rehabilitation program to a monodisciplinary rehabilitation program.

Keywords: cancer survivor, multidisciplinary treatment, acceptance and commitment therapy, quality of life assessment, moderation analysis

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Introduction

Cancer is a highly prevalent disorder and a leading cause of death. In 2020, 9.95 million people worldwide died on the grounds of unsuccessful cancer treatment (WHO, 2021). In Europe, with 132.000 new cancer cases reported in 2020 alone, the Netherlands has the third highest cancer rate regarding its population size (Globocan, 2020). In general, the Dutch population is getting older, especially females and citizens of the provinces Flevoland, Limburg and North Brabant (Centraal Bureau voor de Statistiek, 2020a, 2020b; van de Poll-Franse et al., 2004). In addition, older people are more at risk to receive a cancer diagnosis with an average age of 69 years (Nederlandse Kankerregistratie (NKR), 2021). In that regard, van de Poll-Franse and colleagues (2004) assumed an increase in cancer patients due to the rising number of senior citizens. While this source of evidence is frightening, it is fortunate that an increasing amount of patients referred to as *cancer survivors* withstand this disease due to new technology and treatment instruments. Notably, the number of cancer survivors ascended significantly since 1990, with more than 62% of Dutch patients experiencing a successful cancer treatment in 2020 (Globocan, 2020).

As a consequence of the late onset of disease, the aging Dutch population, and the increased number of cancer survivors, one could easily assume that survivors have also become, on average, older. Thereby, it is essential to acknowledge that patients at an older age face additional comorbidities due to the aging process itself (Leach et al., 2016; van de Poll-Franse et al., 2004). Concerning this development, Mandelblatt and colleagues (2020) argued that older cancer survivors struggle with a higher symptom burden compared to a control group. However, other researchers showed that younger cancer survivors also experienced a higher symptom burden (Esser et al., 2020; Mao et al., 2007). Hence, there is little consensus among experts. More information will be needed to determine if cancer survivors are indeed becoming older and, as a consequence, experience a higher symptom burden because older survivors are more likely to suffer age-related comorbidities. Nevertheless, various cancer

survivors, independent of their age, experience negative consequences after successful cancer treatment because of their oncological experiences (Castellano-Tejedor et al., 2015; Eiser, 1998; Yoon et al., 2020).

Up to 20% of survivors report struggling with low levels of *quality of life* (QOL), which is defined by lower levels of mental health and well-being, as well as physical, psychological, and social difficulties after successful cancer treatment (Arch & Mitchell, 2016; Ganz, 2003; Huang et al., 2017; Hulbert-Williams et al., 2015; Kennedy et al., 2007; Lovelace et al., 2019; Lundh et al., 2013; Mackenzie, 2014; Raque-Bogdan et al., 2015; Runowicz et al., 2016; Schmidt et al., 2018; Seligman, 2011; Wenzel et al., 2002). Typical physical complaints are fatigue (prevalence rate = 28%), disturbance in sleep (prevalence rate = 11-34%), or weight changes (prevalence rate weight gain = 27-47%, prevalence rate weight loss = 32%) (Chen et al., 2010; Gaston-Johansson et al., 1999; Halbert et al., 2008; Jacobsen, 2007; Jacobsen et al., 1999; O'Neill, 1993; Slade et al., 2020; Strollo et al., 2020; Wenzel et al., 2002; Woodworth et al., 2017). Furthermore, psychological difficulties such as anxiety (prevalence rate = 17.9%) or depression (prevalence rate = 11.6%) are commonly experienced (Mitchell et al., 2013; Runowicz et al., 2016; Sellick & Crooks, 1999; Wenzel et al., 2002). Problems at work or within the social environment are examples of cancers' social challenges (Blaney et al., 2013; Effinger et al., 2019; Lee et al., 2020; Reid-Arndt et al., 2009; Reuter-Lorenz & Cimprich, 2013). The sum of all experienced symptoms represents the overall symptom burden and is defined by the term *severity of complaints* in the present study. Thus, the severity of complaints has an impact on survivors' QOL (Huang et al., 2017; Kennedy et al., 2007; Lovelace et al., 2019; Lundh et al., 2013; Mackenzie, 2014; Raque-Bogdan et al., 2015; Schmidt et al., 2018; Seligman, 2011).

Rehabilitation

A possibility to reduce the severity of complaints and increase QOL is to offer cancer survivors a form of a rehabilitation program. Rehabilitation programs should be developed based on well-defined care guidelines, which are recommendations to improve health care quality and safety. Furthermore, guidelines assist the translation of research findings into practice (Stout et al., 2021). Unfortunately, there is a lack of care guidelines for survivors' rehabilitation (Pace et al., 2016; Runowicz et al., 2016; Stout et al., 2021; Worku et al., 2017). Thus, several researchers concluded that the first step in establishing high-quality care guidelines is determining the most important goals for that treatment (Pace et al., 2016; Runowicz et al., 2016; Stout et al., 2021; Worku et al., 2017). According to multiple researchers, the two fundamental goals of rehabilitation programs are to reduce survivors' symptoms and enhance their QOL, preparing the patients to live with and beyond cancer (Runowicz et al., 2016; Stout et al., 2021). Runowicz and colleagues (2016) and Stout and colleagues (2021) recommend the inclusion of physical exercises, psychoeducation, psychotherapy, nutrition counselling, and, if required, pharmacotherapy within their care guidelines.

Multidisciplinary treatment programs comply with the care guidelines and are commonly used in cancer survivors rehabilitation (Hellbom et al., 2011; Ruiz-Vozmediano et al., 2020; Stout et al., 2021). Multidisciplinary treatment programs can be defined as an integrated approach that considers and incorporates all relevant treatment methods into an individual treatment plan (Silbermann et al., 2013; Victorian Government Department of Human Services, 2007). Fundamental is that professionals from various fields combine their expertise and discuss cancer survivors care needs and other impacting factors (Victorian Government Department of Human Services, 2007). Thus, multidisciplinary treatments combine, for example, medical, psychological, relaxational, nutritional and physical treatment options. Since patient's problems are often complex and multifactorial, multidisciplinary

programs appear to be valuable (Nienhuys et al., 2018; van de Poll-Franse et al., 2004). Further support comes from experimental research, which identified multidisciplinary treatment programs as the best method to increase cancer survivors QOL (Hellbom et al., 2011; Ruiz-Vozmediano et al., 2020).

Besides the use of multidisciplinary programs, monodisciplinary programs like *Acceptance and Commitment Therapy* (ACT), *Cognitive Behavior Therapy* (CBT) or *Physical Exercises* are also used for cancer survivor's rehabilitation (Fors et al., 2011; González-Fernández & Fernández-Rodríguez, 2019; Hulbert-Williams et al., 2015; May et al., 2008; Osborn et al., 2006; van Weert et al., 2008; Ye et al., 2018). Monodisciplinary programs use one treatment approach only and are provided by one specialized healthcare professional (Beck et al., 2019). Overall, monodisciplinary rehabilitation programs have been shown to be effective for cancer survivors' rehabilitation (González-Fernández & Fernández-Rodríguez, 2019; Korstjens et al., 2008; Mewes et al., 2012; Osborn et al., 2006).

For instance, several researchers concluded that ACT as a monodisciplinary rehabilitation program effectively reduces survivors symptoms and increases their QOL (Arch & Mitchell, 2016; Feros et al., 2013; Hulbert-Williams et al., 2015; Merikangas et al., 2007). ACT is a transdiagnostic, process-focused and flexible intervention, which could be used for a wide range of disorders (Arch & Mitchell, 2016). A cornerstone of ACT is the *Hexaflex model*. The model comprises six different components: i) being present, ii) defining valued direction, iii) committed action, iv) self as a process and context, v) cognitive defusing, vi) acceptance (Hulbert-Williams et al., 2015). The fundamental goal of ACT is to gain greater psychological flexibility, which leads to greater life satisfaction (Feros et al., 2013; S. C. Hayes et al., 2011). The goal of ACT can be achieved by accepting both positive and negative experiences made through a cancer diagnosis, by committing to meaningful behavior change that matches the patient's values (Greco et al., 2008; Rost et al., 2012; Stanton et al., 2007).

The reduction of symptoms comes as a by-product since the focus relies on accepting difficult experiences (Dimidjian et al., 2016; Feros et al., 2013). So far, both ACT, as a monodisciplinary program, and multidisciplinary treatment programs seem promising to effectively increase QOL and reduce the severity of complaints in cancer survivors (Arch & Mitchell, 2016; Feros et al., 2013; Hellbom et al., 2011; Hulbert-Williams et al., 2015; Ruiz-Vozmediano et al., 2020). However, it is not scientifically proven whether the combination of ACT and multidisciplinary treatment effectively increases QOL and reduces the severity of complaints of cancer survivors.

Another aspect that has not been investigated is whether cancer survivors with higher baseline scores of anxiety, depression or fatigue have lower QOL after the treatment than cancer survivors with low or medium anxiety, depression, or fatigue scores. Previous research concerning the relationship between anxiety, depression, fatigue, and QOL concluded that anxiety, depression, and fatigue positively correlate with each other and a lower QOL in cancer survivors (Brown & Roose, 2011; Nayak et al., 2017; Redeker et al., 2000; Schreier & Williams, 2004). Nevertheless, it is unclear whether the previously mentioned symptoms have a moderation effect on QOL.

Study aim

The first aim is to investigate whether there is a difference in age and severity of complaints among cancer survivors at intake. It is assumed that cancer survivors of the most recent year of recruitment are significantly older and experience more severe complaints compared to previous years because of three factors: the aging Dutch population, the increase of survivors and the late onset of the disease. In addition, the study aims to test the changes between pre-and post-test measurements of multidisciplinary treatment with ACT components on QOL, depression, anxiety, and fatigue. It is expected that QOL increases and that depression, anxiety, and fatigue decrease after the treatment. Furthermore, it is assumed that

cancer survivors scoring high on depression, anxiety, or fatigue experience lower levels of QOL compared to people scoring low or medium on depression, anxiety, or fatigue at the start of the treatment.

Method

Study design

A pre-posttest design was used to examine changes in QOL, depression, anxiety, and fatigue in cancer survivors (Figure 1). The study was carried out from 2017 till 2019 within an ambulant treatment at the Roessingh center in Enschede, the Netherlands. Thus, participants were recruited during that period. An ethical committee did not ethically approve the study. However, participants were fully informed before participation and signed informed consent (Appendix).

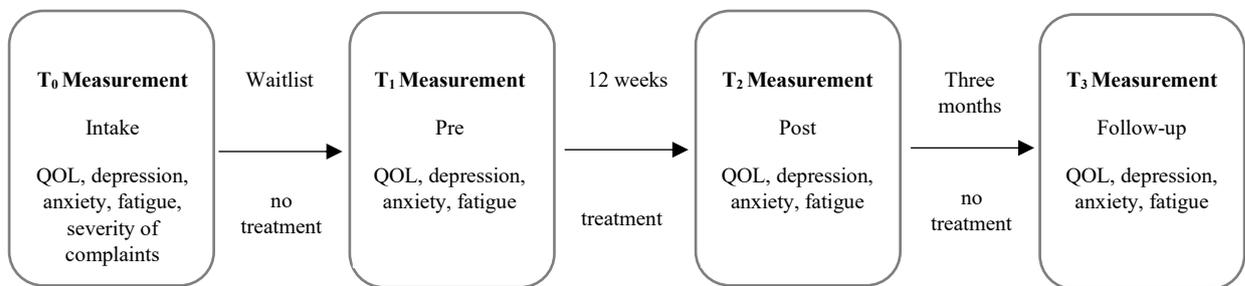


Figure 1. Flow chart of the different measurements and outcome measures used throughout the study

Procedure and participants

Over the three years, 155 cancer survivors were referred by their general practitioners to the rehabilitation program at the Roessingh center. At the initial assessment, prospective clients were informed by a psychologist and a rehabilitation doctor about the treatment and the study purposes. Afterwards, cancer survivors signed an informed consent and completed several screening questionnaires. However, due to low motivation or too severe physical or mental complaints, 73 cancer survivors were further excluded (Figure 2). Those clients were referred to the hospital or another mental health clinic. The remaining clients were assigned to a waitlist by the psychologist because treatment places were not directly available. Nineteen more cancer survivors were excluded because they either declined to participate ($n = 14$), passed away ($n = 3$) or gave other reasons not to participate ($n = 2$). When clients started the

treatment (T₁), they completed several questionnaires. The treatment lasted 12 weeks in total (for a detailed description, see rehabilitation treatment). After the treatment (T₂) and three months later (T₃), clients filled out questionnaires again. Unfortunately, 35 cancer survivors were unavailable for follow-up measurement.

The mandatory requirement for patients' inclusion into the analysis of the current study was completing the study until the post-treatment measurement (T₂). Hence, 64% of the data was excluded because these participants stopped before T₂. This exclusion criterion resulted in 15 cancer survivors who started the treatment in 2017. Five of them were male, and the mean age of cancer survivors in 2017 was 47.93 ($SD = 8.03$, range = 35 – 60). Furthermore, 18 cancer survivors were analyzed in 2018, of whom only three were male. The mean age of cancer survivors in 2018 was 51.28 ($SD = 11.92$, range = 27 – 75). Lastly, in 2019, 15 clients were analyzed with a mean age of 49.73 ($SD = 9$, range = 33 – 64), with only two male participants.

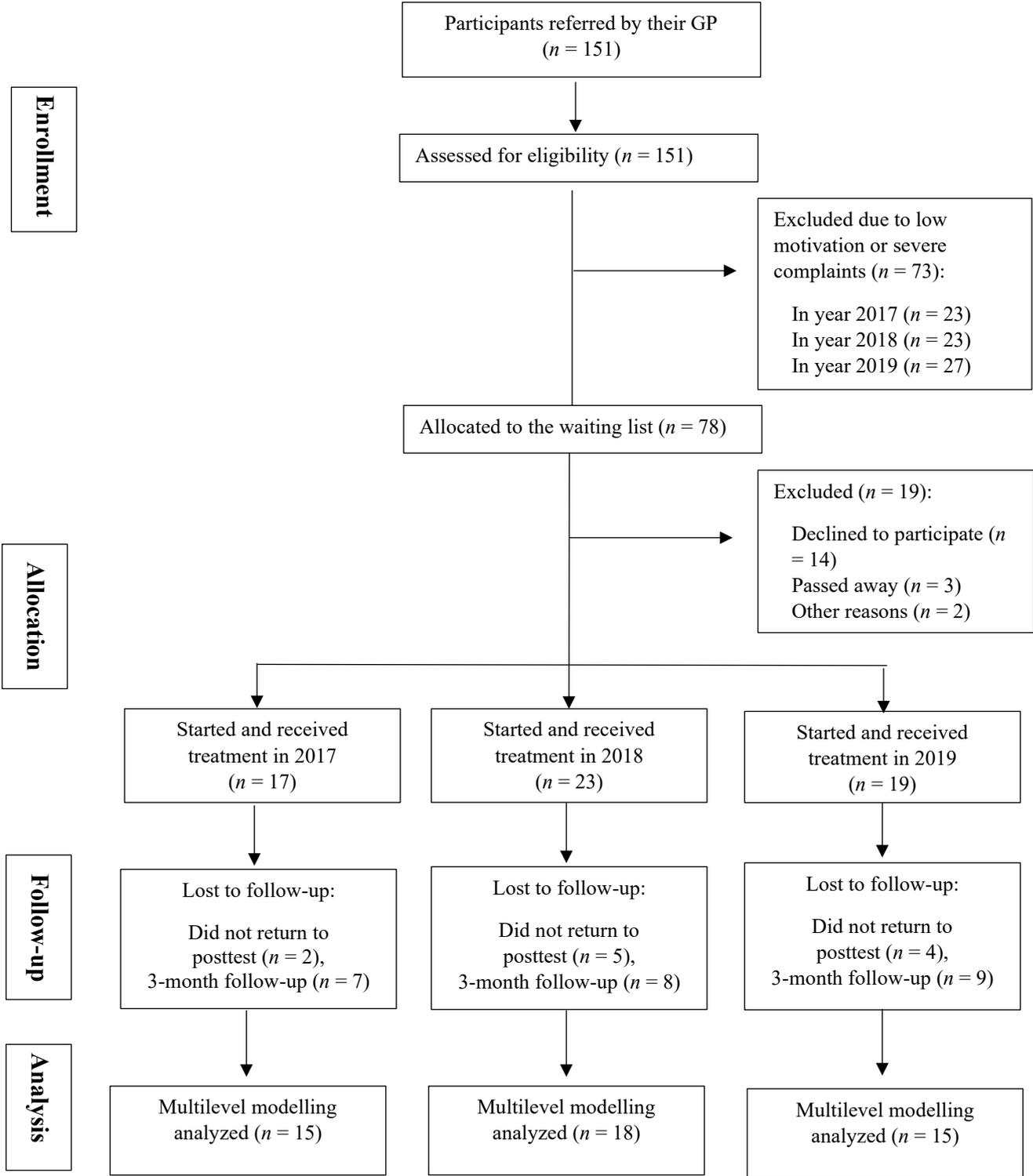


Figure 2. Participant flow chart through the clinical trial.

Materials

All questionnaires were administered in Dutch by Roessingh.

Primary outcome measure

Quality of life. The "European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30" is a 30-item questionnaire used to assess cancer patients' life quality and mental well-being (EORTC-30; Aaronson et al., 1993). The questionnaire contains multi-item scales and six single-item scales. However, the present study used only the two global health status questions because the focus of the hypothesis was on the overall QOL. Thus, participants rated the two global health status questions on a 7-point scale ranging from 1 (very poor) to 7 (excellent). These two global health status questions are: "How would you rate your overall health during the past week?" and "How would you rate your overall quality of life during the past week?". Higher standardized raw scores (0 - 100) indicated higher global health for cancer survivors. In general, the developer of the questionnaire determined acceptable to good internal reliability ($\alpha > 0.7$) and validity for the comprehensive questionnaire (Aaronson et al., 1993). The internal consistency of the two global health status questions for the present study was good on all measurement points ($\alpha_{T0} = 0.76$; $\alpha_{T1} = 0.78$; $\alpha_{T2} = 0.86$; $\alpha_{T3} = 0.83$).

Secondary outcome measures

Anxiety and Depression. The "Anxiety and Depression Inventory" (HADS; Zigmond & Snaith, 1983) was used to measure anxiety and depression in cancer survivors. The inventory consists of 14 Likert scale questions with subscales for anxiety and depression. Each subscale contains seven scale questions. Participants indicated their level of agreement with each statement on a 4-point scale ranging from 0 (strongly disagree) to 3 (strongly agree). Item 7 and 10 needed to be reverse-coded because these items were formulated negatively. Thereby, higher sum scores (0 - 21) indicated higher levels of anxiety and

depression. An example item for anxiety is "I feel tense", whereas an exemplary item for depression is "I can laugh and see things from the happy side". According to Zigmond & Snaith (1983), Cronbach's alpha was high (above 0.85) for each subscale, indicating good internal consistency. However, internal reliability was weak for the present study for anxiety ($\alpha_{T0} = 0.19$, $\alpha_{T1} = 0.16$, $\alpha_{T2} = 0.22$, $\alpha_{T3} = 0.36$) and, also for depression ($\alpha_{T0} = -0.25$, $\alpha_{T1} = 0.07$, $\alpha_{T2} = -0.47$, $\alpha_{T3} = -2.4$). In addition, Zigmond and Snaith (1983) concluded that the questionnaire is a valid measurement to test anxiety and depression.

Fatigue. The multidimensional fatigue index was used to assess fatigue (MFI-20; (Smets et al., 1995). This questionnaire is commonly used among cancer patients by practitioners. The questionnaire contains 20 Likert scale question with subscales for general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation. An example of general fatigue is "I felt tired". The participants indicated their level of agreement with statements on a 5-point scale ranging from 1 (Yes, that is true) to 5 (No, that is not true). Ten items, namely item 2, 5, 9, 10, 13, 14, 16, 17, 18 and 19, needed to be reverse-coded because they were phrased negatively. Higher sum scores (per scale: 4 – 20; complete: 20 – 100) indicated higher levels of fatigue. Cronbach's alpha was high (above .85) for each subscale, according to Smets and colleagues (1995). They also determined that the test is a valid instrument. However, the reliability of the present study was weak for general fatigue ($\alpha_{T0} = -0.08$, $\alpha_{T1} = -0.39$, $\alpha_{T2} = -0.03$, $\alpha_{T3} = -0.08$), weak to acceptable for physical fatigue ($\alpha_{T0} = -0.13$, $\alpha_{T1} = -0.55$, $\alpha_{T2} = -0.27$, $\alpha_{T3} = -0.26$), acceptable to good for reduction in motivation ($\alpha_{T0} = 0.24$, $\alpha_{T1} = 0.54$, $\alpha_{T2} = 0.77$, $\alpha_{T3} = 0.8$), good for reduction in activity ($\alpha_{T0} = -0.88$, $\alpha_{T1} = -1.03$, $\alpha_{T2} = -0.81$, $\alpha_{T3} = -1.09$), and weak for mental fatigue ($\alpha_{T0} = 0.23$, $\alpha_{T1} = 0.14$, $\alpha_{T2} = 0.15$, $\alpha_{T3} = -0.02$).

Severity of Complaints. The researcher assessed individual psychological problems using the Dutch version of the Symptom Checklist-90 (SCL-90; Arrindell & Ettema, 2003) The difference between the Dutch version and the original (American) version

developed by Derogatis and colleagues (1976) is that some items shifted scales (Arrindell & Ettema, 2003; Derogatis et al., 1976). Therefore, the used questionnaire comprises 90 questions with eight subscales. The subscales are: (a) *anxiety* (e.g. How much were you bothered by trembling?), (b) *agoraphobia* (e.g. How much were you bothered by feeling afraid in open spaces or on the streets?), (c) *depression* (e.g. How much were you bothered by low sexual interest or pleasure?), (d) *somatization* (e.g. How much were you bothered by headaches), (e) *cognitive-performance deficits* (e.g. How much were you bothered by having to do things very slowly to ensure correctness?), (f) *interpersonal sensibility* (e.g. How much were you bothered by feeling critical of others?), (g) *anger-hostility* (e.g. How much were you bothered by feeling easily annoyed or irritated?), (h) *sleep difficulties* (e.g. How much were you troubled by falling asleep?). Participants indicated their level of affection for each item on a 5-point scale ranging from 0 (not at all) to 4 (extremely), measuring how much they were affected by each item during the last week. Higher sum scores (Anxiety: 0 – 40; Agoraphobia: 0 – 28, Depression: 0 – 64; Somatization: 0 – 48 ; Cognitive-performance Deficits: 0 – 36; Interpersonal sensibility: 0 – 72 ; Anger-Hostility: 0 – 28; sleep difficulties: 0 – 12) indicated higher severity of complaints. Derogatis and colleagues (1976) determined good internal consistency for each subscale ($\alpha > 0.7$).

Rehabilitation treatment

The intervention followed a multidisciplinary treatment design, including elements of ACT. Therefore, participants had two weekly appointments throughout the 12 week intervention period at the Roessingh center. In detail, seven professions were included in the treatment: an occupational therapist, a psychologist, a doctor, a physiotherapist, a social worker, a sports trainer, and a nutritionist. In addition, this interdisciplinarity treatment was composed of seven different modules: i) the psychoeducation module, ii) the work module iii) the coaching and energy module, iv) individual therapy module v) the physical exercise module, vi) physiotherapy module and vii) the nutrition module (Figure 3). Table 1 provides

an overview of all modules, the duration, and the discussed topics. All modules took place within a group setting besides individual therapy and the nutrition module.

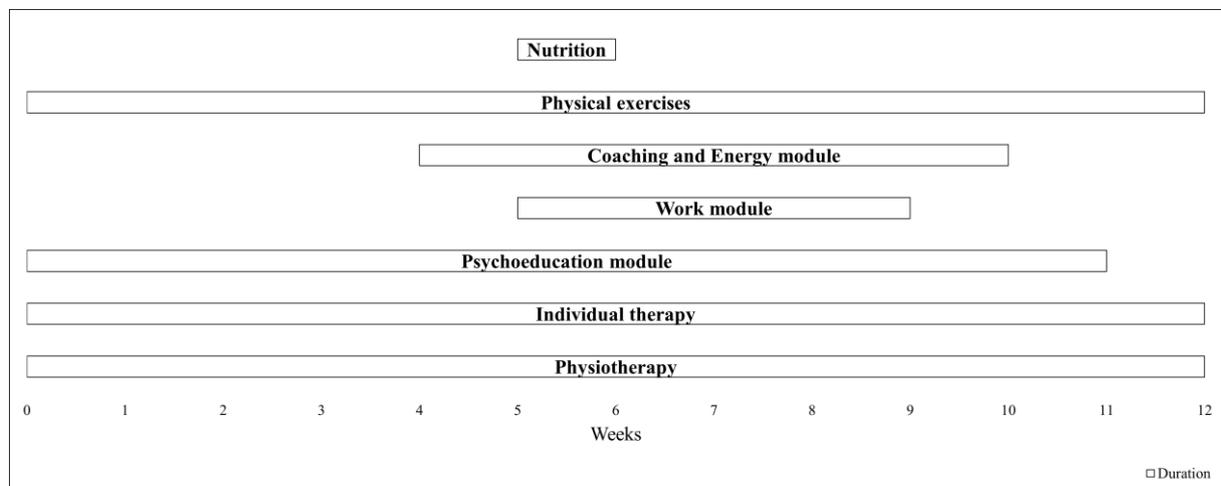


Figure 3. The figure visualizes the seven different treatment modules and their duration over the treatment process

Table 1

Multicomponent treatment overview with topics and duration of the seven modules

Module	Topics	Duration in hours (h)
Psychoeducation module	Rehabilitation and resilience Consequences of surviving cancer The meaning of physical exercises and having an active lifestyle Dealing with emotions Finding a balanced lifestyle	18
Work module	Re-entry into employment Employees' rights Employees' responsibilities	4
Coaching and energy module	Detecting problems and patterns/mechanisms of their daily activities Finding new coping strategies	6
Individual therapy	Patient's emotions concerning cancer and the recovery progress based on Acceptance and Commitment therapy	12

	Individual topics	
Physical exercise module	Diverse sports (swimming walking)	30
Physiotherapy	Relaxation techniques	12
	Mindfulness-training	
	Classical physiotherapy/exercises	
Nutrition module	Adiposity	1
	Underweight	
	Nutrition	
	Development of an eating schedule	

Overall, the therapy is based on ACT. Therefore, the goal of each module was to learn to accept the disorder and shortcomings by gaining awareness of these at first and then discovering a new way to live with the experienced complaints. Consequently, cancer survivors learned to accept their feelings and reevaluated the changes due to these complaints. Therefore, the focus of the therapy was on the positive aspects and ways to achieve a happier life again.

A variety of topics was treated within the seven modules of the rehabilitation program. Thereby, participants did not have any homework assignments, but it was expected that they actively participated during the therapy sessions. During the psychoeducation, the work and the coaching and energy module, cancer survivors worked together with a therapist to learn about diverse cancer and health-related topics. Thus, the therapist provided more detailed information concerning different topics and aspects of the disease and life afterwards. In addition, clients also independently elaborated the topics under the guidance of a therapist. For example, clients shared their experienced difficulties and searched for alternative coping strategies. Resulting from the gained knowledge, clients, for example, independently developed a weekly activity plan. The physical exercise module and the physiotherapy required active physical participation. Hence, cancer survivors performed various sports like

running or swimming during physical exercise. In contrast, during the physiotherapy, participants learned various relaxation techniques and performed classical physiotherapy exercises. The nutrition and individual therapy module were constructed more flexible and on an individual basis. Thus, specific topics and obstacles were discussed during a one-on-one session.

Data analysis

The statistical program IBM SPSS Statistics 24 was used to perform all analyses. To assess whether the three years of recruitment differentiate in age and severity of complaints based on the SCL-90 at intake, descriptive statistics and a Kruskal-Wallis test were used. Thereby, Dunn's post hoc test with a Bonferroni was implemented. A one-way ANOVA was not used because the normality assumption was not fulfilled. Furthermore, one outlier was detected, which was removed. Age and the outcomes of the nine subscales of the SCL-90 were used as the test variables. The year of recruitment was the grouping variable.

Changes in QOL, depression, anxiety and fatigue were analyzed using a series of paired-sample t-tests. In order to perform this analysis, the following assumptions had to be met, namely: i) paired observation, ii) the dependent variable is measured on a continuous scale, iii) no significant outliers in the difference between the two related groups, and iv) the difference should be normally distributed. Because the normality assumption was violated, the nonparametric Wilcoxon signed-rank test was performed instead of paired-sample t-tests. Furthermore, detected outliers were removed.

Moderation analyses were performed using the PROCESS tool (version 3.5) in SPSS, of which its macro was developed by A. F. Hayes (2013). Results were computed using model 1, with a 95% CI, using 5000 bootstrap samples. In the analyses, QOL at post-test assessment (T_2) was the dependent variable (Y), and QOL at pre-test assessment (T_1) was the independent variable (X). The potential moderators, depression, anxiety, and fatigue, were

separately entered as categorical moderator variables (W). Important to acknowledge, depression, anxiety, and fatigue have been transformed into categorical variables beforehand, with cut-off scores at 8 and 12 for depression and anxiety and cut-off scores at 44 and 61 for fatigue (Andic et al., 2020; Bjelland et al., 2002). Since only two participants belonged to the group "low level of fatigue", with a score of 40 and 44, the sample was too small for further analysis. Therefore, the lower cut-off score of fatigue was decreased [low = 0 – 39; medium = 40 – 60; high = 61 – 100]. Consequently, the moderator fatigue was dichotomous. For the analysis, low anxiety, low depression, and medium fatigue were the reference categories.

Results

Year of recruitment differences

Cancer survivors of 2018 were slightly older ($M = 51.28$, $SD = 11.92$) than cancer survivors in 2017 ($M = 47.93$, $SD = 8.03$) and 2019 ($M = 49.73$, $SD = 9$) but the difference was not significant, $p = 0.574$. Additionally, cancer survivors of the three years of recruitment also did not significantly differ in severity of complaints based on the SCL-90 at intake (Table 2). The three year-groups sample size was too small for further in-depth comparison.

Therefore, the remaining analyses were conducted on the total sample.

Table 2.

Sociodemographic Characteristics of Participants and difference between the three recruitment years based on the SCL-90 at Intake

	Recruitment year 2017 ($n =$ 15)	Recruitment year 2018 ($n =$ 18)	Recruitment year 2019 ($n =$ 14)	Chi- square	p
Age, M (SD)	47.93 (8.03)	51.28 (11.92)	49.73 (9)	1.1	0.574
Severity of complaints, M (SD)					
Anxiety	19.13 (7.45)	17.5 (3.9)	19.71 (7.45)	0.30	0.860
Agoraphobia	9.2 (2.57)	8.61 (2.03)	11.07 (5.21)	1.54	0.463
Depression	34.33 (10.31)	34.72 (8.82)	34.36 (10.68)	0.25	0.885
Somatization	24.8 (7.65)	26.94 (6.12)	25.64 (7.48)	0.96	0.620
Cognitive- performance deficits	22.93 (6.39)	22.89 (6.49)	22.14 (5.43)	0.11	0.947
Interpersonal sensitivity	25.67 (6.17)	29.28 (8.83)	24.14 (5.1)	3.4	0.183
Anger-hostility	9.27 (3.47)	8.67 (2.68)	7.93 (1.73)	0.68	0.713
Sleep difficulties	8.67 (3.81)	8.44 (3.49)	9 (3.7)	0.25	0.885

Additional items	14.27 (4.56)	14.39 (3.6)	13.79 (3.19)	0.26	0.880
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Pre- to Post differences

Multiple Wilcoxon signed-rank tests were completed to analyze pre-post changes in QOL, anxiety, depression, and fatigue. Results indicated an increase in QOL after the treatment and a decrease in anxiety, depression, and fatigue (Table 3, Figure 4 - 7).

Table 3

Pre- Post-test difference in Quality of Life, Anxiety, Depression and Fatigue

	Intake (T ₀) <i>M (SD)</i>	Pre-test (T ₁) <i>M (SD)</i>	Post-test (T ₂) <i>M (SD)</i>	Three months follow-up (T ₃) <i>M (SD)</i>
Quality of life	57.04 (16.57)	58.33 (15.59)	68.70 (20.88)	69.44 (17.74)
Anxiety	8.29 (3.86)	9.24 (3.39)	7.13 (3.96)	6.82 (4.34)
Depression	6.53 (3.53)	7.2 (3.51)	5.33 (3.45)	5.32 (4.2)
Fatigue	69.43 (7.99)	68.64 (6.84)	62.21 (8.87)	59.6 (9.49)

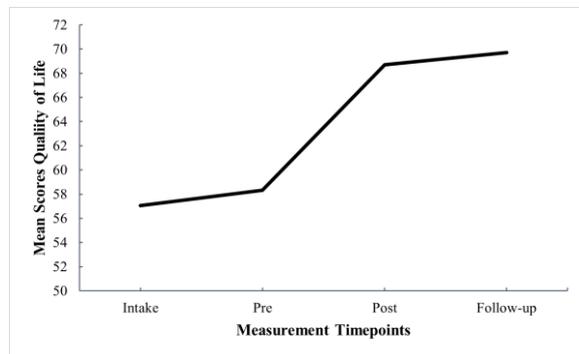


Figure 4. Development of quality-of-life over the study.

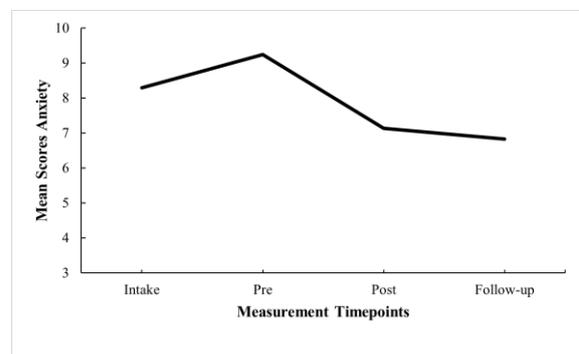


Figure 5. Development of anxiety over the study.

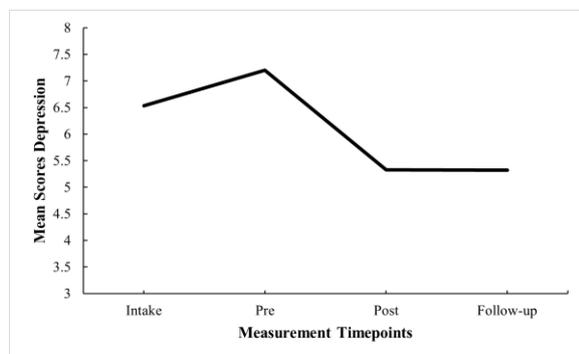


Figure 6. Development of depression over the study.

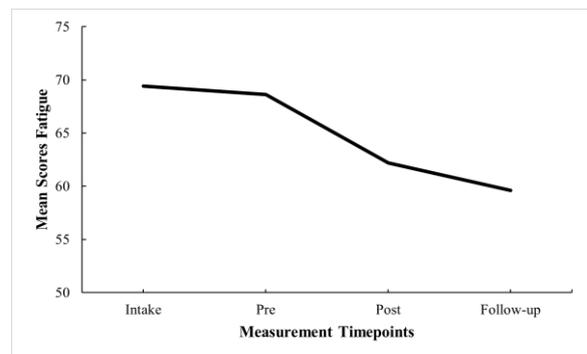


Figure 7. Development of fatigue over the study.

Table 4 provides an overview of all Wilcoxon signed rank tests that were conducted. On average, cancer survivors experienced a significant change from pre- to post-test in QOL, $z = -3.42, p = 0.001$, anxiety, $z = -3.93, p < 0.001$, depression, $z = -3.57, p < 0.001$, and fatigue, $z = -3.82, p < 0.001$. Hence, QOL increased, and anxiety, depression and fatigue decreased significantly. In addition, QOL scores on average also increased significantly between intake and post-test assessment, $z = -3.86, p < 0.001$, while anxiety, $z = -2.28, p = 0.023$, depression, $z = -2.34, p = 0.019$, and fatigue, $z = -4.02, p < 0.001$ decreased significantly within this time frame. In addition, significant improvements were also found for QOL, $z = -2.71, p = 0.007$, anxiety, $z = -3.65, p < 0.001$, depression, $z = -3.26, p = 0.001$, and fatigue, $z = -3.27, p = 0.001$ between pre-test assessment and three months follow-up. Furthermore, QOL, $z = -2.87, p = 0.004$, depression, $z = -2.38, p = 0.017$ and fatigue $z = -3.34, p = 0.001$ changed significant between intake measurement and three months follow-up while anxiety did not change significant, $z = -1.57, p = 0.118$). Lastly, there was also a significant change in anxiety, $z = -2.25, p = 0.025$ and depression, $z = -2.27, p = 0.024$ between intake measurement and pre-test.

Table 4

Wilcoxon signed-rank tests

	Intake vs Pre-test	Intake vs Post-test	Intake vs Three months follow-up	Pre-test vs Post-test	Pre-test vs Three months follow-up	Post-test vs Three months follow-up
Quality of life	-0.34 ns	-3.86***	-2.87**	-3.42**	-2.71**	-1.15 ns
Anxiety	-2.25*	-2.28*	-1.57 ns	-3.93***	-3.65***	-0.2 ns
Depression	-2.27*	-2.34*	-2.38*	-3.57***	-3.26**	-0.57 ns
Fatigue	-1.34 ns	-4.02***	-3.34**	-3.82***	-3.27**	-1.62ns

Note. * $p < .05$, ** $p < 0.01$, *** $p < .001$, ns = not significant

Moderation analysis

Results of the three moderation analysis revealed no significant interaction effects between any of the categorical moderators, anxiety, depression, fatigue, and QOL at pre-treatment assessment (Anxiety: $F(2, 42) = 0.14, p = 0.871, R^2 = 0.005$; Depression: $F(2, 42) = 0.28, p = 0.755, R^2 = 0.011$; Fatigue: $F(1, 41) = 0.1, p = 0.748, R^2 = 0.002$). Table 5 provides an overview of all interactions between QOL at pre-test and the various moderators. Important to acknowledge, low levels of anxiety and depression and medium levels of fatigue were the reference categories. In particular, there was no significant interaction between medium anxiety and QOL at pre-test. This outcome means that there is no difference in regression slopes for QOL between persons in the high anxiety group and the low anxiety group ($B = 0.03, CI(-0.75, 0.8), p = 0.947$). Similarly, no significant interaction was found for high anxiety and QOL at pre-test, which indicates no difference in regression slopes for QOL between persons in the medium and the reference anxiety group ($B = 0.25, CI(-0.74, 1.24), p = 0.611$). Additionally, no significant interaction for medium depression and QOL at pre-test ($B = 0.18, CI(-0.75, 1.12), p = 0.697$) nor high depression and QOL at pre-test ($B = 0.45, CI(-0.85, 1.75), p = 0.486$) were found, indicating that there is no difference between persons in the high, medium, and low depression group. Lastly, there was also no interaction effect of high fatigue and QOL at pre-test ($B = 0.13, CI(-0.71, 0.98), p = 0.748$), meaning that there is no difference in QOL between persons in the high fatigue group and the medium fatigue group.

Table 5.

Moderation analysis: Anxiety, Depression, Fatigue and Quality of Life at Pre-Test on Quality of Life at Post-Test

Moderators	<i>B (SE)</i>	95 % <i>CI</i>	<i>p</i>	<i>R</i> ²
Anxiety				0.005
Medium anxiety	0.03 (0.38)	-0.75 – 0.80	0.947	
High anxiety	0.25 (0.49)	-0.74 – 1.24	0.611	
Depression				0.01
Medium Depression	0.18 (0.46)	-0.75 – 1.12	0.697	
High Depression	0.45 (0.64)	-0.85 – 1.75	0.486	
Fatigue				0.002
High Fatigue	0.13 (0.42)	-0.71 – 0.98	0.748	

Note. *B* is the unique contribution of the interaction item (moderator x quality of life at pre-test assessment) in the prediction of the QOL at post-test assessment; Low anxiety, low depression and medium fatigue were the reference categories.

Discussion

The study's first aim was to investigate whether cancer survivors differ in age and severity of complaints based on the SCL-90 at intake. Results determined that there was no difference among cancer survivors in terms of age and severity of complaints. Consequently, results indicated that each year of recruitment had similar characteristics and preconditions. Thereby, the previous hypothesis that cancer survivors are becoming older because of the aging Dutch population, the late onset of the diagnosis, and an increase in cancer survivors have not been shown to be the case (Globocan, 2020; Nederlandse Kankerregistratie (NKR), 2021; van de Poll-Franse et al., 2004). Since no difference in age was found, it is not surprising that cancer survivors did not differ in terms of symptom burden as a consequence of age-related comorbidities (Leach et al., 2016; van de Poll-Franse et al., 2004). Nevertheless, Mandelblatt and colleagues (2020) showed that older cancer survivors struggle with a higher symptom burden compared to a control group in their randomized-control (RCT) study. In contrast to the present study, Mandelblatt and colleagues (2020) examined only breast cancer survivors who were all older than 60 (range 60 to 98). Since cancer survivors of the present study were, in comparison, much younger, this might explain why Mandelblatt and colleagues (2020) could find a difference in symptom burden while the present study could not. Contrasting, Mao and colleagues (2007) determined that cancer survivors who were younger than 50 experienced a higher symptom burden compared to cancer survivors older than 64. Nevertheless, they did not collect the data themselves but used a national health interview survey, which included 1904 cancer survivors and approximately 2900 participants without a history of cancer. Furthermore, while they stated that younger participants are more affected through experiencing ongoing symptoms compared to older survivors, they did not determine whether the difference was significant. Lastly, Mao and colleagues (2007) only investigated pain, insomnia and distress. Consequently, there was little consensus among researchers on whether older or younger cancer survivors have a higher

symptom burden and lower QOL. However, both, Mandelblatt and colleagues (2020) and Mao and colleagues (2007) agree that age does appear to influence the severity of complaints. A result that is in line with other studies as well (Brown & Roose, 2011; Dunn et al., 2013). To date, no study was found which examined a possible increase in symptom burden over the years. Hence, the present study was the first study, to our knowledge, which investigated whether cancer survivors differ in their symptom burden over the years. Notwithstanding, the present study was not able to reveal the trend of cancer survivors getting older and neither determined a change in symptom burden over the years. Instead, the present study supports the idea that there is no difference in cancer survivor's symptom burden over time.

The second aim of the study was to describe changes in QOL, depression, anxiety, and fatigue over the research period. The study results confirmed that QOL increased from pre- to post-test assessment, between intake and post-test assessment, and between pre-test to three-month follow-up. In addition, depression, anxiety, and fatigue decreased in between those timeframes as well. Lastly, results also showed that QOL increased between intake and three-month follow-up, while depression and fatigue decreased during this time interval. Consequently, QOL increased, and anxiety, depression and fatigue decreased after participating in a multidisciplinary treatment program based on ACT. Previous research showed that cancer survivors QOL increased after participating in a rehabilitation program. For example, Osborn and colleagues (2006) showed that CBT, as a monodisciplinary rehabilitation program, can effectively increase QOL and reduce depression and anxiety in cancer survivors. Yet, Osborn and colleagues (2006) study differ from the present study because Osborn and colleagues (2006) conducted a meta-analysis for monodisciplinary rehabilitation programs. The present study, on the contrary, used a pre-post design to examine the effect of a multidisciplinary program based on ACT. Nonetheless, both studies examined cancer survivors diagnosed with different cancer types and determined an improvement in QOL and symptom burden. Other researchers also showed that ACT, as a monodisciplinary

rehabilitation program, can also effectively decrease anxiety, depression, fatigue and pain and increase vitality (QOL) in cancer survivors (Arch & Mitchell, 2016). Likewise, as in the present study, Arch and Mitchell (2016) examined the intervention on a group-based level and also studied cancer survivors with different cancer types. Furthermore, they used a similar study design, namely a multiple baseline, single-arm design. However, Arch and Mitchell (2016) examined ACT as a monodisciplinary program while the present study's rehabilitation program was only based on ACT. A similar conclusion was gained on the basis of González-Fernández and Fernández-Rodríguez (2019) RCT study, which showed that the ACT administrated on a group-therapy basis was effective in decreasing depression and anxiety and increasing activation compared to the control group. The study design allowed González-Fernández and Fernández-Rodríguez (2019) to conclude that ACT is an effective program for cancer survivors while the present study cannot determine that the treatment was responsible for the positive change because of the absence of a control group. Till now, it appears that monodisciplinary treatment programs seem promising in increasing QOL and reducing the symptom burden for cancer survivors.

Nevertheless, other researchers have also shown the effectiveness of multidisciplinary treatment programs to increase QOL and reduce the symptom burden in cancer survivors. For example, Ruiz-Vozmediano and colleagues (2020) determined that an integrative dietary, physical activity, and mindfulness program enhance the QOL in breast cancer survivors. In contrast to the present study, Ruiz-Vozmediano and colleagues (2020) used an RCT study design which is why they were able to show the effectiveness of a multidisciplinary program. However, they only examined breast cancer survivors, the program lasted six months, and the program was not based on ACT. In addition, they also did not investigate the effect of their program on the symptom burden. Similar conclusions were found in a study by van Weert and colleagues (2005). They examined the effectiveness of a 15-week long multidisciplinary rehabilitation program consisting of individual exercise, sports, psychoeducation, and an

information program for different types of cancer survivors. In particular, they concluded that cancer survivors of the treatment group experienced an increase in QOL and muscle strength compared to the control group (van Weert et al., 2005). Nevertheless, while they were able to show the effectiveness of a multidisciplinary rehabilitation program, the program was not based on ACT, nor did they investigate the impact on symptom burden, as the present study did.

So far, both mono- and multidisciplinary treatment programs appear to be effective for cancer survivor's rehabilitation. In this regard, researchers comparing mono- and multidisciplinary rehabilitation programs for cancer survivors determined that there is no significant difference between these rehabilitation types to increase QOL and reduce the symptom burden (Korstjens et al., 2008; May et al., 2008; Mewes et al., 2012; van Weert et al., 2010). In particular, Korstjens and colleagues (2008) conducted an RCT study that compared QOL changes among different types of cancer survivors who were randomly assigned to one of the following three groups: physical exercises group, physical exercises and CBT group or control group. The intervention lasted 12 weeks in total, and both intervention groups were assessed at baseline, after the rehabilitation and three months later. In contrast, the control group was only examined twice, at baseline and after the treatment. Korstjens and colleagues (2008) concluded that QOL increased in both intervention groups, but no additional effect was found in favor of either intervention group. Similar conclusions were found in the RCT studies by May and colleagues (2008) and van Weert and colleagues (2010), who both concluded that physical exercise, as a monodisciplinary treatment, is not superior to physical exercise combined with CBT. In addition, Mewes and colleagues (2012) assessed the cost-efficacy of multidisciplinary rehabilitation programs for cancer survivors in a review. They determined that multidisciplinary programs are cost-effective and beneficial in decreasing fatigue and physical functioning. However, Mewes and colleagues (2012) did not find an additional effect of multidisciplinary rehabilitation programs over monodisciplinary,

neither in terms of being more cost-efficient nor the better treatment of the symptom burden. Therefore, no concrete conclusion can be made concerning the superior efficacy of mono- or multidisciplinary rehabilitation programs. More particularly, no study, to our best knowledge, examined the difference between a monodisciplinary rehabilitation program, such as ACT, and a multidisciplinary rehabilitation program based on ACT. Therefore, the present study might provide a starting point to investigate further whether ACT in a multidisciplinary rehabilitation program is as effective as ACT used as a monodisciplinary rehabilitation program to increase cancer survivors QOL and reduce their symptom burden.

The last goal of the study was to determine whether different levels of anxiety, depression, or fatigue moderate QOL after treatment. Results suggest that higher baseline levels did not influence QOL. Therefore, QOL seems to increase similarly among cancer survivors regardless of their severity of complaints. That was an unexpected finding, given that previous literature has confirmed a correlation effect between QOL and severity of complaints. For example, Mols and colleagues (2018) showed a negative relationship between anxiety and global QOL and between depression and global QOL. Likewise, to the present study, they used the two global questions of the EORTC-30 as an outcome measurement and the HADS for depression and anxiety. In contrast to the present study, however, Mols and colleagues (2018) examined only colorectal cancer survivors, used a longitudinal study design, and cancer survivors did not participate in a rehabilitation program. Nevertheless, it might be that even though an association was found, that no moderation occurred. In fact, no study, to our best knowledge, investigated whether depression, anxiety, or fatigue moderate QOL in cancer survivors. Therefore, the present study is of value as it primarily investigated a possible moderation effect and did not find one. A potential explanation why the present study did not reveal a moderation effect originates from Keyes' two-continua model, suggesting that well-being and the severity of complaints are two distinct concepts (Keyes & Lopez, 2009). Thus, the model assumes that well-being and psychopathology correlate but do not have a

causal effect on each other. Therefore, scoring high on psychopathology does not necessarily lead to experiencing low levels of QOL because both variables change independently. The model holds validity if one considers that cancer survivors' QOL increased and depression, anxiety, and fatigue decreased throughout the study. Hence, it is possible that the QOL and symptoms correlate but do not have a causal effect on each other. The present study adds to a growing concept of literature showing that psychopathology and well-being are two distinct concepts. Additionally, it is the first study investigating whether anxiety, depression, or fatigue moderate changes in QOL in cancer survivors.

Strengths and Limitations

A strength of this study was that real cancer survivors had been examined. Furthermore, the study was the first to investigate pre to post changes in cancer survivors after participating in a multidisciplinary rehabilitation program based on ACT. Additionally, in our best knowledge, the study was also the first research that investigate whether anxiety, depression, or fatigue moderate change in QOL of cancer survivors. Besides these strengths, the study has some limitations as well.

The first major limitation of this study is the absence of a control or comparison group. Therefore, results should be interpreted cautiously and are not meant to determine whether Roessingh's treatment can enhance the QOL. In other words, the study design does not allow the performance of an effectiveness analysis because of the absence of a control group. Additionally, the study examined cancer survivors of only three consecutive years and, as a consequence, was not able to demonstrate the possible change in the age of cancer survivors. For example, Griffiths and colleagues (2012) explained that any disruptive shift could lead to a social change. Considering this explanation and that no significant change occurred from 2017 until 2019, it might be that a possible change in age or symptom burden remains unnoticed. Furthermore, the study did not investigate the relationship between age and the

severity of complaints. Hence, it could only be concluded that participants of different years of recruitment did not differ in age or severity of complaints in any meaningful fashion.

Additionally, no claims could be made in terms of the relation between age and severity of complaints. Lastly, the data is characterized by a large fluctuation in the number of participants due to varying degrees of participation in follow-up measurement. This shortcoming is a known problem in research (Xi et al., 2018). Therefore, only patients were included who at least completed the post measurement.

Future direction and Recommendation

This study shows promising effects that multidisciplinary treatment programs based on ACT seem to increase QOL and significantly reduce the severity of complaints. Continuable, several intriguing questions for future studies arose. The next step should now be comparing Roessingh's rehabilitation program to a control group to determine the effectiveness of the treatment (Stolberg et al., 2004). Commonly, researchers suggest using an RCT study design to determine effectiveness (Richardson, 2000; Stolberg et al., 2004). However, RCT studies require a large sample size, which is why it is not a feasible solution for Roessingh.

Alternatively, Roessingh could assign the potential treatment patients to a 12-week waitlist, parallel to the start of the intervention, as it was done before by Lerman and colleagues (2012) to determine the effectiveness of the treatment. Thereby, participants on the waitlist could serve as a control group. Since Roessingh already has a waitlist, one would only need to set a waiting time of 12 weeks to generate a waitlist-control group. Afterwards, cancer survivors on the waitlist-control group can be offered a rehabilitation place. Overall, a study design including a waitlist-control group is commonly used in practice (Lerman et al., 2012; Richardson, 2000; Von Ah et al., 2012).

In addition, a question that remained unanswered is whether mono- or multidisciplinary rehabilitation programs are superior. Therefore, several researchers concluded that further research is needed to answer the superiority question (Korstjens et al.,

2008; Mewes et al., 2012; van Weert et al., 2010). Hence, future research should compare the effectiveness of mono- and multidisciplinary rehabilitation programs for cancer survivors. More specifically, future research could examine whether there is a difference in QOL and symptom burden for cancer survivors after completing either an ACT rehabilitation program or Roessingh's multidisciplinary treatment program. In consultation with Roessingh, cancer survivors could either participate in Roessingh's current multidisciplinary treatment program or complete an ACT exclusive program extracted from Roessingh's multidisciplinary approach.

Furthermore, researchers are divided by disagreements about whether older or younger cancer survivors experience a more significant symptom burden (Mandelblatt et al., 2020; Mao et al., 2007). Therefore, several researchers advise further investigate whether age influences the symptom burden (Brown & Roose, 2011; Dunn et al., 2013; Mandelblatt et al., 2020; Mao et al., 2007). Hence, future research might assign participants according to their age into different age groups to further investigate whether they differ in terms of symptom burden. Assuming that a one-way ANOVA could detect an age-specific difference in symptom burden, the outcome could be helpful to tailor rehabilitation programs for cancer survivors potentially age-specific needs. Alternatively, Ruspini (1999) suggests the use of a longitudinal study design to detect a possible society change. However, this study design is time and cost expensive which is why the previous mentioned solution might be more appropriate.

Lastly, future researchers whose data is characterized by a large number of missing data due to a loss in follow-up measurements are encouraged to use the recommendation by Xi and colleagues (2018). They recommend using a mixed model approach whereby missing data are stimulated by regressing all available pre-and post-test values over treatment and assessments. The approach assumes some variance-covariance structure for the repeated measure (Xi et al., 2018).

Conclusion

Present results cast a new light on multidisciplinary rehabilitation programs which are based on ACT for cancer survivors by showing positive pre-post changes in QOL, anxiety, depression, and fatigue for participants. Cancer survivors showed an increase in QOL and a decrease in anxiety, depression, and fatigue throughout the study. While the present study favors multidisciplinary rehabilitation programs, researchers are divided by disagreements whether monodisciplinary rehabilitation programs are more valuable than multidisciplinary for cancer survivors. On the basis of the current discussion concerning the superiority question and the study's results, clinicians are encouraged to investigate whether ACT as a monodisciplinary rehabilitation is equally as effective as a multidisciplinary rehabilitation program based on ACT. Thereby, it is also essential to include a waitlist control group parallel to the rehabilitation start to determine valid conclusions. Nevertheless, the present results add to a growing corpus of research evidence showing a high contribution of after-cancer care for all cancer survivors.

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Appendix

Informed consent

Dit vragenboekje is ten behoeve van het intakegesprek voor een revalidatieprogramma voor oncologie

Gegevensbestand en onderzoek

Graag zouden wij uw antwoorden uit dit boekje willen gebruiken voor ons gegevensbestand. Met de gegevens van u en andere patiënten kunnen we onze revalidatieprogramma's verbeteren. Ook zouden uw gegevens in de toekomst gebruikt kunnen worden voor wetenschappelijk onderzoek.

Om gebruik te mogen maken van uw gegevens voor het gegevensbestand en/of wetenschappelijk onderzoek hebben wij uw toestemming met handtekening nodig. Indien u toestemming geeft dan kunt u dat te allen tijde weer intrekken. Uw gegevens worden vertrouwelijk behandeld¹. Uw gegevens worden los van uw naam, adres of patiëntnummer verwerkt en zijn nooit rechtstreeks te herleiden.

Wanneer u geen toestemming geeft, heeft dat nooit invloed heeft op uw behandeling.

Ik geef toestemming om mijn gegevens te gebruiken voor het gegevensbestand van Het Roessingh, centrum voor revalidatie, Enschede.

- ja
- nee

Ik geef toestemming om mijn gegevens te gebruiken voor wetenschappelijk onderzoek van Roessingh Research & Development Enschede

- ja
- nee

Datum:

Handtekening:

¹ volgens de gedragscode Gezondheidsonderzoek van de Stichting Federatie van Medisch Wetenschappelijke Verenigingen www.fmwv.nl