

The Effectiveness of oncologic rehabilitation: A Systematic Scoping Review

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Abstract

Background: The survival rate of cancer is increasing and nowadays it is often treated as chronic illness, since survivors complain about a variety of symptoms after the treatment. A multidisciplinary approach is recommended by guidelines and experts, in order to enhance the variety of complaints cancer survivors experience. The aim of this thesis was to provide an overview of the current knowledge regarding multidisciplinary treatment for cancer rehabilitation and to investigate the effectiveness of different intervention options on Quality of Life (QOL) and Cancer related Fatigue in cancer survivors.

Methods: A systematic research was conducted in the electronic databases PubMed, Web of Science and PsycINFO from February 2021 to April 2021. For each database, cancer-, oncology-, rehabilitation-, rehab-, cancer survivorship-, multidisciplinary intervention-, and RCT-related keywords were used. Eligible inclusion criteria were randomized controlled trials, English language, multidisciplinary rehabilitation interventions for cancer survivors and published in the last 15 years (2006 – 2021). Children (≤ 17) were excluded.

Results: Four RCT-studies were analyzed in more detail. Not all studies evaluated on Fatigue as the primary measure, but it was provided as one of the measures in all articles. Quality of Life was also not the primary measure in all studies, but was at least one of the measures in all articles. In total, two out of four studies reported statistically significant changes on Fatigue. Regarding Quality of Life, two out of the four studies described statistically significant changes.

Conclusions. The effects of multimodal interventions on improving Quality of Life and reducing Fatigue in cancer survivors differ and the exact impact remains uncertain. Thus, further research with a higher number of included studies in the form of a meta-analysis is needed to make evidence-based statements about the effectiveness.

Keywords: cancer rehabilitation, cancer survivor, multidisciplinary intervention, quality of life, fatigue, randomized controlled trials

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The Effectiveness of oncologic rehabilitation: A Systematic Scoping Review

According to the International Agency for Research on Cancer, the number of cancer deaths worldwide in 2020 was estimated to be around 9.96 million (Xi & Xu, 2021) and following cardiovascular diseases, cancer remains the second most common cause of death in many countries (Ma & Yu, 2006). Before 1980, for more than two thirds of all cancer patients the disease ended deadly, while nowadays more than the half of them can hope to be cured permanently, since there were major improvements in the areas of prevention, early detection and treatment of oncological diseases (Deutsches Krebsforschungszentrum, 2019). The survival statistics vary depending on the age of the patient, the sex and the cancer type and range from 98% for testicular cancer to 1% for pancreatic cancer (Cancer Research UK, 2020). In the Netherlands, 1 in 8 women will develop breast cancer at some point in their lives and it is the most prevalent type of cancer in the country (National Institute for Public Health and the Environment, 2018). But despite being the most common oncologic disease in women, it is not the one with the highest mortality, and 87% of women with a breast cancer diagnosis survive at least 5 years following the diagnosis and over 82% survive at least 10 years (Zentrum für Krebsregisterdaten, 2021). Even though the high survival rate may indicate that most of the cancer patients get cured from an oncologic disease, it does not mean that they are not suffering from a vary of symptoms after the treatment (Institute of Medicine and National Research Council, 2006) and cancer is therefore sometimes considered as a chronic illness (Phillips & Currow, 2010).

Cancer as chronic illness

Cancer survivors can be limited in various aspects of life after their treatment, as they often continue to experience a range of symptoms that can manifest in fatigue, psychological

distress, and limitations in mobility, communication, and cognition (Institute of Medicine and National Research Council, 2006). A study gave insight that 36% of cancer survivors suffer from a moderate fatigue and 12% from severe fatigue (Kuhnt et al., 2009). However, the causes behind the pathological exhaustion are different, and the complaints of the affected people differ as well (Deutsches Krebsforschungszentrum, 2017).

Due to progress and improvements in health care and research and the higher survival rate of cancer patients as a result, the understanding of the long-term impact of cancer and its treatment becomes more important (Firkins, Hansen, Driessnack & Dieckmann, 2020) and providing psycho-oncological counseling and other interventions for cancer survivors are often important components of today's after care (Weis et al., 2007). However, there are still major deficits in care and it is important to improve this and to investigate which interventions have proven to be effective in alleviating symptoms (Weis et al., 2007). This is important not only with regard to the health economic aspect, but above all with regard to the physical and mental health of the patients (Weis et al., 2007).

Quality of Life and Fatigue in cancer survivorship

The inclusion of "Quality of Life" in the evaluation of medical interventions has increased and it is striking that there is no general definition of QoL, which complicates the evaluation in medicine (Dimenäs, Dahlöf, Jern & Wiklund, 1990). Dimenäs, Dahlöf, Jern and Wiklund (1990) have come to the conclusion that QoL is composed of three components: Subjective well-being, Health, and Welfare. While subjective well-being functions as the central component, and refers to the individual's perception of his or her life situation, the component health describes a subjective and objective assessment of physical and mental condition, while well-being focuses on objective environmental factors (Dimenäs, Dahlöf, Jern & Wiklund, 1990). They therefore believe that the assessment of QoL in medicine

should ideally take these three main factors into account, with subjective well-being and health playing a particularly important role (Dimenäs, Dahlöf, Jern & Wiklund, 1990).

Since every aspect of the survivor's life can be affected by the disease and its treatment, a meta-analysis examined the Quality of Life in long-term cancer survivorship and found that the Quality of Life in cancer survivors is significantly impacted 2 to 26 years after the diagnosis (Firkins, Hansen, Driessnack & Dieckmann, 2020). Regarding the Quality of Life of cancer survivors, there are various aspects, which can be affected (Institute of Medicine & National Research Council, 2006). A Quality of Life model applied to cancer survivors shows that there are different components such as Physical Well Being and symptoms, which includes functional activities, strength, pain, fatigue, overall physical health, fertility and sleep and rest, Psychological Well Being, which includes control, anxiety, depression, enjoyment/leisure, fear of recurrence, cognition/attention, distress of diagnosis and control of treatment, Social Well Being, which includes family distress, roles and relationships, affection/sexual function, appearance, enjoyment, isolation, finances and work and Spiritual Well Being, which includes the meaning of illness, religiosity, transcendence, hope, uncertainty and inner strength (Institute of Medicine & National Research Council, 2006). The model highlights the importance of acknowledging different components when it comes to Quality of Life in cancer survivorship (Institute of Medicine & National Research Council, 2006).

A study has shown that moderate to severe depression was reported in 17% and anxiety in 9% of cancer survivors, and both were higher in women than in men ($p < 0.001$) (Götze et al., 2019). The study also found out, that cancer survivors, who were under the age of 60 years were more depressed and anxious compared to the general population ($p < 0.001$) (Götze et al., 2019), which underlines the influence of biological aspects such as age.

Research has shown that depression was also significantly associated with Fatigue in cancer

survivorship (Kuhnt et al., 2009). The study concluded that moderate fatigue in cancer survivors had a prevalence of 36% and severe fatigue of 12% (Kuhnt et al., 2009). Furthermore, fatigue was also associated with anxiety, sleep difficulties, adjustment to the illness, pain, dyspnoea, age and lacking social support (Kuhnt et al., 2009). This illustrates that certain symptoms can influence and reinforce each other. This assumption is also supported by the biopsychological model, which determines that the complaints of cancer survivors are affected by psychological, biological and social aspects in their life (Novy & Aigner, 2014). In order to meet the needs of patients, it is therefore particularly important to ensure the right treatment and effective interventions.

Mono- and multidisciplinary interventions

A distinction is made between programs, which are monodisciplinary based, such as Cognitive Behavioural Therapy (CBT), Acceptance and Commitment Therapy (ACT) or Physical Activities and Training (Mathew, Doorenbos, Jang & Hershberger, 2020; Dieli-Conwright et al., 2018; Aricò, Raggi & Ferri, 2016) and multidisciplinary based programs. Monodisciplinary based programs approach the complaints by using one intervention method only, and have shown significant effects in the rehabilitation of cancer survivors (Mathew, Doorenbos, Jang & Hershberger, 2020; Dieli-Conwright et al., 2018; Aricò, Raggi & Ferri, 2016). Research has shown that a monodisciplinary program containing ACT led to significant psychosocial improvements in anxious cancer survivors (Arch & Mitchell, 2015), and thus may be considered as effective intervention, in order to increase the Quality of Life of cancer survivors (Arch & Mitchell, 2015; Feros et al., 2013). Interventions, which are exercise and activity based have also shown that they have a positive effect on the quality of life, pain, fatigue and physical function of patients (Möller, Beck, Rydén & Malmström, 2019). Multidisciplinary based programs are taking advantage of different interventions, by

combining them in a program to address all aspects of complaints (Integraal Kankercentrum Nederland, 2017). Furthermore, in multidisciplinary based programs, the patient can benefit from the expertise of a vary of professionals of different fields, such as specialist nurses, oncologists etc. (Kesson, Allardice, George, Burns & Morrison, 2012). Since multidisciplinary programs follow the cancer rehabilitation guideline (Integraal Kankercentrum Nederland, 2017; Hellbom et al., 2011), they are often provided in cancer rehabilitation, especially when the patients complaints are complex and interrelated (Integraal Kankercentrum Nederland, 2017). Thus, multidisciplinary programs are recommended in cancer survivorship rehabilitation, since the symptoms and complaints of the patients are often interrelated and therefore affecting each other (Hellbom et al., 2011). Depending on the severity of the symptoms, the intervention, the general circumstances and wishes of the patient, these intervention programs can be provided as inpatient or outpatient treatment and thus take place at home, in a hospital, a practice or in a rehabilitation clinic (Integraal Kankercentrum Nederland, 2017; Leitlinienprogramm Onkologie, 2016).

A few studies were published to date on the effectiveness of multidisciplinary based programs in oncological rehabilitation, and have shown significant results. Research demonstrated an enhanced Quality of Life and healthy lifestyle in breast cancer survivors by using a multimodal based program, containing physical activity, integrative dietary and mindfulness program (Ruiz-Vozmediano et al., 2020). The study also stated that cancer symptoms may be better managed by implementing a multidisciplinary program instead of monodisciplinary interventions (Ruiz-Vozmediano et al., 2020). Furthermore, several research imply that studies report multidimensional interventions have shown at least significant benefits over usual care, which was most noticeable in fatigue and physical functioning complaints (Mewes, Steuten, Ijzerman & Van Harten, 2012; Kesson, Allardice, George, Burns & Morrison, 2012; Adamsen et al., 2009).

Research objective

Since the amount of cancer survivors will further increase in the future, and the burden of complaints is affecting many different aspects of the patient's life, a multimodal approach regarding their complaints is recommended by experts (Cadet, Davis, Elks & Wilson, 2016; Integraal Kankercentrum Nederland, 2017). A multidisciplinary program also indicates a patient centered approach by providing qualified health care by different professionals (Cadet, Davis, Elks & Wilson, 2016). Thus, cancer rehabilitation facilities can provide a multidisciplinary approach of holistic care, by combining the knowledge of different professionals, and the effectiveness of evidence based various interventions, such as psychological, nutritional, mindfulness and physiology services, and improve the cancer survivor's life (Cadet, Davis, Elks & Wilson, 2016). However, although different studies have demonstrated significant effects of multidisciplinary rehabilitation programs, there is consensus among researchers that the effects of multidisciplinary rehabilitation programs still warrant further research (Ruiz-Vozmediano et al., 2020; Hellbom et al., 2011; Riedl et al., 2017; Loh & Musa, 2015; Bennett et al., 2016). This scoping review aims to provide an overview of the effectiveness of multidisciplinary interventions in oncological rehabilitation of adult cancer survivors regarding their Fatigue and Quality of Life. Furthermore, by addressing this gap in the literature, this review also aims to contribute bundled information, in regard to incorporating current study results, in order to improve the approach in oncological rehabilitation.

Methods

Search strategy

For the systematic scoping review, searches for studies were conducted in the electronic databases PubMed, Web of Science, and PsycINFO, from February 2021 to April 2021. Randomized Controlled Trials (RCTs) were searched in each database by using cancer-, oncology-, rehabilitation-, rehab-, cancer survivorship-, multidisciplinary intervention-, and RCT-related keywords.

































Study Selection


First, articles were searched and identified through databases. Secondly, duplicates were recognized and removed. Thirdly, the titles and abstracts of the articles were screened. The full texts were screened after, and finally, the inclusion and exclusion criteria were considered. Eligible inclusion criteria were: (1) Randomized Controlled Trials (RCTs), (2) English language, (3) multidisciplinary rehabilitation interventions for cancer survivors, (4) evaluating on Fatigue and Quality of Life and (5) published in the last 15 years (2006 – 2021). Children (≤ 17) were excluded. The focus was placed on RTCs, as these are the most proven standard to measure cause-effect relationships between an intervention and the outcome (Hariton & Locascio, 2018).


Quality Assessment


The risk of bias was evaluated by using the Cochrane Risk of Bias tool (Higgins & Thomas, 2021). The risk of bias of the included studies was judged by two independent reviewers (CK & SB). Afterwards, differences in the assessment were addressed and a consensus was made. Finally, the supervisor of the study (GJP) assessed and approved the final proposal for the risk of bias assessment.

Table 1. *Risk of bias*

First author, year	Selection bias <i>Random sequence allocation</i>	Selection bias <i>Allocation concealment</i>	Performance bias <i>Blinding of participants</i>	Performance bias <i>Blinding of personnel</i>	Detection bias <i>Blinding of outcome</i>	Attrition bias <i>Incomplete outcome</i>	Reporting bias <i>Selective reporting</i>	Other bias <i>other sources of bias</i>
Adamsen, 2009								
Fillion, 2008								
O'Neill, 2018								
Rummans, 2006								

 Low risk of bias

 Unclear risk of bias

 High risk of bias

Results

Selection of Included Studies

The initial search in the databases PubMed, Web of Science and PsycINFO generated 621 records. Within these generated records, 66 were identified as duplicates and therefore got removed. Screening the 555 records regarding titles and abstracts, resulted in the exclusion of 536 records that did not meet the exclusion criteria. The remaining 19 records and their full

texts were assessed for eligibility. Of these 19 records, seventeen records were excluded because the interventions were not multidisciplinary or did not evaluate Fatigue or QOL and therefore did not meet the criteria. The remaining two records and two additionally hand searched records were included in the systematic review. The selection steps are visualized in the flowchart below (see Figure 1).

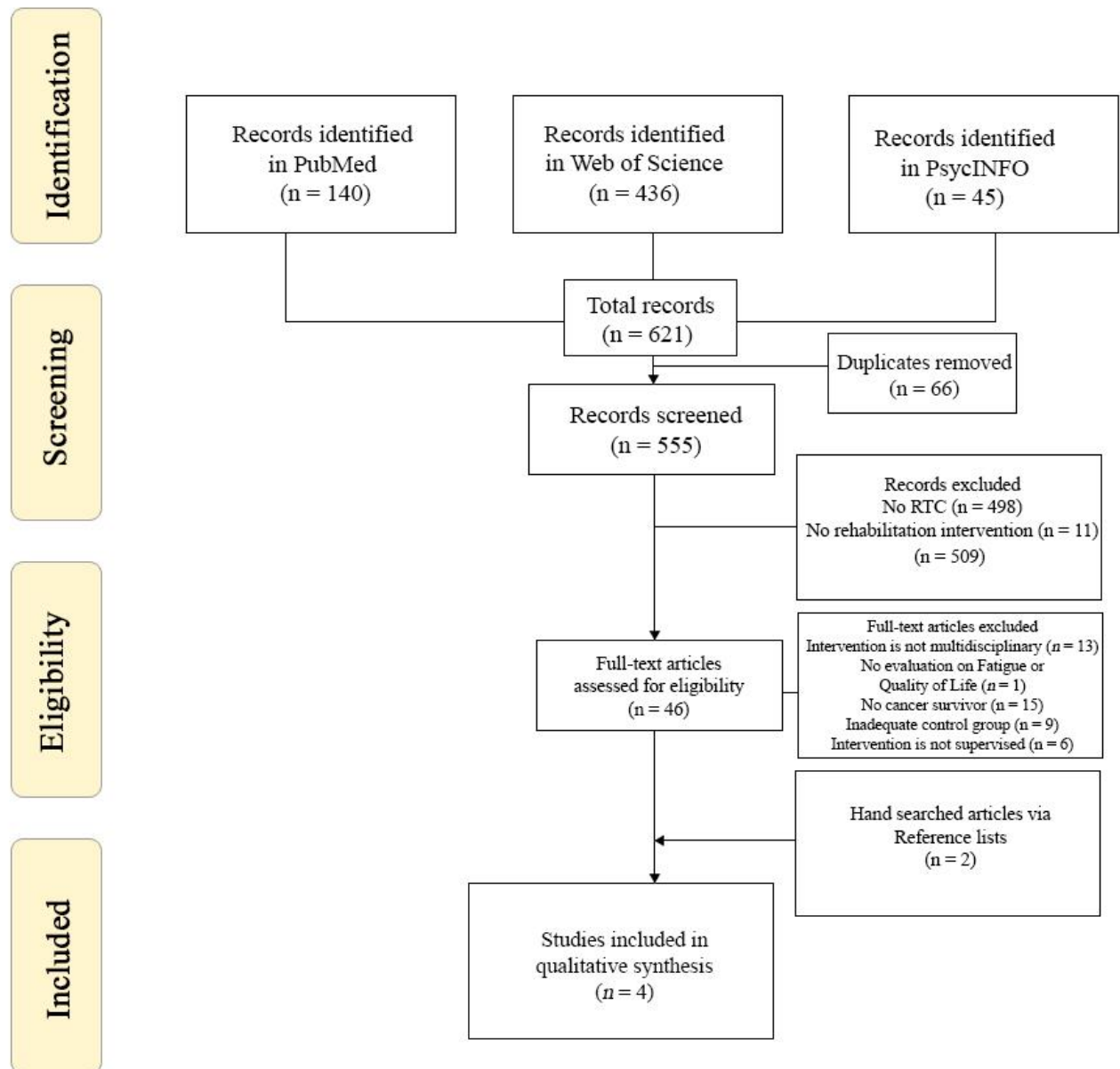


Figure 1. *Flowchart literature search*

Characteristics of the Included Studies

The included studies and their demographic characteristics are demonstrated in Table 2

Table 2.

Demographic Characteristics of final Studies

First author, year of publication	Disorder (%)	% Female (n total)	Mean age (SD)	Time since first diagnosis in years (SD)
Adamsen, 2009	21 different cancer diagnoses (17 with solid tumours, 4 with malignant haematological diseases) 48% evidence of disease 52% no evidence of disease	73% (196)	Control 47.2 (10.6) Intervention 47.2 (10.7)	Control 0.25 Intervention 0.23
Fillion, 2008	Breast cancer (100%)	100% (87)	52.47 (9.91) Control 51.84 (10.25) Intervention 53.09 (9.65)	n/a
O'Neill, 2018	Esophagogastric cancer (100%)	18.60% (8)	Control 64.14 (10.46) Intervention 67.19 (7.49)	n/a Time post-surgery, Control 2.8 (19.56) Intervention 1.96 (15.23)
Rummans, 2006	Colorectal cancer (38%) Primary head and neck cancer (17%) Lung cancer (15%) Primary brain tumours (12%) Other cancer type (18%)	35.92% (37)	Control 59.4 (10.62) Intervention 59.7 (11.49)	n/a but within 5 years

Interventions

Population characteristics. Of all (4) RCTs on behavioural therapeutic interventions, two were conducted in Europe (Ireland & Denmark) and two were conducted outside Europe

(Canada & the United States of America). One of the study samples consisted only of females (Fillion, 2008), while the other studies consisted samples of females and males.

Intervention characteristics

A description of the interventions of the final studies is provided in the following.

Table 3.

Intervention descriptions of final studies

First author, year of publication	Intervention name (n)	Format (guidance)	Questionnaires	Duration in weeks (n sessions)	Control group (n)	Retention rate post treatment (n)	Follow up in weeks	Outcome measure; p values
Adamsen, 2009	Multimodal high intensity exercise intervention; Standard medical care + participating in group based multimodal high intensity exercise intervention including high intensity cardiovascular and resistance training, relaxation and body awareness training and massage (134)	Supervised by trained nurse specialists and physiotherapist	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), Medical Outcomes Study Short Form (MOS SF-36)	6 (9 hours per week)	Conventional medical care & allowance to freely increase physical activity (135)	Intervention (118) Control (117)	-	Fatigue (p = .02) (MOS SF-36) Physical functioning (p = .01) Role physical (p = .007) Vitality (p = <.0001) Role emotional (p = .02) Mental health (p = .04) Physical component scale (p = .02) Mental component scale (p = .004)
Fillion, 2008	Brief Intervention for Fatigue Management; Group psychotherapy and physical activity (48)	One hour consisted supervision of walking training by a kinesiologist or a trained research nurse, 1.5 hours psycho-educative fatigue management sessions were codirected by 2 oncology nurses; Training for these nurses in cognitive behavioural approaches was provided and they were supervised by a health psychologist (10 hours, in addition to 6 hours of reading)	Medical Outcomes Study Short Form 12 (SF-12), Multidimensional Fatigue Inventory (MFI)	4 (Four weekly group meetings of 2.5 hours and 1 short telephone "booster session" (5-15 minutes))	Usual-care (46)	(44) (43)	12	Fatigue Group Effects T2 (p = .03) Physical Quality of Life T1 (p = .03) Mental Quality of Life T2 (p = .04)
O'Neill, 2018	Multidisciplinary Rehabilitative Program (RESTORE Program); Exercise, dietary counselling and group education (21)	Aerobic and resistance training were prescribed, Dietary Counselling from a registered nurse, Group education delivered by multidisciplinary team including a surgeon, dietitian, physiotherapist, occupational therapist and psychotherapist specialized in mindfulness	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)	12 (7 Group Education sessions)	Standard clinical care (22)	(21) (22 T0, 19 T1, 18 T2)	12, 36	Cognitive function T1 Intervention < Control (p = .031)
Rummans, 2006	Structured, multidisciplinary intervention for strategies designed to improve participants quality of life: Educational materials, CBT strategies, question & answer period, sharing, reflecting, relaxation and physical activity (57)	Education materials, Structured sessions conducted by a physical therapist followed by educational information, cognitive-behavioural strategies for coping with cancer, open discussion with group leaders and other participants and support from the overall experience with group leaders and other participants, guided relaxation exercise. Each session was led by psychiatrist or psychologist, depending on the theme of the session: an advanced practice nurse, a certified hospital chaplain or a licensed social worker cofacilitated the session	Spritzer QOL Uniscale, Linear Analog Scales of Assessment (LASAs) of QOL	4 (Eight 90-minute sessions, 3 days per week)	Standard medical care as recommended by oncologist (58)	(49) (54)	8, 27	Overall Quality of Life T1 Intervention > Control (p = .047) QOL Intervention group T1 (p = .009) T1 Improvement of Intervention group Physical symptom reduction (p = .022), emotional well-being (p = .046), social well-being (financial issues) (p = .025), legal concerns (p = .048), spiritual well-being (p = .06)

Notes. CBT = Cognitive Behavioural Therapy

T0 = Baseline

T1 = Post-Treatment

T2 = Follow-up

Results

Fatigue

The effects of the interventions on cancer related fatigue were assessed in all of the four included studies (Adamsen et al., 2009; Fillion et al., 2008; O'Neill et al., 2018 & Rummans et al., 2006). The study of Adamsen et al. (2009) stated a significant effect in Fatigue (EORTC QLQ-C30) in favour of the intervention group for the primary outcome after six weeks. A significant reduction of the fatigue score of -6.6 points (95% confidence interval -12.3 to -0.9) was found in the intervention group compared to the control group ($p= 0.02$). The simple effect contrasts in the study of Fillion et al. (2008) showed a significant difference between the intervention group and the control group for fatigue (MFI) at the 3-month follow-up. Women, who were in the intervention group manifested a lower level of fatigue at the follow-up, compared to women who took part in the control group ($p= 0.03$) (Fillion et al., 2008).

In the study of O'Neill et al. (2018), in which the intervention group received the RESTORE program, there were no significant effects on fatigue (EORTC QLQ-C30) reported.

There were also no significant effects on fatigue (Linear Analog Scales of Assessment of QOL) described in the study of Rummans et al. (2006).

Quality of Life

The effects of the interventions on Quality of Life were assessed in all of the four included studies (Adamsen et al., 2009; Fillion et al., 2008; O'Neill et al., 2018 & Rummans et al., 2006). Regarding the global health status/quality of life (EORTC QLQ-C30) the intervention in the study of Adamsen et al. (2009) showed no improvement.

The study of Fillion et al. (2008) reported a significant group difference post-intervention (T1) for physical quality of life. Immediately after the intervention (T1), women who took part in the intervention group of this study showed a significant higher level of physical quality of life (SF-12, PCS-12; Physical Component Summary) compared to women who took part in the control group ($P = .04$) (Fillion et al., 2008). Regarding the mental Quality of Life (SF-12, MCS-12; Mental Component Summary) there were no interaction or main effects reported, which demonstrated that the intervention and the control group improved equally on mental health quality of life overtime ($p = >.05$) (Fillion et al., 2008). Nevertheless, an ad hoc simple effect contrast was able to detect a significant effect ($p = .04$) at the 3-month follow-up, which suggests that the improvement of mental Quality of Life in the intervention group was more important than the increase of the control group (Fillion et al., 2008).

The study of O'Neill et al. (2018) reported no changes in health-related quality of life (HRQOL, EORTC QLQ-C30), except for the cognitive function, which was higher in the control group immediately post-intervention (T1) ($p = .031$). Any other HRQOL functional and symptom scores were comparable between the intervention and control group at all measurements (O'Neill et al., 2018).

The overall Quality of Life (Spritzer QOL Uniscale, Linear Analog Scales of Assessment of QOL) in the study of Rummans et al. (2006) was maintained by the experimental group at the end of the intervention, while the control group showed a significant decrease in quality of life. The primary end point analysis indicated that it was 9 points higher in the experimental group than in the control group ($p = .047$) (Rummans et al., 2006). Furthermore, the intervention group was able to achieve a 3-point increase from baseline, whilst a 9-point decrease from baseline was reported for the control group ($p = .009$) (Rummans et al., 2006). Additionally, the number of participants in the intervention group

describing this significant increase, was two times higher compared with the control group ($p = .025$) (Rummans et al., 2006). Participants reporting a significant decrease in Quality of Life after 4-weeks (post-intervention), measured by an 8-point decrease from the baseline scores, made up 54% of the control group and only 33% of the intervention group ($p = .0312$) (Rummans et al., 2006). Moreover, a significant effect between both groups was also reported for the spiritual well-being ($p = .003$), in favour of the intervention group (Rummans et al., 2006). However, a difference between the treatments was only observed after 4 weeks, which was immediately after the intervention ($p = .037$) (Rummans et al., 2006). During the 5 months after the intervention, the intervention group was able to maintain or even increase their quality of life, while the Quality of Life in participants of the control group leisurely returned to the baseline level (Rummans et al., 2006). However, the statistical difference between the intervention and the control group in Quality of Life was not statistically significant at weeks 8 and 27 anymore (Rummans et al., 2006). Further, the analysis of the scores of the Linear Analog Scales of Assessment, revealed four areas where the intervention group improved, while the control group did not, from baseline to post-intervention at week 4 (Rummans et al., 2006). A significant difference of the mean scores of the intervention and control group was reported regarding physical symptom reduction ($p = .022$), emotional well-being ($p = .046$), social well-being (financial issues) ($p = .025$) and legal concerns ($p = .048$) and spiritual well-being ($p = .06$) (Rummans et al., 2006).

Discussion

This systematic scoping review aimed to investigate the effectiveness of multidisciplinary intervention programs in oncologic rehabilitation regarding fatigue and Quality of Life. Furthermore, this systematic review intended to provide an overview of current existing studies

related to the research topic. This systematic review suggests that two of the presented multidisciplinary interventions have statistically significant effects on cancer related fatigue or QOL, while being compared to an adequate control group. One out of the four studies can be considered as unusual, since there were no significant effects on fatigue and/or QOL (O'Neill et al., 2018), except for the cognitive function, which was even higher in the control group rather than the intervention group.

However, in regard to the follow-ups of the studies (Fillion et al., 2008; O'Neill et al., 2018; Rummans et al., 2006), the reported significant effects were usually not long lasting, except for one study (Rummans et al., 2006). While comparing the follow-up scores of the studies, it can be suggested that the described effects flattened out in time (Fillion et al., 2008; O'Neill et al., 2018; Rummans et al., 2006). Even in the study, in which the intervention group was able to maintain their QOL for a longer time period, the difference between the experimental group and the control group slowly narrowed to a non-significant score in the following five months (Rummans et al., 2006). Thus, it can be assumed that nearly all of the evaluated interventions lack in the longevity of their effects (Fillion et al., 2008; O'Neill et al., 2018; Rummans et al., 2006). Thus, it is questionable whether multidimensional intervention programs are necessarily preferable to monodimensional intervention programs. Particularly in view of the high costs (van Rooijen et al., 2019) associated with multidimensional approaches, further research is needed to determine whether multidimensional programs are significantly more effective than monodimensional ones.

Regarding cancer related fatigue, the intervention programs provided in the studies of Fillion et al. (2008) and Adamsen et al. (2009), seem to be the ones with the highest effectiveness. In both studies the intervention groups were able to reduce their fatigue, while the other two studies (O'Neill et al., 2018; Rummans et al., 2006) reported no significant effects on fatigue. The effect size of the improvement in fatigue (0.33) in the Adamsen et al.

(2009) study indicates a small to medium clinically important change (Cohen; Nakagawa & Cuthill; King, as cited in Adamsen, 2009), but their results differ from reports of a meta-analysis which suggests that the effect of exercises may be too small to have a clinically relevant meaning (effect size=0.13,95% CI -0.06 to 0.33) (Schmitz et al., as cited in Adamsen, 2009). The other two studies, which did not report any significant changes in fatigue, would support this, since they also contained physical training elements, but without an effect on fatigue (O'Neill et al., 2018; Rummans et al., 2006). Thus, the intensity of the exercise might be an explanation for the significant effects on fatigue in two of the studies (Adamsen et al., 2009; Fillion et al., 2008), since both of them indicated exercises of a higher intensity. Furthermore, in the study of Fillion et al. (2008), cancer related fatigue was the main target of the intervention program. Thus, this might also have affected the significant effects. A systematic review analyzing the effects of supervised physical activity interventions on cancer related fatigue came to the conclusion that combined aerobic and resistance exercises should be considered as part of rehabilitation programs for cancer patients in order to reduce their complaints (Meneses-Echávez, González-Jiménez & Ramírez-Vélez, 2015). Nevertheless, another systematic review reports that the effects of exercises on cancer related fatigue in adults, still lack of certainty, but at least it can be assumed that exercise interventions do not appear to increase the fatigue (Kelley & Kelley, 2017). It is thus likely that indicating exercises in rehabilitation programs for cancer patients may at least lead to positive outcomes. Comparing the results of the investigated studies with those of a study examining the effects of a monodimensional intervention based on physical training, no differences in Fatigue or QoL were observed in the intervention group compared to the control group (Dhillon et al., 2017). This may indicate that a targeted combination of multiple interventions may have a stronger impact on QoL and Fatigue in cancer survivors, however, again, the data are not yet sufficient to draw final conclusions. It is always advisable to adapt

the cancer survivorship health care to individual needs, and to weigh which intervention approach would best help regarding the patients individual complaints.

Regarding the effects of the interventions on Quality of Life in cancer patients, the four studies included in this synthesis differed in their results. In one out of the four studies (Adamsen et al., 2009) the multidisciplinary intervention had significant effects on improving vitality, aerobic capacity, muscular strength, physical and functional activity and emotional well-being but not on Quality of Life. The study of O'Neill et al. (2018), which evaluated the impact of a multidisciplinary rehabilitative program on cardiorespiratory fitness, also showed no significant effects on Quality of Life. However, there are already systematic reviews that suggest improvements in cardiopulmonary fitness, which are exercise-related, have a considerable impact on health-related Quality of Life (Sweegers et al., as cited in O'Neill, 2018). The two other studies reported significant effects regarding QOL (Fillion et al., 2008; Rummans et al., 2006), which the intervention groups were able to maintain or increase in the follow-up (Fillion et al., 2008; Rummans et al., 2006). Although both intervention programs had a duration of 4 weeks, a current systematic review and meta-analysis, which aimed to analyze the effects of high-intensity training on health-related Quality of Life in cancer patients and survivors came to the conclusion that exercise programs may need to have a longer duration than 8 weeks, with a high-intensity training frequency of two times per week and a total duration of at least 120 minutes per week, in order to address health-related Quality of Life in an optimal way (Lavín-Pérez et al., 2021). However, the mentioned meta-analysis is the first one to address the effects of high-intensity training in regard to health-related Quality of Life, and therefore further research is urgently needed to support the recent findings (Lavín-Pérez et al., 2021). One explanation for the different results could be the theory that QoL is composed of several components and is therefore shaped very individually (Dimenäs, Dahlöf, Jern & Wiklund, 1990). This assumption would also support focusing on,

and addressing, the survivor's individual complaints in each case. According to another review it can be at least assumed that exercise-based interventions are effective in the short and long term in order to improve the Quality of Life in cancer survivor, and that CBT also showed benefits (Duncan et al., 2017).

In conclusion, it can thus be stated that although multidisciplinary interventions for cancer survivors have shown to be effective in reducing fatigue and increase or maintaining Quality of Life, it cannot be generalized due to different results in comparison with recent research. Since the effects differ from study to study and it still is not clear which components may contribute to the effect sizes, multiple studies have reported the effectiveness of intervention programs (Duncan et al., 2017; Lavín-Pérez et al., 2021; Sweegers et al., as cited in O'Neill, 2018, Rummans et al., 2006; Fillion et al., 2008; Adamsen et al., 2009; O'Neill et al., 2018). Thus, multidisciplinary interventions can lead to a reduction of fatigue complaints and increase the QOL in cancer survivors, however it has to be taken into consideration, that there is still a lot of research required, in order to analyze what component of the intervention program leads to the desired results and if it is really necessary to provide multimodal therapy to every cancer survivor, since there are also reports of monodisciplinary interventions with significant effects on typical cancer survivors complaints (Arch & Mitchell, 2015; Feros et al., 2013).

Quality of the studies and Limitations

A strength of this systematic review is, that it supports recent findings regarding the effectiveness of interventions on QOL, that could help to provide a feasible and structured multidisciplinary intervention for cancer survivors (Ruiz-Vozmediano et al., 2020). Since the survival rates of cancer patients will increase in the future, it is important to highlight suitable interventions in order to reduce or diminish the common complaints cancer survivors

experience (Firkins, Hansen, Driessnack & Dieckmann, 2020). Thus, this systematic review mainly supports the current research, since there were significant effects reported regarding fatigue and QOL. Additionally, it also provides an overview of different multidisciplinary programs and their results, which can be beneficial for further research on this topic. Another strength of this review is, that all of the studies investigated on the effects of the intervention programs regarding fatigue and QOL (Adamsen et al., 2009; Fillion et al., 2008; O'Neill 2018; Rummans et al., 2006).

However, the limitations of this systematic review also have to be considered. One of the limitations is the use of different questionnaires, which makes a comparison more difficult. While two of the studies used the EORTC QLQ-C30 questionnaire, the two other studies consisted of the MFI and the Linear Analog Scales of Assessment of QOL (Adamsen et al., 2009; Fillion et al., 2008; O'Neill 2018; Rummans et al., 2006). Therefore, fatigue and QOL was not only evaluated with different questionnaires, but also in different detail and depth, since the items are not the same (Adamsen et al., 2009; Fillion et al., 2008; O'Neill 2018; Rummans et al., 2006). Even though the EORTC QLQ-C30 is a very common multidimensional assessment of health-related QOL, there is still a growing discrepancy between the measured items and the rapidly evolving treatment environment (Blazeby et al., as cited in O'Neill, 2018). Therefore, the authors of one of the four described studies stated that during group discussions it was revealed that their intervention program still seemed to had benefits on physical, mental and social well-being, and that the participants of the experimental group may have benefited regarding QOL qualitatively and subjectively in a dimension, which cannot be evaluated by modern HRQOL tools (O'Neill et al., 2018).

Another concern is the multidisciplinary aspect of the interventions, thus it cannot be assumed which specific component leads to the desired significant effects, or if the multidisciplinary design itself is responsible for it, since there are also studies that report

significant effects by only using monodisciplinary interventions, such as ACT alone (Arch & Mitchell, 2015; Feros et al., 2013).

A last limitation would be the small number of studies included in this systematic review and their heterogenous results, since this is not sufficiently informative. However, the different outcomes may highlight again the requirement for more research in this field.

Future Research and Recommendation

Upcoming systematic reviews in the future should include more studies and focus on providing comparable outcome measures. Most ideal would be studies that use the same questionnaires, in order to make a comparison easier and valid. It would also be reasonable to do studies with more participants, in order to be able to generalize the results for the population. Since the effectiveness of multidisciplinary interventions for cancer survivorship rehabilitation have not been fully researched yet, future studies should also focus on examining the impact that each component of the multimodal program may hold. Meta-analysis has shown different results, and therefore the impact of each component remains uncertain (Duncan et al., 2017; Lavín-Pérez et al., 2021; Sweegers et al., as cited in O'Neill, 2018). Additionally, it is recommended to investigate the impact of a component alone, as well as combined, since mono- and multidisciplinary interventions appear to be nearly equally helpful and effective for cancer survivors (Korstjens et al., 2011).

Conclusion

It can be concluded, that there is still research needed in order to make generalizations and to improve the health care for cancer survivors. Furthermore, it is not only in the interest of the cancer survivors, who suffer from various symptoms to get a feasible intervention. In regard to the health care expenses, it is also important to consider an effective intervention to

reduce not only the complaints but also the costs for the rehabilitation care (Lorgelly & Neri, 2018). Furthermore, it is important to investigate to what extent multimodal therapy approaches are really better suited to alleviate certain symptoms and complaints in cancer survivors. Since monodimensional approaches also show significant effects with regard to symptoms such as anxiety or fatigue, and are more cost-effective, it is important to weigh up which intervention approaches should be pursued (Korstjens et al., 2011; Arch & Mitchell, 2015; Feros et al., 2013). Although many experts agree that a multimodal approach addresses more areas and is therefore well suited (Integraal Kankercentrum Nederland, 2017) for the various symptoms and complex problems of cancer survivors, there is still a lack of studies that clearly show an advantage over monodimensional approaches. Future research should also examine the impact of the place, where the interventions are being provided, since there could be differences between hospitals or specific oncologic rehabilitation centers, as they tend to be specialized in cancer care and there is a lack of studies, which evaluate the impact of the treatment environment.

It can be concluded that this systematic review supports current research and the results, that a multidisciplinary intervention program is at least feasible and may be effective in cancer survivorship rehabilitation, even though the studies reported different results. The trend of current research definitely supports the assumption that specific interventions may have a statistically significant impact on fatigue and QOL. However, it is important that further research is done in the future, in order to address the limitations of this review, which were described in the previous section and to offer new insights into the effectiveness of multidisciplinary interventions for cancer survivors, especially to examine the differences between mono- and multidisciplinary based interventions more, but also to investigate the impact of each component in a multidisciplinary intervention. This systematic scoping review still highlighted the importance of an ideal treatment program for cancer survivors, not only

regarding their symptoms and burdens, but also in regard to costs in the health care system. All in all, it can be concluded, that significant effects were reported, but the comparability between the studies still lacks, and the real impact of an intervention component is not certain and does not allow a generalized statement.

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