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Exercise Intervention Features to Improve Physical Activity Levels in Young Adults with a Cancer Diagnosis: A Systematic Review

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Abstract

Exercise intervention features to improve physical activity levels in young adults with a cancer diagnosis: A systematic review.

Objective: To identify the different interventions focused on increasing Physical Activity (PA) levels in Young Adults with cancer (YAwC), as well as the features and benefits of the existing exercise interventions for this population.

Design: Systematic review.

Methods: Selected studies were identified from searches in the PubMed and Web of Science databases. In the search, different filters were used, such as Randomized Control Trials (RCTs), Randomized Trials (RTs), human trials and trials with adults aged 18 to 44 years, Control Trials (CTs) and trials written in English.

Results: A total of thirty-one articles met the inclusion criteria, five of which included theoretical-based interventions. The other six studies used an exercise intervention, and only one study performed a mixed program. The findings of these studies showed that different modalities of exercise interventions increased the level of PA. The main characteristics of these programs were that they included exercise and behavioral interventions, with duration of 12 weeks (2 to 4 days per week), a range of intensity between 55% and 70% of the Maximum Heart Rate (MHR), and supervised sessions.

Conclusion: The results of this review support that these specific programs for YAwC not only improve their levels of PA, healthy parameters, and lifestyle but also improve their family, economic and social environments.

Keywords: Young adults; Cancer; Physical activity; Exercise

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Introduction

Young Adults with a Cancer diagnosis (YAwC) are an important target population due to the high impact that this population has on the economy and in different dimensions of society [1]. YAwC are defined as patients between 18 and 45 years old with a cancer diagnosis, and in 2012, incidences of 43,000 new cancer cases as well as 15,000 cancer-associated deaths were reported in this population [2]. The Spanish Society of Medical Oncology (SEOM) has estimated 16,000 new cases of cancer in young adults in 2022 [3].

Although the incidence is rising in YAwC, mortality is decreasing in developed countries thanks to new effective treatments, [4] increasing the number of prevalent cases. These individuals, with their expected lifespan, play an important role in their families, which has a high impact on the economy and society because of the major effects of premature morbidity [2,4].

Regarding data from the European Cancer Information System (ECIS), the most common cancers in this population in 2020 were breast cancer, testicular cancer, thyroid cancer, non-Hodgkin lymphoma, melanoma, and uterine cancer, cancers of the Central Nervous System (CNS) and colorectal cancer. Moreover, young adults with certain types of cancer, such as Hodgkin's

lymphoma, non-Hodgkin lymphoma, germ-cell tumors, melanoma, and thyroid carcinoma, have shown better prognoses than their older counterparts [4]. In contrast, regarding other cancers, such as breast and prostate cancer, young patients, who are commonly diagnosed with more aggressive and advanced-stage tumors, present lower survival rates [5-8]. This situation involves YAwC in intensive chemotherapy schemes, which are associated with higher side effects and long-lasting comorbidities, which prevent to recover of a normal life [9].

Cardiac side effects [10] are observed, especially if chemotherapy combinations contain anthracyclines, which have been related to a hazardous rise in heart failure of 10.7% in Hodgkin's lymphoma survivors, even 25 years after cancer diagnosis [11]. Another cancer-associated side effect is cachexia (muscle mass loss), which not only reduces functionality and tolerance to anticancer therapies [12-14] but also has a high impact on patients' psychosocial environments, such as leading to a negative body image or problems with self-esteem [15]. However, the impacts of these side effects in this population in the long term have not been well studied [16].

Physical Activity (PA) and exercise oncology programs during and after cancer treatments have been established as effective tools to improve cancer patients' quality of life and reduce other cancer comorbidities. Combined exercise (aerobic and strength exercises) with moderate-vigorous intensity is the most common and effective intervention in exercise oncology [17-20], achieving improvements in VO2 max levels, insulin sensitivity, body composition, muscle strength and reducing fatigue and fat mass [18].

However, participants included in most of the exercise oncology studies presented a mean age over 50 years old, which suggests that YAwC are not sufficiently represented in the included samples. In addition, the young population presents distinctive characteristics in treatments, pre- and post-diagnosis lifestyles and general interests that need to be studied to better understand how exercise impacts the health and motivation of YAwC [19].

Regarding the lack of information about the impacts of exercise in YAwC, the purpose of this review was to identify the different interventions focused on increasing PA levels in YAwC, as well as the features and benefits of the existing exercise interventions for this population.

Methods

Design

A systematic review was performed to determine the PA levels and effects of exercise on the levels of PA, quality of life and health of YAwC, presented in Randomized Trials (RTs) and Randomized Control Trials (RCTs). In addition, the methodological quality and results of the selected studies were discussed.

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review (PRISMA) statement [21].

Literature search and selection criteria

The search strategy was to identify relevant papers published before September 01st, 2022. The electronic databases (PubMed and Web of Science) were systematically searched by combining the following Boolean operators and keywords: "cancer OR lymphoma OR Hodgkin lymphoma OR lymphoma no Hodgkin AND leukemia AND sarcoma AND malignant tumor OR all cancers" AND "young adults OR young adult survivors cancer OR young people" AND "exercise program OR exercise intervention OR physical exercise OR endurance exercise OR strength exercise OR resistance exercise OR physical activity OR combined exercise program". In addition, the filters of "RCT, RT, humans, and 18 to 44 years" were included in PubMed, and "CT and English written" were included in Web of Science.

A first abstract screening was developed to identify paper issues and types of interventions. Second, potential eligible manuscripts were evaluated based on the following selection criteria: 1) RCT or RT; 2) the mean age of the sample was between 18 and 45 years; 3) the participants had to present a diagnosis of any type of cancer in the previous 5 years; 4) papers with any measurement of any physical activity level parameter; 5) interventions with a maximum duration of six months; and 6) papers written in English. Systematic reviews, meta-analyses, editorials, case reports, cross-sectional studies and case series studies were excluded.

Selection of studies

For the selection of the studies, the titles and abstracts found with the search strategy were independently screened by two researchers (M.C. and L.G.). Then, the full text of the screened studies was obtained, and each paper was reviewed using the predefined eligibility criteria.

Data extraction and assessment of methodological quality

Two authors independently conducted the search and data extraction (M.C. and L.G.). Relevant data of the studies were extracted by the previously mentioned authors following the PRISMA guidelines [21]. The investigators extracted the following information: First author's last name; year of publication; population, including sample size, sex, age, cancer type and stage of the illness; exercise interventions, including the type of intervention, if it was supervised, and the frequency, duration, intensity, and level of adherence; outcomes as the measurements and instruments used; and the main results including the statistical analysis used. A third independent investigator (S.C.) reviewed the quality of the selected papers.

The methodological quality of the studies was assessed using the PEDro scale, which is based on the Delphi list [22]. The PEDro scale assesses the methodological quality of randomized trials, with possible scores up to 10 points. Scoring was based on the information available in the published version.

Assessment of methodological quality and quantitative analysis

The methodological quality of the 13 studies included in this review was evaluated using the PEDro scale, a specific tool that assesses the quality of randomized clinical trials. In this sense, trials with scores less than 4/10 present low methodological quality, and trials with scores over 4/10 are considered high methodological quality RCTs. The PEDro scale evaluates the following items, and the results of our evaluation are shown in Table 1:

1. Eligibility criteria specified: this criterion relates the external validity, but it is not used to calculate the PEDro score.
2. Random allocation
3. Concealed allocation

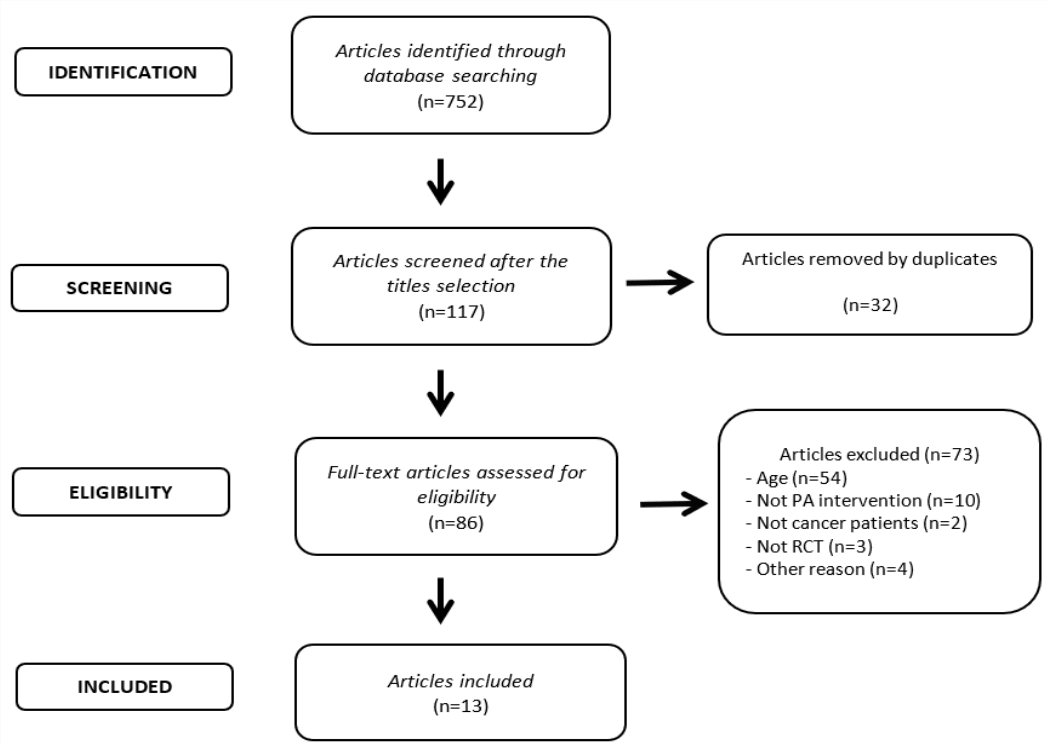

Figure 1: PRISMA Flow diagram.

4. Groups similar at baseline
5. Subject blinding
6. Therapist blinding
7. Assessor blinding
8. Less than 15% dropout
9. Intention-to-treat analysis
10. Between-group statistical comparisons.
11. Point measures and variability data.

The scores of methodological quality of all the analyzed studies ranged from 6 to 7 out of 10, which are considered to indicate "high" methodological quality on the PEDro scale (scores greater than or equal to 6/10).

Regarding the items of the PEDro scale, only those related to the process of blinding were not included in any of the studies, suggesting the difficulty of this practice in this type of study. With respect to the other items, most were followed in the selected studies, suggesting appropriate internal validity.

Results

Selection of studies

Figure 1 presents the PRISMA flow diagram. The initial search strategy identified a total of 752 studies. Thirty-one duplicated studies were removed. One hundred-seventy studies were selected out of the remaining 721 based on the title and abstract information. In the manuscript analysis, a total of 73 studies were excluded because the participants' ages were not reported or their ages were out of range, they did not include any PA intervention, the studied populations were not cancer patients, and the studies were not RCTs. Finally, 13 studies were included in the review that fully met the inclusion criteria.

Characteristics of the studies

Features of the sample: The main inclusion criteria of the studies were the absence of medical conditions or contraindications that precluded exercise or PA due to cardiovascular disease.

Related to the sample characteristics, age, stage of the illness, type of cancer and sex were collected in all the studies, while stage of cancer was reported in only seven of them. Seven studies included patients in early cancer stages (from I to IIIA), survivors and only patients with primary cancer (metastatic or secondary cancer patients were not included) [23-29] and three studies reported data including patients in advanced or metastatic stages (IIIB, IIIC and IV) [23,26,27]. Cancer stage was not reported in five of the included studies [30-34].

Time from diagnosis was collected in six of the twelve selected studies, of which three were performed during the first year after diagnosis [23,25,27]; one included woman who were cancer free 5 years after diagnosis [26]; and the last two included participants who were diagnosed with cancer in the past 10 years [30,31]. In six studies, this information was not reported [24,28,29,32-34].

Twelve studies enrolled a total of 973 young adults with a cancer diagnosis who had an average age of 32.9 years. Regarding the sex of the participants, 81.1% were female, and only 18.9% were males, despite both sexes being included in nine of these studies [23,24,25-34].

The most common types of cancers were breast cancer (63.6%); Hematologic cancer, such as lymphomas and leukemias (16.7%); testicular cancer (8.7%); gynecologic cancer, such as endometrial or

Table 1: Methodological quality of the 13 included studies.

Author year	2	3	4	5	6	7	8	9	10	11	Total
Jesper 2014 [24]	+	+	+	-	-	-	+	+	+	+	7/10
Erickson et al. [32] 2021	+	+	+	-	-	-	+	+	+	+	7/10
Valle et al. [23] 2013	+	+	+	-	-	-	-	+	+	+	6/10
Rabin et al. [30] 2011	+	+	+	-	-	-	+	+	+	+	7/10
Ibrahim et al. [25] 2017	+	+	+	-	-	-	+	+	+	+	7/10
Bloom et al. [26] 2008	+	+	+	-	-	-	+	+	+	+	7/10
Thorsen et al. [27] 2005	+	+	+	-	-	-	-	+	+	+	6/10
Rabin et al. [30] 2015	+	+	+	-	-	-	+	+	+	+	7/10
Atkinson et al. [33] 2021	+	+	+	-	-	-	+	+	+	+	7/10
Salchow et al. [34] 2021	+	+	+	-	-	-	+	+	+	+	7/10
Wurz et al. [28] 2021	+	+	+	-	-	-	+	+	+	-	6/10
Wurz et al. [29] 2021	+	+	+	-	-	-	+	+	+	-	6/10
Total	12/12	12/12	12/12	0/12	0/12	0/12	10/12	12/12	12/12	10/12	

cervical cancer (5.25%); and other tumors (5.5%). Only two studies, with 96 patients, were performed under treatment conditions (chemotherapy) [24,32], while the other ten studies, with a total of 877 enrolled YAwC survivors, were performed without treatments [23,25-31,33,34].

Features of the interventions

Exercise interventions: We evaluated studies with three types of interventions: Five with theoretical-based interventions, six with exercise interventions and one with workshop activities.

Regarding theorical-based interventions, the type of exercise that patients performed by themselves was collected in only two of the five studies. In both of these studies, aerobic activities were performed by the patients [23,31]. Regarding the six studies with exercise interventions, the selected type of exercise was described in all of them: One study developed whole-body resistance training [24]; four studies involved combined exercise (mixing aerobic and resistance training) [28,29,33]; one study reported an intervention based on upper limb training [25]; and in the last study, patients decided what type of activity they performed, with walking observed as the most common activity [27]. The study that included workshop activities described an intervention based on strength exercises for breast cancer patients [26].

Intensity and instruments of control in exercise interventions: Three of the five included studies with theoretical-based interventions reported moderate-intensity activity to improve PA levels [23,30,31]. Two of them scheduled exercise intensities in a range of 55% to 70% of the Maximum Heart Rate (MHR) [30,31]. The third study only described the performance intensity from light to moderate, without HR specifications [23]. However, in the other two studies, PA intensity was not reported [32,34].

On the other hand, the seven studies with exercise interventions showed different intensities depending on the type of exercise performed [24-29,33].

In this sense, five studies included combined interventions [25,27-29,33]. In these studies, aerobic exercise intensity was adjusted based on the patient's physical condition or fatigue level, reaching intensities between 50% to 85% of the MHR and from 40% to 75% of the heart rate reserve. In addition, not only the intensity but also the number, frequency and duration of the sessions were registered during the program, ensuring an adequate progression in the exercise load [25,27-29,33]. For strength exercise intensity, the first study adjusted intensity to achieve from 10 RM to 20 RM, based on the patient's level of fitness [25]. In the second study, intensity was established in >80% of 10 RM [33]. The third study evaluated the patient's subjective experience of tiredness (between 13 and 15 on the Borg Scale) [27]. Nevertheless, in the last two studies, the intensity of the strength intervention was not reported [28,29].

One study only performed a strength exercise intervention, establishing an intensity from 15 to 10 Repetitions Maximum (RM), reevaluating the RM in the middle of the program [24]. Finally, one study included workshop activities using elastic bands, but the intensity was not reported [26].

Level of adherence and follow-up: Seven studies reported adherence to the intervention or follow-up of the patients' activities [23,24,27,28,31,33,34]. Adherence data were collected in these seven studies, assessed by means of Facebook posts, such as the number of PA sessions and step entries and the setting of weekly goals in one study [23]; by means of types of activities in another study [27]; and by means of collecting attendance, which was between 60% to 90% for adherence to the program in the rest of studies [24,28,31,33,34]. Only two of the studies also reported a follow-up 12 weeks and 6 months after the intervention [31,33].

Level of outcome achievement

Levels of PA: Eight of the nine studies where the levels of PA were measured reported improvements in the levels of PA in YAwC and survivors after the intervention [23,25,26,30-34]; two of them obtained an increase in light and moderate minutes of PA (113, 8-135 min/week) in the Intervention Groups (IGs) [23,31]. Another study showed an increased mean of 23.7 MET-h/week in the IG, compared to a mean of 14.6 MET-h/week in the Control Group (CG) [25]. One study showed that 37.5% of the IG met the ACSM criteria for PA, compared to 10% of the CG after the intervention [30].

Two studies showed improvements in both groups after the intervention [33,34]. In one of them, an increase was observed in vigorous PA, but in the follow-up, only the IG showed increased vigorous PA levels [34]. In the other study, both groups were sufficiently active after 10 weeks and 6 months (LS>23) [33]. An

Table 2: Studies selected in this review.

Authors	Year	Population n, sex, cancer type, study type	Exercise or physical activity intervention type, supervised, frequency, duration, intensity	Main objective	Instruments main objective	Other objectives	Adherence and follow up	Achievement of objectives	Results
Jesper et al. [24]	2013	49, males, 18-50 years, germ cell cancer patients, RCT.	Resistance exercise, supervised, 3 times a week for 9 weeks, 15RM and 10-12RM.	To examine the effects of resistance exercise in concentrations of selected cytokines, QOL and fatigue.	Blood test, QOL, and EORTC.	RF PF Bone marrow Toxicity Adherence	Adherence: 70% attended sessions	No	Chemotherapy reduced RF and PF and increase PCLs. Positive correlation between plasma TNF cytokine levels and pulmonary toxicity. PCLs were unaffected by RT. Higher IL-6 cytokine levels increased fatigue and reduced QOL.
Erickson et al. [32]	2021	47, males and females, 18-39 years, any type of cancer, pilot RCT.	Theorical-based intervention, not supervised, 12 weeks, setting walking goals, measuring steps/day.	To improve self-management of fatigue.	Accelerometer, PAAI, SRI for Physical Activity, and PROMIS.	Self-efficacy, self- regulation and outcomes related to PA levels and fatigue severity.	None	No	There were no significant differences between the groups for any of the variables. Fatigue levels increased in the CG but decreased in the IG. Total PA increased in the IG and decreased in the CG. Self-efficacy decreased in the CG but remained the same in the IG. Self-regulation increased in both groups.
Valle et al. [23]	2013	86, males and females, 21-39 years, all types of cancer excluding nonmelanoma skin cancer, RT.	Social cognitive theory, not supervised, 12 weeks, moderate to vigorous intensity.	To evaluate the efficacy of a behavioral intervention to Improve PA levels.	GLTEQ	QOL Body weight BMI Adherence	Adherence: 66%, 7% Adherence: 66,7% goal-setting. 71,7% PA and steps entries	Yes	The IG PA level increased by approximately 135 min/ week more than the CG levels for light PA. The IG reported an increase of 237 min/ week compared to 75,7 min/week in the CG for total minutes of PA. Participants who set the highest goals with at least 10 weekly goals reported higher vigorous PA.
Rabin et al. [30]	2011	18, males and females, 18-39 years, all types of cancer excluding nonmelanoma skin cancer,	Internet-based PA, behavioral intervention, not supervised, 12 weeks, <70% MHR.	To assess the level of PA, mood, and fatigue after the internet-based PA intervention.	PAR POMS.	NR	None	Yes	37.5% of the IG was meeting the ACSM criteria for PA compared to 10% of the CG. Intervention participants had greater reductions in fatigue from baseline to 12 weeks compared to controls.
Ibrahim et al. [25]	2017	59, females, 18-45 years, stage IV breast cancer, RCT.	Upper limb mobility, strength, and endurance. Supervised and home based, 2 times for 12 weeks, 10 minutes of a cardiovascular exercise as a warm-up then 8-10 reps RM and 20 reps RM. At least 30 minutes per session.	To assess the effectiveness of the exercise program in upper limb dysfunction and pain.	Disability of Arm, Shoulder and Hand questionnaire	Levels of PA	None	Yes	The IG showed an increased mean of 23.7 MET- h/week, compared to the CG mean pf 14.6 MET-h/week. Women in the intervention group showed better scores on the carrying heavy objects test. 86% of the women returned to work decrease of 8.5 h/week 89% resumed prior work activities.

Bloom et al. [26]	2008	404, females, <50 years, breast cancer survivors, RCT.	Mixed program with theory and practice methodology based on "healthy behavior workshops", supervised,6 hours a day per month for 3 months.	To improve the knowledge about breast cancer, diet, increase PA levels and communication with family through workshops.	21 Likert-formatted items. Block's Fruits and Vegetables and Fat screeners. METs Likert type scale from 1 frequently to 4 never	NR	None	Yes	77% of the women who had begun the exercise program after the workshops reported an increase of PA. Increased knowledge levels for breast cancer. Did not improve diet or family's communication.
Thorsen et al. [27]	2005	111, males and females, 18-50 years, lymphomas, breast, gynecologic or testicular cancers, RCT.	Home-based, flexible training program, resistance, and endurance exercise, supervised, home-based, 14weeks, minimum of 2 sessions per week, 13-15 on the Borg Scale and 60-70% of the MHR. At least 30 minutes per session.	To evaluate the effects of program on CRF and QOL parameters.	Å strand-Rhyming indirect test of maximal oxygen uptake, EORTC QOL, and Hospital Anxiety and Depression Scale.	Adherence	Adherence: The mean number of activities performed was 2.6 and 1.9 in the IG and the CG, respectively.	Yes	VO2max increased by 6.4 ml/kg 1/min1 in the IG and by 3.1 ml/kg 1/min1 in the CG. Did not improve QOL, fatigue levels, anxiety, or depression. A dose-response association existed between the number of minutes spent exercising per week and changes in VO2max from baseline to post intervention in all patients.
Rabin et al. [30]	2011	35, males and females, 18-39 years, all types of cancer, RCT.	Theory-based intervention, endurance exercise, not supervised, to obtain at least 5 days per week, 12 weeks, 55-69% of the MHR. Mindfulness, 4 days per week. At least 30 minutes per session.	To examine the feasibility of the intervention to increase PA levels, fitness, and mood.	PAR, One Mile Walk Test, POMS.	Follow-up	Adherence: 77% completed the intervention Follow-up: Patients maintained improvements 12 weeks later.	Yes	The IG performed at least 113.8 minutes of moderate PA. Treadmill walk test time was reduced by 1.06 in the IG. Mood disturbance did not show significant differences between the groups, but it improved after the intervention in both groups. Patients maintained improvements12 weeks later. Did not improve mood.
Atkinson et al. [33]	2021	43, males and females, 15-25 years, hematological malignancy, or solid tumor, RCT	Structure exercise intervention. Aerobic and resistance exercise, supervised sessions in the hospital or community-based gymnasiums, 12 weeks, 2 sessions per week, moderate intensity 50%- 60% of the MHR and high intensity >85% MHR, 2-3 sets of 8-12 repetitions at >80% of 10 RM.	To improve CRF, as measured by VO2peak, muscular strength and flexibility, fatigue scores, and QOL.	Cycle ergometer with gas analysis. Hydraulic hand grip and leg dynamometer. Maximal push-ups test, sit-up test, Sit and Reach Flexibility Test, and back scratch test, spirometer. Pediatric QOL Inventory, FACIT-F, GLTEQ, BMI, waist circumference and Common Terminology Criteria for Adverse Events.	Follow-up Adherence	Follow-up: At 6 months there were significant differences in body mass and BMI favoring the EG. Adherence: 90% attended sessions	Yes	Vo2peak in the exercise group EG was 33,8 compared to that of 29,6 in the CG. Percent VO2max predicted was 87,6% *vs.* 77,4% in the EG and CG, respectively. In strength and flexibility only, maximal push-up number was greater in the EG compared with that in the CG. No differences in QOL and fatigue. No significant differences in leisure time PA, but both groups were sufficiently active after 10 weeks and 6 months LSI>23. Body mass and BMI did not change after 10 weeks. No adverse events occurred during the supervised exercise sessions.

Salchow et al. [34]	2021	89, males and females, 15-39 years, solid tumor, leukemia, or lymphoma, RCT.	Trans theoretical Model intervention, not supervised, personalized plan with goals; 12 weeks; not reported days per week.	To improve vigorous PA behavior.	International Physical Activity Questionnaire. EORTC	Amount and intensity of PA, QOL, activity preference, and reasons for not participating	Adherence: 77.5%	No	There were no differences between the groups in vigorous PA after the intervention. Only the IG showed increased parameters of vigorous PA days, hours, and MET scores at follow up. The time spent sitting was reduced in both groups from baseline to post intervention. Only the IG maintained these values at follow up. QOL showed no significant differences in either group after the intervention. Preferred activities were resistance training, swimming, yoga, cycling and running. The reasons for not participating were distance, a lack of time, never liking PA, feeling too weak and others.
Wurz et al. [28]	2021	16, males and females, 15-39 years, all types of cancer, pilot RCT.	Physical exercise intervention, supervised only 6 weeks, individualized baseline assessment results, 12 weeks, 4 sessions per week 25-45 minutes, 2 strength sessions 1–3 sets of 6–12 repetitions, 2 aerobic sessions 40-75% of the heart rate reserve	To know if it is feasible to use neuroimaging with executive functioning tasks to assess neural activity changes following a PA intervention.	3 Tesla Siemens Biograph MAGNETOM MR-PET scanners.	Changes in neural activity after 12 weeks of the PA intervention.	Adherence: 67%	Yes	Participants' executive functioning task performance data did not show differences in errors of commission, omission, and reaction time. There were significant differences in neural activity after 12 weeks of the PA intervention. Regions of the brain responsible for working memory, planning complex movements, cognitive and motor control, response inhibition and decision-making may show increases in their neural activity due to PA.
Wurz et al. [28]	2021	16, males and females, 15-39 years, all types of cancer, pilot RCT.	Individualized PA program, supervised only 6 weeks of resistance training, 12 weeks, 4 days/week 25-45 minutes, 2 resistance training sessions 1-3 sets of 6-12 repetitions, aerobic training sessions were unsupervised 40–75% of the HRR	To observe the self-perceptions of this population.	Self-report questionnaire covering personal and medical factors. Qualitative interviews for self-perceptions.	To understand how PA may contribute to self-perceptions after cancer treatment.	None	Yes	Participants showed positive changes in self-worth following cancer treatments. Frustrations, discontent were feelings the participants compared to their physical abilities pre cancer to post treatment. Only those who had performed physical activity before cancer had major confidence levels and saw themselves capable of being physically active. The PA intervention positively impacted their physical capacity, patients felt surer of

RCT: Randomized Control Trial; RT: Randomized Trial; CT: Clinical Trial; RM: Repetition Maximum; MHR: Maximum Heart Rate; HRR: Heart Rate Reserve; QOL: Quality of Life; PA: Physical Activity; CRF: Cardiorespiratory Fitness; EORTC: European Organization for Research and Treatment of Cancer; PAAI: Physical Activity Assessment Inventory; SRI: Self-Regulation Index; PROMIS: Patient-Reported Outcomes Measurement Information System; GLTEQ: Godin Leisure Time Exercise Questionnaire; PAR: Physical Activity Recall; POMS: Profile of Mood States; METs: Metabolic Equivalent of Task; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; BMI: Body Mass Index; RF: Renal Function; PF: Pulmonary Function; PCLs: Plasma Cytokines Levels; RT: Resistance Training; IG: Intervention Group; CG: Control Group; ACSM: American College of Sport Medicine; VO2max: Maximum Oxygen Consumption: VO2peak: Peak Oxygen Consumption; LSI: Leisure Score Index; FV: Fruit and Vegetables

increase in PA after the workshops was reported in 77% of the participating women [26].

Finally, only one study described a dose-response relationship correlating the number of minutes of exercise per week with the changes observed in VO2 max from baseline to the post intervention assessments [27].

Body composition and fitness capacity: Curiously, body composition was assessed in only two studies, and body weight, body mass and BMI were the only parameters measured. It should be noted that after the intervention in the first study, the IG lost 2.1 kg of body weight; however, no changes in BMI were observed [23]. In the second study, body mass and BMI did not show changes after 10 weeks of intervention [33].

PF and RF were measured in one study, but the RT intervention did not improve these parameters in YAwC during chemotherapy [24]. In addition, it should be noted that one study observed an increase in neural activity after 12 weeks of the PA intervention [28]. Related to upper limb function, only improvements in carrying heavy objects were significant in women with breast cancer [25].

Fitness capacity was assessed in three studies, and a significant improvement was observed in all these studies [27,31,33]. Strength and flexibility were evaluated in one study, where only the IG performed better in the maximal push-up test. Flexibility did not show significant differences between the groups [33].

Quality of life, fatigue, and mood: QoL was measured in five studies [23,24,27,33,34]. Four of them did not report changes after the intervention [23,27,33,34]. Only one showed a reduction in QoL for patients who reported high levels of IL-6 [24].

Fatigue was measured in five studies [24,27,30,32,33]. In two of them, fatigue was reduced after the theoretical-based intervention [30,32] and two others did not show changes after the intervention [27,33]. Finally, one study showed a positive correlation between fatigue and IL-6 levels in patients undergoing chemotherapy [24].

Regarding mood, anxiety or depression, improvements were not observed in any study [27,30,31].

Other outcomes: Nine studies assessed other interesting outcomes that are included in Table 2 [24-26,29,31-34], highlighting the positive correlation between plasma TNF cytokine levels and pulmonary toxicity [24]. Adaptations in time returning to work after cancer [25], knowledge about breast cancer [26], PA levels after 12 weeks [31] 6 months of follow-up, sitting time [34] and changes in self-perception [29,32] were other interesting assessments in the selected papers.

Discussion

Features of an exercise intervention to increase PA levels in YAwC

The novelty of this review is that it focused on describing different existing interventions to promote PA in YAwC, with the objective of analyzing the features and benefits of these programs in the target population because of its interesting profile. The overall quality of the included studies was high, although the number of studies found in this population was low, limiting the capability to draw decisive conclusions about the results of these interventions. Despite this, a total of 973 patients were recruited in the twelve selected studies [23,24,25-34].

The main result of this review shows an increase in PA levels after different modalities of exercise interventions in this population [23,25,26,30-34]. Nevertheless, mixed interventions, including exercise and educational programs, supervised interventions, interventions with a duration of 12 weeks, interventions maintaining a frequency between 2 to 4 days per week, and interventions with a range of intensity from 55% to 70% of the Maximum Heart Rate (MHR), were the main characteristics of the programs that obtained the best results for improving PA levels in YAwC.

A previous review supports our conclusion that young adult cancer patients have increased PA levels after different PA programs. As we described previously, face-to-face and mixed (exercise and theoretical) interventions and supervised sessions were the most prominent features of these studies. However, in this review, there was a lack of information about the specific dose of exercise needed to improve physical conditions depending on the illness stage (under treatment, metastatic or survivors) [35].

In line with our population, PA levels are not collected in most of the studies evaluating older cancer patients (>60 years). Moreover, interventions for older cancer patients are usually face-to-face, supervised by qualified intervention staff, not theoretical-based programs and include more integrative interventions, including nutritional counseling [36].

Considering that only 40% of healthy young adults are meeting the PA levels recommended by the World Health Organization [37], and taking into account that cancer is an illness that reduces PA levels in this population, [38,39] more interventions are essential. In this sense, previous studies have reported two appropriate stages during the cancer process when physical activity interventions are more effective: After diagnosis and during treatment [39]. In line with this, our review elucidates the features that an exercise intervention should have to be effective in improving PA levels in this population.

In addition, it is important to highlight that individuals in this age group are the most financially productive members of their societies, with a longer life expectancy and an important role in caring for their families [40]. Nearly 32% of young adult cancer survivors reported low social functioning over time [41]. In addition, YAwC may receive intensive chemotherapies due to their age and substantial tolerance of treatments. However, the appropriate management of side effects and toxicity of treatments are essential not only for increasing quality of life but also for preventing other comorbidities that may reduce life expectancy in YAwC [40,42]. Despite the benefits of exercise for cancer patients, low PA levels have been reported by young adult patients after diagnosis and during treatment [38].

Other benefits of exercise interventions for YAwC

Our review has observed that exercise interventions are related to multiple benefits in this population. Specifically, improvements in fitness capacity [27,31,33] and reductions in body weight were reported [23] in the included studies. Regarding fatigue, only two studies that included theoretical-based programs showed significant reductions [30,32]. In line with the results of one of the included studies [28], PA interventions might be able to mitigate cancer-related cognitive impairment in the long term in YAwC, improving their QoL, [43] although more studies are needed in this sense. Other studies support the findings described in this review, such as improvements in health parameters, changes in fitness capacity, and reductions in different cancer treatment side effects [44].

On the other hand, different studies that evaluated QoL, [23,24,27,33,34] proinflammatory cytokine levels [24], and mood [27,30,31] did not report significant changes. In addition, an interesting finding was that changes in PA (moderate intensity) and the benefits observed in the aerobic fitness intervention were maintained 12 weeks after at the end of the program [31].

However, the majority of physical exercise oncology research has involved samples including older adult patients (18 to 80 years), [19,45] showing a lack of knowledge for this particular population. In general, physical exercise is related to improving different health outcomes and side effects in cancer patients, such as physical function, fatigue, quality of life, anxiety, depression, bone health, and lymphedema. However, it is crucial to individualize the exercise dose according to the type of patient, the stage of the disease, and the patient's baseline physical level [19].

How can interventions be improved in this population?

First, it is important that studies describe the exercise dose used in the intervention, as it might contribute to the application and transfer of this knowledge to exercise community programs.

Second, it is mandatory that studies describe how the exercise is adapted for the participants, considering not only the initial level of every patient but also the secondary effects and other possible comorbidities developed during cancer treatments.

Third, half of the studies reported the level of adherence to the intervention, assessed by the percentage of the assisted sessions or by the number of proposed activities developed. Related to adherence, the included studies reported a mean close to 75%, which is considered a low level of adherence (it should be over 75%) [46,47]. In this sense, different strategies to improve patient adherence and motivation, such as the type of activities or including different items of the CALO-RE taxonomy, should be considered to improve exercise interventions for this population [46].

Related to the second method of adherence assessment, the means of the number of activities performed were 2.6 and 1.9 (per week) in the IG and CG, respectively [27]. Regarding the follow-up, no changes were observed in the adherence level 12 weeks after the end of the intervention, indicating that the effects of the program were long lasting [31].

To the best of our knowledge, this study represents an attempt to systematically review the existing information about different strategies to improve physical activity levels in YAwC. This review suggests that YAwC need specific educational and exercise interventions to increase their PA levels and include exercise in their lifestyles. This behavioral change may not only benefit the patients' health in the short and long term but also their family, economic and social environments.

Study Limitations

The main limitation was the small number of studies included due to a lack of research in this population. In addition, the variability observed in the interventions used limits the capability to extrapolate the observed results. Despite this, all patients included in these studies were survivors, which homogenize the conclusion to YAwC in this situation. Other limitations include the lack of centers and professionals specialized in exercise oncology. The implementation of oncology exercise units and the recommendation of patients by health care professionals to community programs are needed.

Clinical Implications and Future Lines of Research

This review highlights the need for more studies that evaluate the impact of exercise on YAwC, particularly those undergoing treatment for metastatic disease. Other interesting avenues for research are to assess the cost-effectiveness of exercise interventions for YAwC and to evaluate how the side effects of the treatments affect not only the social and economic environments but also the life expectancy of these patients. In addition, other health parameters and long-lasting side effect prevention should be analyzed in the future.

Conclusion

This current review provides the required evidence that both theoretical and exercise interventions increase PA levels in young adults with a cancer diagnosis. The most useful finding was that the features of the exercise interventions in this population significantly improved PA levels, including both theoretical and exercise interventions. In addition, it was observed that fitness capacity, body weight and fatigue improved after the programs, which had a positive impact on the patients' health.

Related to these patients, it was observed that mixed interventions allowed YAwC to maintain appropriate PA levels even during treatment, making patients more capable of meeting daily and family needs. Future research should include different items of the CALO-RE taxonomy to increase adherence levels to the programs.

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