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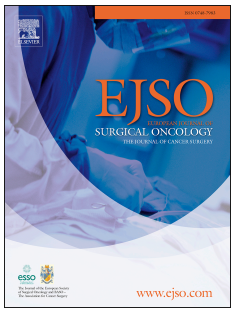

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Effect of physical exercise on the quality of life of women surviving breast cancer: systematic review with meta-analysis of randomized clinical trials

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Abstract

Introduction: Women surviving breast cancer (WSBC) may experience reduced quality of life (QoL) due to disease-associated manifestations and undergone treatment. Engagement in physical exercise (PE), and subsequent effects on physical capacity and social and emotional wellbeing, are known to enhance QoL.

Method: this systematic review meta-analysed the impact of PE, compared to respective control groups, on QoL in WSBC. Randomized clinical trials published up to December 2023 were searched in PubMed Medline, PsycInfo, EMBASE, Web of Science, LILACS, Cochrane Central, Scopus, and Google Scholar. Selected papers were catalogued in Endnote® and remaining documents exported to Rayyan®. Data analyses utilized the RoB2 tool, Revman®, and GRADE for classification of certainty of evidence. Values of change in measurements between baseline and post-intervention were meta-analysed, with standardized mean differences calculated as effect size.

Results: 3,313 documents were identified, with 36 meeting our eligibility criteria, and 35 quantitatively analysed. The meta-analysis revealed that PE, irrespective of modality,

significantly improved QoL, as assessed by the Short Form Health Survey 36 (SF-36) global health perception scale (SMD= 0.43; CI95%: 0.12 to 0.73; p=0.006), FACT-G (SMD= 0.56; CI95%: 0.13 to 0.99; p≤0.01), FACT-B (SMD= 0.73; CI95%: 0.38 to 1.08; p=0.0003), and EORTC QLQ-C30 (Global health, SMD = 0.98; 95% CI: 0.49 – 1.47; p<0.00001). Subgroup analyses showed that combination of aerobic and resistance exercises yielded the most significant increase in QoL. SF-36 subdomains showed moderate to high certainty of evidence.

Conclusion: PE is effective in improving QoL in WSBC, particularly when combining aerobic and strength exercises. Robust public policies must encourage PE not only to reduce cancer risk but also to promote QoL improvement in WSBC.

Keywords: Physical Exercise; breast cancer; Quality Of Life; physical activity.

1. Introduction

Quality of life (QoL) is a multidimensional aspect of human existence encompassing factors such as physical and mental health, socialisation and emotions, social security, wealth and purchasing power, among others [1]. According to the World Health Organization (WHO), QoL is defined as an individual's perception of their position in life within the context of the culture and value systems they are a part of, as well as their position in relation to objectives, expectations, standards, and concerns [2].

Over time, considerable understanding has been gained on this topic, with associations between QoL and various health problems and respective clinical outcomes robustly identified. Therapeutic process involving breast cancer (BC) treatment significantly influences QoL, particularly on physical and emotional conditions, which in turn play a crucial role in the wellbeing of survivors [3,4]. Some studies have assessed QoL of women surviving breast cancer (WSBC), aiming to understand the impact of the disease on the survivors' social, physical, and psychological needs [5,6]. The primary factors believed to influence QoL of WSBC are clinical, sociodemographic, and psychosocial conditions [7].

Consequently, complementary multidisciplinary interventions are necessary to restore or improve clinical conditions of individuals who have undergone BC treatment, with a primary focus on improving QoL and promoting wellbeing [8,9,10]. Multidisciplinary actions are pivotal in mitigating the impacts that BC causes on health. The promotion of a healthy lifestyle, including participation in social activities and regular physical exercise, has been associated with enhanced QoL [11]. Conversely, a sedentary lifestyle, inadequate diet, alcohol consumption, and smoking, are well established risk factors for the health of BC survivors, and addressing such issues contribute to QoL improvement [8, 12].

In the context herein presented, the practice of physical exercise emerges as a complementary intervention capable of restoring the physical capacity of BC survivors who have completed chemotherapy and radiotherapy [13,14]. Beyond managing symptoms of stress and depression, and the promotion of overall wellbeing, physical exercise enhances immune

function and the cardiopulmonary system [15]. Physical exercise is instrumental in recovering the physical conditions of BC survivors, encompassing aspects such as increased muscle strength, fatigue control, body composition, and sleep quality. Social and emotional factors, including manifestations of anxiety, depression, and stress, which are elements directly linked to the QoL of WSBC, can also be improved by physical exercise [11,15,16,17].

Previous systematic reviews with meta-analyses have explored randomized clinical trials (RCTs) and identified a significant association between physical exercise and QoL in WSBC [6, 18, 19]. However, those systematic reviews often overlook findings in different domains of instruments assessing QoL and the types of physical exercises adopted in therapeutic interventions. QoL Domains and Subscales uniquely delineate specific aspects of an individual's life that are most affected by their health condition and treatment. By offering a more granular assessment than a singular overall QoL score, these measures facilitate a more nuanced interpretation of outcomes. This, in turn, enables the development of more precisely targeted interventions aimed at addressing specific challenges experienced by individuals. Accordingly, the present study aims to systematically investigate the effect of physical exercise on QoL of post-treatment WSBC, addressing gaps in the literature and providing an updated perspective on the topic.

2. Method

This is a systematic review with meta-analysis that followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses – PRISMA – protocol [20]. The review is registered on the International Prospective Register of Systematic Reviews platform – PROSPERO (CRD42021253384).

The research question was structured according to the PICO acronym. The Population investigated was women survivors of breast cancer (WSBC); the Intervention was physical exercise programs; the Comparison was physical activity *versus* inactivity; the Outcome was QoL. The primary question asked was: “In women who are breast cancer survivors, does physical exercise compared to physical inactivity influence QoL?”

2.1 Search Strategy

The search terms and respective synonyms were based on descriptors indexed in the Medical Subject Heading (MeSH), Embase Subject Headings (EMTREE), and Descriptors in Health Sciences (DeCS). The search terms included “Breast Tumors”, “Breast Neoplasm”, “Breast Mammary,” “Cancer; Breast Neoplasm”, “Unilateral Exercise, Physical”, “Exercise, Muscle”, “Training, Resistance”, “Lifting, Weight”, “Conditioning, Human Physical”, “Resistance Training”. The search strategies developed included Boolean operators AND and OR. We did not employ the term “quality of life” directly in the search as to capture a broader range of studies on physical exercise in WSBC, aiming to find studies that have addressed QoL indirectly, or as a secondary outcome.

The databases searched included the Latin American and Caribbean Center for Health Sciences Information (LILACS), PubMed Medline, PsycInfo, EMBASE, Web of Science, Cochrane Central, and Scopus. Google Scholar was also searched. The reference lists of eligible studies were consulted to ensure no potentially eligible study was missed in database searches. The search was conducted in November 2022, with an update in February 2025.

2.2 Eligibility Criteria

RCTs conducted with women aged 18 years or older, breast cancer survivors, who had completed treatment with surgery (total or partial mastectomy), chemotherapy and or radiotherapy, were included. The intervention considered in our investigation was a systematized physical exercise program involving health components such as flexibility, assessment of the cardiac and respiratory system, endurance, and muscular strength. QoL, the outcome of interest in this review, was considered if assessed with any validated instrument, as detailed later. The definition of control group in our investigation involves, within each included RCT, groups of participants who did not perform physical exercise and or programmed physical activity, receiving only usual care, such as regular clinical monitoring (Table 1).

2.3 Study Selection Process

The documents retained from the database search were exported to Endnote® Software web version, the duplicates were removed, and the remaining documents exported to Rayyan® (Qatar Computing Research Institute). The selection process, including phases I (identification by title and abstract) and II (screening and full reading), were separately and independently performed by two reviewers (DSMN and CRNL). Discrepancies were resolved with the input of a third reviewer (LPMO). Authors were contacted by email for additional information when needed. The study selection process is summarised in a PRISMA flowchart (Figure 1).

2.4 Bias Risk Assessment

The risk of bias for the QoL outcome was assessed using the Risk of Bias (RoB 2) tool [21]. The risk of bias assessment was conducted independently by two reviewers (DSMN and CRNL), and a third reviewer (LPMO) consulted when necessary. General risk of bias was categorized as: 1) low risk, when all domains were judged as low risk; 2) some concerns, when at least one domain had some concerns and no domain was considered high risk; and 3) high risk, when at least one domain was judged as high risk, or multiple domains were judged as some concerns [21].

2.5 Data Extraction and Analysis

Data were recorded in a Microsoft® Excel spreadsheet, including author, year of publication, country, study design, sample, age group, time of diagnosis, type and frequency of physical exercise, instruments used for outcome evaluation, primary results, main conclusions, and study limitations. After qualitative data analysis, quantitative data were collected for meta-analyses. Three conditions were considered: (a) combination of studies evaluating the effect of resistance and aerobic exercises; (b) studies with only resistance exercises as intervention; and (c) studies with only aerobic exercises as intervention.

The values of change in measurements between baseline and post-intervention, and respective standard deviations, were used for meta-analyses. The values of change were adopted for our analyses, rather than actual scores before and after intervention, because all studies included in our analyses presented values of change as outcome. Mean and standard deviation were calculated from median, with minimum and maximum values, or mean with confidence interval or standard error. This information was used to estimate missing data [22,23].

The standardized mean difference (SMD) was calculated as the effect size, considering different measurement scales. Values were grouped using the generic random-effects inverse variance method [24].

The inconsistency test (I^2) assessed heterogeneity, with I^2 values close to 25% indicating low heterogeneity, >50% moderate heterogeneity, and >75% high heterogeneity [23,24]. A two-tailed p-value of ≤0.05 was considered statistically significant, and the analyses were performed using Review Manager software, version 5.0 (The Cochrane Collaboration).

The quality of evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) framework, based on our specific outcomes of interest. The GRADE system categorises the certainty of evidence into four levels: high, moderate, low, and very low. This classification is determined by evaluating key factors, including risk of bias, consistency of findings, directness of evidence, and precision of effect estimates. Studies classed as having high-certainty evidence provide results that we have considered reliable and reproducible, whereas those with low or very low certainty indicate substantial limitations that may undermine our confidence in their findings. In our investigation, the various instruments assessed demonstrated differing levels of evidence certainty, as detailed in the next section.

3. Results

3.1 Selection Process

This review identified 3,313 documents. After duplicate identification, 858 studies were excluded. In the selection process based on titles and abstracts, 2,371 studies were excluded, leaving 68 studies for full-text review. Of these, 48 studies were excluded for various reasons, including not meeting eligibility criteria (e.g., not using a validated questionnaire), presenting secondary data from studies already included in the review, studies involving women undergoing BC treatment, studies including male participants, or having a different study

design, or including other types of cancer. Accordingly, our review comprised 36 studies for qualitative analysis. One study involving relaxation exercises was not included in the quantitative synthesis of the meta-analysis (Figure 1).

3.2 Qualitative Synthesis

3.2.1 Studies and Regions

This review includes a total of 3,588 WSBC. In-person intervention durations varied from two weeks [25] to 52 weeks [11], covering studies published between 2003 [26] and 2021 [11] (Table 1).

Out of the 36 studies analysed, most were conducted in the Americas (k=15), distributed across the USA (k=11) [17, 27, 28, 29, 30, 31, 32, 14, 33, 34, 35], Canada (k=2) [26, 36], Argentina (k=1) [37] (Schad et al., 2023) and Brazil (k=1) [38] (Table 1).

In Europe, 12 studies were conducted across nine countries: United Kingdom (k=3) [39, 40, 41], Spain (k=4) [13, 42, 43, 44], France (k=1) [25], Italy (k=1) [45], Germany (k=1) [46], Greece (k=1) [47], and Finland (k=1) [48]. Studies were also identified in Asia (k=7), including four from South Korea [49, 50, 51, 52], two from Iran [53, 54], and one from Turkey (k=1) [55]; and two from Australia (k=2) [56, 11] (Table 1).

3.2.2 Instruments

Among the instruments adopted to assess QoL, the most commonly used was the Short Form Health Survey 36 (SF-36, k=12), followed by the Functional Assessment of Cancer Therapy-Breast (FACT-B, k=8), the Functional Assessment of Cancer Therapy-General (FACT-G, k=10), and the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30, k=10). Other instruments used included the Life Styles Inventory (LSI, k=1), Quality of Life (k=1), developed by [57], Patient-Reported Outcomes Measurement Information System (PROMIS, k=3), Short Form SF-12 (k=1), Health-related Quality of Life (HRQL, k=1), and the Cancer Rehabilitation Evaluation System Short Form (CARES-SF, k=1) (Table 1).

3.2.3 Interventions

Various types of physical exercises were conducted in the studies included for analyses. Fourteen studies jointly evaluated the effects of aerobic and resistance exercises [17,13, 38, 45, 31, 50, 42, 46, 43, 47, 25, 56, 11, 55], while 19 studies implemented aerobic exercise as an intervention [27, 28, 29, 49, 26, 39, 30, 40, 36, 51, 41, 52, 14, 34, 48, 53, 35, 37, 54]. Only two studies used resistance exercises as an intervention [33, 44]), and one used a relaxation modality [32].

3.2.4 Impact of Physical Exercise on QoL

For the studies that incorporated both resistance and aerobic exercise as interventions (k=14), the variation in frequency, duration of each session, and intervention time were notably different. For instance, while [50] applied training with 32 minutes per session at a weekly frequency of 5 times a week for 4 weeks, [17] recommended 150 minutes of aerobic exercise, with 50 minutes daily, plus two sessions per week of strength exercise, over a period of 52 weeks.

Despite substantial variation in frequency, exercise duration, and intervention period, the majority of studies that evaluated both aerobic and resistance exercise (k=14) found a significant QoL improvement for women in the intervention group [17,13, 38, 45, 31, 50, 42, 46, 43, 47, 25, 56, 55]. Only one study did not observe a significant improvement in QoL [11]. In that case, despite an increase in QoL score after the intervention in both groups (1.56 point for the intervention group vs. 0.38 point for the control group; p = 0.266), the difference between groups was not significant. Notably, this was the only study that used the PROMIS protocol [11].

3.2.5 Aerobic Exercise

Among the studies using only aerobic exercise as intervention (k=19), variations in protocol were observed, including differences in intervention duration, ranging from six [14] to 52 weeks [48]; exercise frequency, from once a week [40, 48] to 5 times a week [27, 29,34, 41, 51]; and aerobic exercise duration, ranging from 13 [35] to 90 minutes daily [49].

Among the studies with intervention involving aerobic exercise, several have identified a significant improvement in QoL (k=7) [26, 29, 39,41, 49, 51, 54] or at least in the general health status subdomain (k=6) [27,28, 29, 30, 37, 40]. Such improvements were observed despite differences in intervention protocols and the use of various instruments to assess QoL.

However, in other studies (k=4), an improvement in QoL after intervention was noted, but with no significant difference compared to the control group [14, 34, 48, 52]. In those studies, interventions lasting 6 to 12 weeks and the use of different intervention protocols and QoL assessment tools (SF-12, EORTC QLQ-C30, FACT – G or B) were observed. Only one study concluded that the intervention did not promote an improvement in QoL of WSBC [48]. In that study, optional home training was planned twice a week, with weekly training with a physiotherapist, and QoL was assessed using the EORTC QLQ-C30.

3.2.6 Resistance exercise

In the intervention involving only resistance exercise (k=2), [33] adopted a protocol with training twice a week over 26 weeks. The authors did not identify an improvement in the global Cancer Rehabilitation Evaluation System Short Form (CARES-SF) score in either group (-2.2 points in the intervention group vs. -0.7 points in the control group, p=0.08). Similarly, [44] conducted an intervention with a resistance training protocol, including load progression starting at 40% and going up to 70% of moderate intensity, performed twice a week for 60

minutes per session over 12 weeks. The intervention group showed a mean change of 1.5 in the Physical Well-Being (PWB) subscale of the FACT-B, compared to 0.8 in the control group, but this difference was not statistically significant (p = 0.374).

Our review identified only one study, [32], that adopted an intervention with relaxation techniques (Tai-Chi-Chuan), three times a week for 12 weeks. The authors observed that the intervention group showed significant improvements in QoL, measured by the Health-Related Quality of Life (HRQL), with an average increase of 4.34 points, versus 2.66 points in the control group (p<0.001).

3.3 Effect of Physical Exercise on Quality of Life: Meta-analyses

Analyses of the overall effect of physical exercise, irrespective of modality, on QoL of WSBC, according to the instruments used, are presented in Table 2 and Forest Plots (Supplementary Figures S1 to S30). The meta-analysis of studies using the SF-36 instrument identified a significant improvement in quality, both in general health perception (SMD= 0.43; CI95%: 0.12 to 0.73; p= 0.006), as well as in all other areas of the instrument.

High heterogeneity was observed in most findings. However, no heterogeneity was observed in the SF-36 mental function domain (SMD= 0.40; CI95%: 0.25 to 0.55; p≤0.00001; I^2=0) and mental component score (which summarizes the subdomains Vitality, Social role functioning, Role: emotion, and Mental functioning), (SMD= 0.41; CI95%: 0.23 to 0.58; p≤0.00001; I^2=0) (Table 2). For the physical component score (which summarizes the subdomains physical functioning, Roles: physical, bodily pain, and general health perceptions), moderate heterogeneity was observed (SMD= 0.61; CI95%: 0.28 to 0.95; p = 0.0003, I^2=67%) (Table 2).

Studies using the Functional Assessment of Cancer Therapy (FACT-General) and its additional module to assess individuals with breast cancer (FACT-Breast) also indicated an improvement in QoL with physical exercise, regardless of modality. The overall effect was significant when using FACT-G (SMD=0.56; CI95%: 0.13 to 0.99; p≤0.01, I^2=84%) and FACT-B (SMD=0.73; CI95%: 0.38 to 1.08; p=0.0003, I^2=84%), respectively. However, for the Functional Wellbeing and Additional Concerns subdomains, no improvement in scores was observed (p=0.06 and p=0.14, respectively).

Similarly, the 36-item European Organization for Research and Treatment of Cancer Core Quality of Life (EORTC QLQ-C30) instrument indicated that physical exercise intervention showed a significant improvement in the individual's global health (SMD = 0.98; CI95%: 0.49 – 1.47; p<0.00001, I^2=90%), with separate analyses in the emotional functioning (SMD= 0.55; CI95%: 0.18 to 0.92.; p<0.00001, I^2=82%) and social functioning (SMD= 0.33; CI95%: 0.01 to 0.65; p=0.0001, I^2=76%) domains being significant.

However, the module evaluating individuals with breast cancer specifically (EORTC QLQ-C23) did not identify improvements in the different subdomains (body image, arm symptoms, breast symptoms, sexual functioning, future perspective, sexual enjoyment, and side effects of treatment) after intervention with physical exercise. Noteworthy, analyses employing the EORTC QLQ-C23 only included three studies (Table 2). [50] utilized only three domains of this

instrument (Body image, Arm symptoms, Breast symptoms); whilst the remaining two [48,53] utilized all instrument domains.

Our analyses consider different numbers of studies (k) to evaluate QoL and varied according to data presented in the original studies included in this protocol (global and subdomains). Due to substantial heterogeneity identified in most findings, in addition to the meta-analysis by instruments used, we carried out subgroup analyses considering different types of exercises used in the intervention, as presented in Table 2 and Forest Plots (Supplementary Figures S1 to S30).

The meta-analysis result by subgroups, considering the type of exercise performed in the intervention, identified that aerobic exercise combined with resistance exercise promoted a greater increase in QoL when compared to aerobic exercise only. A significant improvement was observed in all domains of the SF-36 QoL questionnaires, except for the emotional role (p=0.09). In the subgroup analysis, heterogeneity in some domains of the SF-36 was reduced, and there was no heterogeneity in the subdomain of mental function and mental component score (I^2=0%).

The meta-analysis of studies that carried out intervention with aerobic exercise identified a significant improvement only in the SF-36 physical function (SMD=0.26; 95% CI: 0.12 – 0.40; p=0.0002), but with an effect smaller than that observed in the group that performed aerobic training combined with resistance training (SMD=1.02; 95% CI: 0.41 – 1.63; p=0.001). However, the analysis of the SF-36 physical function domain did not show heterogeneity in aerobic exercise (I2=0%) *versus* strength exercise combined with aerobic exercise (I^2=89%) (table 3).

Strength exercise combined with aerobic exercise showed a greater increase in the overall score on the FACT-B instrument (SMD=1.29; 95% CI: 0.58 – 2.00; p=0.0003) compared to aerobic exercise (SMD=0.49; 95% CI: 0.20 – 0.78; p=0.0009), with significant improvement for both modalities combined. However, heterogeneity was lower for the analyses covering aerobic exercise (FACT-G, I^2=47% and FACT-B, I^2=35%) *versus* strength exercise combined with aerobic exercise (FACT- G, I^2=93% and FACT-B, I^2=84%) (table 4).

The positive effect of physical exercise on QoL identified in studies that employed the EORTC QLQ-C30 instrument remained in the subgroup that performed aerobic exercise combined with resistance exercise, both in the global health domain (SMD=1.47; 95% CI: 1.02 – 1.91; p<0.00001) as well as in the other domains of the instrument. Absence of heterogeneity was also observed in the domains of cognitive function, emotional function, and social function. However, the subgroup tested with aerobic exercise did not show a significant improvement in QoL (SMD=0.47; 95% CI: 0.01 – 0.94; p=0.05) (Table 5). Lastly, subgroup analyses such as the EORTC QLQ-C23 questionnaire were not possible due to the limited number of studies included in our review.

3.4 Risk of Bias

Risk of bias analysis of eligible clinical trials included in this review conducted using the RoB 2 instrument showed that among the 36 studies assessed, the majority (64%, k=23) presented

a low risk of bias [11, 13, 17, 26, 30, 31, 33, 35, 36, 37, 39, 40, 41, 42, 44, 46, 48, 51, 52, 53, 54, 55, 56] (Figure 2).

Twelve studies (33%) were classed as having a moderate risk of bias [14, 25, 27, 28, 29, 32, 34, 38, 45, 47, 49, 50], due to reasons including lack of information and methodological shortcomings, such as inadequate detail on randomization and the blinding of study participants. Only one study (3%) was classed as having a high risk of bias [46], primarily due to unclear information about the randomization process (Figure 2).

3.5 Analysis of the Certainty of Evidence

The analysis of studies employing the SF-36 instrument showed moderate certainty of evidence for social function (k=9) and physical component score (k=5). High certainty of evidence was observed for the subdomains of mental function (k=9) and mental component score (k=5). Studies employing the FACT instrument, specifically in the emotional wellbeing subdomain (k=10) and the breast cancer subscale (k=9), presented moderate certainty of evidence. Studies employing the EORTC QLQ-C30 showed moderate certainty of evidence only in the social function subscale (k=8), and the EORTC QLQ-C23 in sexual function (k=2) and sexual behaviour (k=2) (Supplementary tables S1, S2, S3, and S4).

4. Discussion

This systematic review with meta-analysis appraised 36 RCTs assessing the impact of physical exercise on post-treatment QoL of WSBC. Our findings show a positive influence of physical exercise on QoL, with variations based on the type of exercise. Notably, we have found that combined aerobic and resistance training had stronger effects than either modality alone.

Low QoL among WSBC has been documented, as the therapeutic process negatively impacts the lives of affected women [4, 7]. Guidance on promoting a healthy lifestyle, including regular physical exercise, may contribute to improvement in QoL [11].

Currently, exercise guidelines for WSBC are based on general adult recommendations, such as those from the American College of Sports Medicine (ACSM) and the World Health Organization (WHO). These guidelines suggest engaging in 3 to 5 sessions per week, totalling at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity activity, aiming to support cancer prevention and promote an active lifestyle throughout the cancer journey, from diagnosis through to post-treatment recovery [8, 58, 59]. While these recommendations are broadly applicable, particularly since much of the supporting evidence comes from studies involving cancer survivors, they often lack the practical specificity needed to address common limitations faced by patients. Initiatives such as Exercise is Medicine, endorsed by the ACSM, emphasize the importance of progressive and individualized exercise prescriptions for clinical populations. However, formal guidelines still fall short in detailing how to tailor programs to the unique clinical and personal realities of each woman [58].

Exercise recommendations must be personalised to meet the specific needs of survivors, many of whom face physical and emotional challenges after treatment. These may include reduced upper limb mobility following surgery (mastectomy or lymph node dissection), risk of lymphedema, pain, fatigue, psychological distress, and altered body image. Such factors can significantly impact both the capacity and motivation to engage in regular physical activity. Therefore, personalised interventions which include gradual progression, functional recovery, and emotional support, are crucial to improving adherence and achieving lasting outcomes in both physical and psychological rehabilitation [42, 60, 61].

Our systematic review has underscored methodological differences among clinical trials, primarily concerning the type of physical exercise used (aerobic exercise combined with resistance exercise or just aerobic exercise) and varying intervention protocols, particularly regarding the number of days per week and time spent daily on physical exercise. Additionally, differences in guidance methods further complicate synthesizing the currently available evidence to propose specific and practical recommendations for WSBC.

To enhance our understanding of the findings, we conducted a subgroup analysis within our meta-analysis, where the RCTs were grouped based on the instrument utilised to assess the outcome of interest and the type of intervention. However, despite our efforts, the subgroup analysis could not completely elucidate the heterogeneity observed in the findings.

While all instruments used in the reviewed studies are validated, they employ different metrics, even when assessing the same construct, such as "global health." The most frequently employed instrument for assessing QoL was the SF-36, a multidimensional questionnaire consisting of 36 items spanning eight domains (physical functioning; roles: physical; bodily pain; general health perceptions; vitality; social role functioning; role: emotion; mental functioning). It is noteworthy that the SF-36 subdomains cannot be aggregated, and are interpreted individually [63]. The distinct metrics employed by the various instruments across different studies cannot be interpreted equivalently, making direct comparisons challenging. For example, while the SF-36 evaluates QoL across domains, the FACT-Breast emphasises clinical cancer aspects, and the EORTC-23 focuses on treatment-related adverse effects. Recognising metrics variations underscores the need for a standardised approach to QoL assessment in WSBC to enhance study comparability and reliability.

Considering the ability of the instruments to interpret subdomains individually, we found it relevant to conduct a meta-analysis with the different domains available in the eligible clinical trials individually. This approach allowed the inclusion of a greater number of studies, presenting data from the domains separately, also facilitating a nuanced interpretation of various aspects, such as physical, emotional/mental, and social wellbeing, which in combination constitute the concept of QoL. Consequently, evidence of beneficial effects of physical exercise interventions in QoL domains, assessed by the SF-36 and FACT, was found among WSBC.

The SF-36, widely used to assess QoL in individuals with diverse clinical conditions, appears more suitable for the population under investigation, particularly women not undergoing

treatment at the time of the study. The SF-36 yielded the best level of evidence, ranging from moderate to high, in the domains of Social Role Functioning and High Mental Functioning. Additionally, moderate certainty of evidence was identified for the Physical Component Score, while a high certainty of evidence was established for the Mental Component Score.

Distinct instruments designed to assess QoL in women currently suffering with BC, such as the FACT-Breast and the EORTC-23, stand out for exploring issues associated with clinical conditions and adverse effects of cancer treatment. However, when assessing BC survivors specifically, such questions might not be appropriately scored. Our review uncovered evidence of beneficial effects of physical exercise in different FACT domains, with no significant effect observed when QoL was assessed by the EORTC-23. The latter may be attributed to methodological issues and the limited number of studies utilizing the EORTC, or to the specificity of the instrument.

We acknowledge the adoption of different instruments by different RCTs, along with diverse intervention approaches for physical exercise, including face-to-face guidance, telephone guidance, emails, and periodic meetings. We further acknowledge variation in exercise modality, daily time, weekly frequency and duration of intervention among the different protocols included. Despite these methodological differences, the results suggest positive effects of physical exercise on QoL of WSBC after treatment. This diversity of protocols can be interpreted as positive, suggesting that different types of programs, when well planned, can be effective. Future research can explore how to adapt interventions in an individualised manner, respecting different contexts, needs, and possibilities.

Previous reviews have identified a positive association between physical exercise and quality of life in WSBC [6, 18, 19]. Our findings reinforce this evidence, demonstrating that the benefits of physical exercise are sufficiently consistent to be detected by different QoL assessment instruments, such as FACT-G, FACT-B, EORTC QLQ-C30, SF-36 and their respective domains. Combining aerobic exercise with strength training has shown particularly positive effects.

The findings of our review advocate that WSBC incorporate aerobic exercise combined with resistance training into their routine, preferably under the supervision of a qualified professional. Home-based interventions with appropriate guidance, whether online in real time, online streaming, individual, or in small groups, can be viable alternatives for those who do not have access to direct supervision, ensuring the continuity of exercise practice in a safe and effective manner.

Variation in physical exercise prescriptions should also be considered, as different modalities (aerobic, resistance, combined) elicit distinct physiological and psychological adaptations that impact QoL. For example, while aerobic exercise enhances cardiovascular fitness, weight management, and fatigue reduction, resistance training on the other hand improves muscle strength and bone health, which all are key concerns for WSBC. Additionally, factors such as frequency, intensity, and prescription delivery mode influence adherence and long-term sustainability. Given individual differences in physical capacity, clinical condition, treatment history, nutritional status, and psychological well-being, a one-size-fits-all approach is

inadequate. Personalised, adaptable exercise interventions are crucial to maximising effectiveness, accessibility, and long-term QoL improvements for WSBC.

We have considered factors influencing adherence to physical exercise protocols, particularly the role of supervision in those interventions. Our findings show that several studies incorporated some form of exercise supervision, with interventions ranging from professional oversight to self-management, or remote support. Notably, in-person supervision is frequently associated with higher adherence rates, which, in turn, contribute to more substantial QoL improvements. Adherence emerges as a critical determinant of intervention efficacy, as non-compliance attenuates any anticipated benefit of exercise. While supervised protocols demonstrate superior adherence, their implementation in real-world settings presents considerable logistical and resource-related challenges. To maximise intervention effectiveness, prioritising supervised programs, whether conducted in-person or virtually, should be considered essential to enhance adherence and optimise health outcomes.

Our review features the strength of high methodological quality applied during the review process. An extensive search in databases yielded a substantial number of articles, facilitating data grouping and standardization. Such database afforded the completion of a comprehensive meta-analysis to evaluate the overall effect, alongside subgroup analyses that considered not only the type of intervention but also the instrument used to evaluate the effect of physical exercise on QoL of WSBC. Our inclusion criteria strictly comprised RCTs, and a consistent methodological approach was followed in the search for articles and in the analyses conducted on the quality of the studies. Our analyses encompassed risk of bias, subgroup analysis, sensitivity analysis, and certainty of evidence.

The methodological quality of the RCTs included in our investigation was determined via the Risk of Bias (RoB 2) instrument (Fig 2), as recommended by Cochrane to assess the risk of bias in clinical trials [64]. The results show that two-thirds were classified as low risk of bias, and one-third as moderate risk. These findings reflect the advancement of research in this area, evidencing the scientific commitment to methodological rigor. The assessment of the quality of evidence identified the SF-36 instrument as the one that provided the most consistent results, with moderate to high levels of certainty in certain domains. At the same time, limitations of our investigation include the several methodological differences in the clinical trials appraised, especially those related to the actual exercise intervention models adopted across studies, as well as the protocols employed to assess the QoL outcomes. We resolved this major obstacle by analysing subgroups as different types of exercise and different instruments, running the meta-analysis considering subgroups.

The present study highlights that while physical exercise is a vital element of health interventions, it must be embedded within a broader, holistic framework to achieve sustained improvements in QoL for WSBC, including psychological and social support. Our findings demonstrate that both aerobic and combined aerobic with resistance exercises contribute significantly to enhanced QoL, as herein evidenced by improvements across global and domain-specific scores in validated assessment tools. Notably, the combination of aerobic and resistance training yielded superior outcomes than either modality alone. These results underscore the need for personalised exercise prescriptions that account for individual clinical

profiles, including cancer type, treatment history, and physical capacity. Our study further advocates for the integration of psychological and social support alongside physical interventions and calls for the development of evidence-based public policies to institutionalise physical exercise as a critical health intervention known to not only reduce the risks of oncological diseases but also known to promote improvements in QoL after cancer treatment.

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Table 1: Summary of the characteristics of the studies included in the review (k=36).

Author, Year	Country	Sample (intervention/control)	Intervention/Time/Frequency	Duration of intervention	Instrument for outcome	Main results
Strength and aerobic exercise (n=13)						
Aydin et al., 2021 [55]	Turkey	48/24	Exercise group**:** Aerobic exercise (walking and cycling) 5x in the week, 50 minutes at 50-60% of maximum heart rate + resistance training 2x in the week, 60 minutes. Usual care (control group)**:** Encouraged to maintain their usual physical activity levels and received the same informational exercise booklet as the intervention group but did not participate in any supervised exercise program.	12 weeks	EORTC QLQ-C30	The intervention group showed improvement, with a reduction of 10,5 vs. 0,5 points on the score ($p < 0,01$).
Baglia *et al.*, 2019 [17]	USA	121 / 61	Exercise group**:** 150 minutes per week of moderate intensity aerobic exercise (with guidance to perform 50 min per day) + 2 sessions per week of strength exercise.	52 weeks	SF-36 FACT - G FACT - B	The intervention group showed an improvement in the General Health Status domain (SF-36) with an increase of 3.0 points vs. a reduction of -0.5 points in the control group ($p=0.01$). The intervention group had greater functional improvement of cancer

			Usual care (control group): No exercise prescription; monthly contact for educational support and monitoring of adherence to aromatase inhibitor (AI) use.			general therapy - FACT-G (8.0 vs. 1.2 points, p=<0.01) compared to the control.
Casla *et al.,* 2015 [13]	Spain	94 / 45	Exercise group: Strength and aerobic exercise 44 minutes, 2 x weekly. Usual care (control group): Participants were instructed to maintain their usual behavior, without changes to physical activity or diet. At the end of twelve weeks, they were offered participation in exercise classes for ethical reasons and to reduce attrition and contamination.	12 weeks	SF-36	The intervention group showed an improvement in the General Health Status (SF-36) domain, with an increase of 12.11 vs. 7.82 points in the score (p < 0.01).
Castro-Filha *et al.,* 2016 [38]	Brazil	24 / 12	Exercise group: 10 minutes of aerobics + 40 min strength 3 x week, 50 min per session, at submaximal intensity. Usual care (control group): No specific intervention (only clinical monitoring).	12 weeks	SF-36	The intervention group showed an improvement in the General Health Status (SF-36) domain, with an increase of 9.2 vs. a reduction of -3.5 points in the control group (p<0.05).

De Luca *et al.*, 2015 [45]	Italy	20 / 10	Exercise group: 30 min aerobic exercise + 40 min strength + 20 min warm-up, relaxation and rest = 90 minutes each session, twice a week. Usual care (control group): Participants maintained usual activities without starting any new formal exercise program (e.g., joining a gym or walking group) during the study.	24 weeks	FACT - G	The intervention group showed an improvement in quality of life (FACT G) of 13.2 points vs. a reduction of -4.8 points in the control group (p=0.05).
Dieli-Conwright *et al.*, 2018 [31]	USA	100 / 50	Exercise group: 80' of aerobics, twice a week (walking, running on a treadmill, rowing machine and stationary bike / strength training on machines with three sets of 10 repetitions at 80% intensity for the upper limbs and 60% for the lower limbs) and 50' of strength training training, once a week. With a certified professional. Usual care (control group): Participants were instructed not to start any new formal	16 weeks	SF-36	The intervention group showed an improvement in the General Health Status domain (SF-36) with an increase of 7.1 points vs. a reduction of - 2.1 points in the control group (p<0.01).

			exercise program during the study period.			
Do *et al.,* 2015 [50]	South Korea	62 / 30	Exercise group**:** Aerobic exercise and strength 32 minutes/ 5 x a week. Usual care (control group)**:** No rehab program (weeks 1–4); exercise encouraged after.	4 weeks	EORTC QLQ-C30	The intervention group showed an improvement in the global health domain of the (EORTC QLQ-C30) by 22.2 points vs. a reduction of -3.7 points in the control group (p=<0.01).
Galiano-Castilo *et al.,* 2016 [42]	Spain	81 / 37	Exercise group**:** Aerobic exercise and strength 39 minutes/ 3x a week. Usual care (control group)**:** Received basic written exercise advice; asked to report activity changes.	8 weeks	EORTC QLQ-C30	The intervention group showed an improvement in the global health domain of the (EORTC QLQ-C30) with an increase of 13.67 points vs. 2.48 points in the control group (p <0.01).
Heim *et al.,* 2007 [46]	Germany	63 /31	Exercise group**:** Aerobic exercise and strength 32 minutes/ 2 to 3x a week. Usual care (control group)**:** Multidisciplinary rehabilitation program including group exercise, education, physiotherapy, and psycho-oncological support.	13 weeks	FACT-G	The intervention group showed an improvement in the global health domain of the (EORTC QLQ-C30) with an increase of 10 points vs. 1 point in the control group (p < 0.01).

Herrero *et al.,* 2005 [43]	Spain	16 /8	Exercise group**:** 10' of physical exercise + 70' of strength training + 10 minutes of stretching/ 3x a week. Usual care (control group)**:** Maintained habitual sedentary lifestyle (<30–60 min walking, 3x/week); no strenuous exercise.	8 weeks	EORTC QLQ-C30	The intervention group showed an improvement in quality of life with an increase of 29 points vs. a reduction of -8 points in the control group ($p<0.05$).
Kaltsatou *et al*., 2011 [47]	Greece	27 / 13	Exercise group**:** Greek dance (low-intensity at the start and high-intensity from the 15th week onwards) and strength with machines of varying resistance / 3x a week / 10-minute warm-up, 25 minutes of dancing and 25 minutes of strength. With a professional specializing in dance. Usual care (control group)**:** Continued with usual daily routine.	24 weeks	LSI	The intervention group showed an improvement in quality of life with an increase of 0.30 points vs. 0.28 points in the control group ($p<0.01$).
Reves *et al.,* 2021 [11]	Australia	159 / 80	Exercise group**:** Telephone counseling session (six weekly and 10 bi-weekly calls)	52 weeks	PROMIS	The intervention group showed no significant improvement in quality of life

			with aerobic exercise guidance 210 min/week and encouragement of strength training 2-3 sessions/week. Usual care (control group): Participants received study materials and feedback after each assessment, along with a summary of the results.			with an increase of 1.56 points vs. 0.38 points in the control group (P >0.05).
Kwiatkowski *et al.,* 2013 [25]	France	251 / 115	Exercise group: Walking on flat ground or cycling on a cycle ergometer and strength training for lower and upper limbs, supervised by a physiotherapist 5 times a week / 120 minutes per session. Usual care (control group): The patients in the control group continued with their usual daily routine (sedentary).	2 weeks in person, with follow-up measures for up to 24 months	SF-36	The intervention showed an improvement in the General Health Status domain of the SF-36 by 9.5 points compared to the control (p =0.000006), with an increase of 25.9% vs. 14.5% in the control group (p<0.05).
Milne *et al.,* 2007 [56]	Australia	58 / 29	Exercise group: Sessions supervised by exercise physiologists for stationary bike and trampoline. Strength training consisted of 12	12 weeks	FACT - G FACT - B	The intervention group showed an improvement in quality of life (FACT-G) of 15.8 points vs. a reduction of -5.5 points in the control group (p=<0.01).

			different exercises / 2 sets of 10 to 15 repetitions / 25 minutes of aerobic exercise and no identified time for strength training / 3 times a week. Usual care (control group): They were asked not to participate in exercise during this period.			The intervention group showed an improvement in quality of life (FACT-B) of 20.8 points vs. a reduction of -5.3 points in the control group (p=<0.01).
Aerobic exercise (n=17)						
Baruth *et al.,* 2015 [27]	USA	32 / 12	Exercise group: Aerobic exercise with walking for 30 minutes a day, 5 times a week. Usual care (control group): Instructed to maintain their usual physical activity levels, with contact only during follow-up visits. After the study, they received a counseling session, materials, and a pedometer.	12 weeks	SF-36	The intervention group showed an improvement in the General Health Status domain (SF-36) with an increase of 6.9 points vs. a reduction of - 5.8 in the Control group (no p-value).
Basen-Engquist *et al.,* 2006 [28]	USA	60 /25	Exercise group: 90' group meetings every week for 16 weeks and every two weeks for 8 weeks (21 sessions in	26 weeks	SF-36	The intervention group showed an improvement in the General Health Status domain (SF-36) of 77.4 points vs. 67.1 points for the control group (p<0.01).

			total). Physical exercise for at least 30 minutes a day. Usual care (control group)**:** Received written materials on breast cancer survival (excluding physical activity) and two follow-up correspondences during the 6-month intervention period, with no group meetings.			
Cadmus *et al.*, 2009 [29]	USA	74 / 37	Exercise group**:** 30-minute walk in a gym supervised by exercise physiologists, 5 times a week. Usual care (control group)**:** Informed they could exercise independently, but the study's exercise program was unavailable.	26 weeks	SF-36 FACT-G	The intervention group showed an improvement in the General Health Status domain (SF-36) of 1.5 points vs. 1.4 points in the control group ($p<0.05$). The intervention group showed an improvement in quality of life (FACT-G) 3.7 points vs. 3.4 points in the control group ($p=<0.05$).
Cho *et al.*, 2006 [49]	South Korea	55 / 27	Exercise group**:** Low-intensity aerobic exercise, consisting of a warm-up, main exercise and cool-down, administered for 90 minutes, twice a week for a total of 10 weeks.	10 weeks	Quality of Life (Instrument developed by Chae & Choe)	The intervention group showed an improvement in quality of life, increasing by 0.8 points vs. -0.1 points for the control group (p-value not reported).

			Usual care (control group): Did not participate in any group rehabilitation program.			
Courneya *et al.*, 2003 [26]	Canada	52 / 28	Exercise group: 15' of aerobic exercise in the 1st to 3rd weeks, with a systematic addition of 5 minutes every 3 weeks, closing at 35 minutes for the 13th to 15th weeks, 3x a week. The warm-up and cool-down periods consisted of 5 minutes. Usual care (control group): Did not undergo training.	15 weeks	FACT-G FACT-B	The intervention group showed an improvement in quality of life (FACT-G), 5.8 points Vs. 0.5 points in the control group ($p<0.05$). The intervention group showed an improvement in quality of life (FACT-B), 9.1 points Vs. 0.3 points in the control group ($p<0.01$).
Daley *et al.*, 2007 [39]	United Kingdom	108 / 38	Exercise group: Moderate-intensity walking at a university center, with an exercise specialist. 3x week / 50 minutes. Cognitive-behavioral techniques have also been explored. Usual care (control group): Instructed to maintain their usual lifestyle, without engaging in structured exercise programs, with	8 weeks and 24 weeks	FACT - G FACT - B	The intervention group showed an improvement in quality of life with a difference to the control group of 9.80 points for FACT G ($p<0.01$) and 13.14 points ($p<0.01$) for FACT B.

			follow-up only during scheduled consultations.			
Demark-Wahnefried *et al.*, 2015 [30]	USA	697 / 348	Exercise group: Walking, group and personalized guidance, with updates provided by telephone and/or e-mail between each group session. Weekly sessions of 60 minutes. Usual care (control group): Received written materials, were advised to follow weight reduction guidelines, and had two contacts: at baseline and six months.	24-week analysis (108-week cohort)	SF-36	The intervention group showed an improvement in the subscale representing the state of vitality (SF-36) 4.6 points vs. 1.9 points in the control group (p=0.05).
Farajivafa *et al.*, 2023 [54]	Iran	89/44	Exercise group: Walking, balance exercises, and stretches, starting with 15 min/session, 2 days/week, progressing to 50-60 min/session, 3-5 days/week, for 3 months, with intensity monitored using the talk test, weekly telephone calls for adherence tracking, and an exercise logbook for tracking.	12 weeks	EORTC QLQ-C30	The intervention group showed a significant improvement in the global health domain of the (EORTC QLQ-C30), increasing from 50 (31.2) to 75 (25), while the control group went from 66.6 (33.3) to 75 (16), with a significant difference between the groups ($p < 0.01$).

			Usual care (control group)**:** Did not participate in the exercise program. Received monthly phone calls for monitoring only, with no encouragement for physical activity or specific guidance.			
Fields *et al.,* 2016 [40]	United Kingdom	40 /20	Exercise group**:** Group training supervised by an instructor with outdoor Nordic walking. 1x per week / 60 minutes. Usual care (control group)**:** They did not receive the intervention or direct exercise guidance but were contacted biweekly to monitor symptoms, completed all assessments, received educational materials, and were offered a Nordic walking program after the study.	12 weeks	SF-36	The intervention group showed an improvement in the General Health Status domain (SF-36) with an increase of 5 points vs. a reduction of -3 points in the control group (p-value not reported).
Fillion *et al.,* 2008 [36]	Canada	87 / 43	Exercise group**:** Face-to-face group guidance 1 x a week / 2.5 hours (1 hour for walking + 1.5 hours for psycho-educational guidance) / for 4	12 weeks	*SF-12*	The intervention group showed an improvement, although not a significant one, in the subscale representing the General Physical State (SF-12), 4.61

			weeks + 15-minute telephone reinforcement on week 9. They also received 20-minute muscle relaxation recordings to listen to daily. Usual care (control group): Usual medical care for breast cancer treatment, without participation in the stress management/physical activity intervention.			points vs. 1.76 points in the control group (p=0.81).
Kim *et al.,* 2011 [51]	South Korea	45 / 22	Exercise group: Telephone counseling combined with an e-book containing guidelines for moderate intensity exercise / 5 times a week / 30 minutes a day. Usual care (control group): Without structured intervention.	12 weeks	EORTC QLQ-C30	The intervention group showed an improvement, although not significant, in the global health domain of the (EORTC QLQ-C30) 11.69 points vs. 4.34 points in the control group (p > 0.05).
Lahart *et al.,* 2016 [41]	United Kingdom	80 / 40	Exercise group: Telephone counseling with the goal of accumulating 30 minutes of moderate-intensity exercise a day, 3-5 days a week.	26 weeks	FACT - G FACT - B	The intervention group showed a non-significant improvement in FACT-G quality of life, 2.28 points vs. 0.29 points in the control group (p= 0.234). The intervention group showed an improvement in FACT-B quality of life,

			Usual care (control group): Received only standard physical activity information and was instructed to maintain their current lifestyle during the study, without participation in a structured intervention.			5.85 points vs. 1.09 points in the control group ($p<0.05$).
Lee *et al.*, 2014 [52]	South Korea	59 / 28	Exercise group: Guidance from a self-management platform on the web, with advice on how to improve and plan exercise, eating behavior, the importance of weight control, etc. Participants recorded the type, intensity and duration of exercise, and had to access the platform twice a week. A recommendation of 30 minutes of exercise per day, or at least 150 minutes per week. Usual care (control group): Received a 50-page educational brochure on exercise and diet, but without structuring.	12 weeks	EORTC QLQ-C30	The intervention group showed an improvement, although not significant, in the global health domain of the EORTC QLQ-C30, 3.3 points vs. 0.5 points for the control group ($p>0.05$).

Nyrop *et al.,* 2017 [14]	USA	62 / 31	Exercise group**:** Guidance to practice moderate intensity exercise for at least 150 minutes a week. Usual care (control group)**:** Was instructed to wait for 6 weeks without any activity, receiving informational materials only after that period.	6 weeks	FACT-G	The intervention group showed an improvement, although not significant, in quality of life - 1.48 points vs. 0.07 points in the control group (p=0.09).
Rogers *et al.,* 2009 [34]	USA	41 / 19	Exercise group**:** Face-to-face guidance and counseling for moderate-intensity exercise, 150 minutes a week, 3 to 5 times a week. Usual care (control group)**:** Received general physical activity materials from the American Cancer Society, without specific behavior change instructions.	12 weeks	FACT-G FACT-B	The intervention group showed an improvement in FACT-G, but not significantly, 4.5 points vs. control 2.9 points (p= 0.63). The intervention group showed an improvement in FACT-B, but not significantly, 5.5 points vs. 3.2 points in the control group (P = 0.57).
Saarto *et al.,* 2012 [48]	Finland	573 / 237	Exercise group**:** Supervised and/or home training with the help of a physiotherapist. Supervised training consisted of different classes (step aerobics and circuit classes).	52 weeks	EORTC-QLQ-C30	The intervention group did not promote any change in the global health domain of the (EORTC QLQ-C30), 4.2 points vs. 5.6 points (p=0.43).

			Home training was optional (walking, Nordic walking or aerobic training, jumping jacks and jumps similar to step aerobics)/ 2x a week for home training / 1x a week for supervised training / for 30 minutes. Usual care (control group): The control group was instructed to maintain their usual physical activity levels and exercise habits throughout the study, without participating in any supervised or home-based training intervention.			
Schad et al., 2023 [37]	Argentina	60/24	Exercise group: The exercise program consisted of six weekly one-hour Argentine tango sessions, with a total duration of 6 weeks. Usual care (control group): Continued their usual daily activities during the six-week waiting period and received	6 weeks	EORTC-QLQ-C30	The intervention group showed a change in the global health domain of the (EORTC QLQ-C30), with an increase of 4.7 points in the intervention group compared to a decrease of -1.19 points in the control group (p=0.10).

			no structured physical activity intervention.			
Shobeiri *et al.*, 2016 [53]	Iran	60 / 30	Exercise group**:** Aerobic exercise 30 minutes, 2x a week. Usual care (control group)**:** They were instructed to maintain their sedentary lifestyle for 10 weeks.	10 weeks	EORTC QLQ-C30	The intervention group promoted improvement in the global health domain of the (EORTC QLQ-C30), 33.03 points Vs. 5.13 points in the control group ($p<0.01$).
Swisher *et al.*, 2015 [35]	USA	23 / 10	Exercise group**:** Aerobic exercise 30 minutes a day, 3x a week at the gym and 2x at home. Usual care (control group)**:** They received written materials on healthy eating and physical activity suggestions but did not receive specific counseling or supervision and were not instructed to avoid changes in diet or exercise.	12 weeks	FACT-B	The intervention group showed an improvement in quality of life, an increase of 14 points vs. a reduction of -6.1 points in the control group ($p<0.05$).
Strength Exercise (n=1)						

Maldonado et al., 2022 [44]	Spain	32/28	Exercise group: Training with load progression starting at 40% and going up to 70% moderate intensity exercise guidelines / 2x a week / 60 minutes daily. Usual care (control group): Performed home-based walking (≥10,000 steps/day) without resistance training.	12 weeks	FACT-B	The intervention group showed a mean change of 1.5 (0.6) in the PWB subscale of the FACT-B, compared to 0.8 (0.6) in the control group, with a mean difference of 0.7 (−0.9 to 2.4), but this difference was not statistically significant (p = 0.37).
Ohira *et al.,* 2006 [33]	USA	86 / 43	Exercise group: Supervised resistance exercise twice a week, with no minimum or maximum time for performing the nine common bodybuilding exercises (for chest, back, shoulder and arm muscles, as well as buttocks, hips and thighs). Usual care (control group): No structured training or supervision, but only continued their usual activities or lifestyle.	26 weeks	CARES-SF	The intervention showed no significant improvement in the overall CARES-SF score in either group. There was a reduction of -2.2 points vs. -0.7 points in the control group (p=0.08).
Relaxation Exercise (n=1)						

Mustian *et al.*, 2004 [32]	USA	21 /10	Exercise group: Tai Chi Chuan / 60 minutes a day/ 3x a week. Usual care (control group): Did not participate in the interventions	4 weeks to 16 weeks	HRQL	The intervention group showed an improvement in QoL with an increase of 4.34 points vs. 2.66 in the control group (P<0.01).

Table 2 - Overall effects of physical exercise on health-related quality of life (HRQoL), according to the instruments used.

Scale/*Subscales*	***k***	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**
SF-36					
Physical functioning	10	1293	0.63 [0.34, 0.93]	Tau² = 0.16; Chi² = 45.86, df = 9 (P < 0.00001); I² = 80%	P < 0.0001
Roles: physical	9	706	0.54 [0.20, 0.87]	Tau² = 0.19; Chi² = 33.43, df = 8 (P < 0.0001); I² = 76%	P = 0.002
Bodily pain	9	714	0.62 [0.23, 1.01]	Tau² = 0.28; Chi² = 45.81, df = 8 (P < 0.00001); I² = 83%	P = 0.002
General health perceptions	9	706	0.43 [0.12, 0.73]	Tau² = 0.14; Chi² = 27.43, df = 8 (P = 0.0006); I² = 71%	P = 0.006
Vitality	10	1326	0.44 [0.18, 0.69]	Tau² = 0.11; Chi² = 33.82, df = 9 (P < 0.0001); I² = 73%	P = 0.0008
Social role functioning	9	706	0.40 [0.09, 0.71]	Tau² = 0.15; Chi² = 29.36, df = 8 (P = 0.0003); I² = 73%	P = 0.01
Role: emotion	8	623	0.33 [0.01, 0.65]	Tau² = 0.14; Chi² = 23.68, df = 7 (P = 0.001); I² = 70%	P = 0.04
Mental functioning	9	706	0.40 [0.25, 0.55]	Tau² = 0.00; Chi² = 6.29, df = 8 (P = 0.61); I² = 0%	P < 0.00001
Physical component score	5	517	0.61 [0.28, 0.95]	Tau² = 0.09; Chi² = 12.04, df = 4 (P = 0.02); I² = 67%	P = 0.0003
Mental component score	5	517	0.41 [0.23, 0.58]	Tau² = 0.00; Chi² = 2.49, df = 4 (P = 0.65); I² = 0%	P < 0.00001
FACT					
FACT - General	10	590	0.56 [0.13, 0.99]	Tau² = 0.40; Chi² = 56.56, df = 9 (P < 0.00001); I² = 84%	P < 0.01
FACT - Breast	10	603	0.73 [0.38, 1.08]	Tau² = 0.23; Chi² = 37.50, df = 9 (P = 0.002); I² = 84%	P = 0.0003
Physical well-being	12	727	0.51 [0.15, 0.86]	Tau² = 0.31; Chi² = 58.25, df = 11 (P < 0.00001); I² = 81%	P = 0.03
Social/family well-being	11	664	0.34 [0.10, 0.58]	Tau² = 0.09; Chi² = 23.48, df = 10 (P = 0.009); I² = 57%	P = 0.006
Emotional well-being	11	664	0.38 [0.19, 0.57]	Tau² = 0.03; Chi² = 14.79, df = 10 (P = 0.14); I² = 32%	P < 0.0001
Functional well-being	12	727	0.28 [-0.01, 0.57]	Tau² = 0.19; Chi² = 41.21, df = 11 (P < 0.0001); I² = 73%	P = 0.06
Breast cancer subscale	9	546	0.51 [0.31, 0.70]	Tau² = 0.02; Chi² = 10.40, df = 8 (P = 0.23); I² = 23%	P < 0.00001
Additional concerns	2	130	0.50 [-0.17, 1.16]	Tau² = 0.16; Chi² = 3.09, df = 1 (P = 0.08); I² = 68%	P = 0.14
EORTC QLQ-C30					
Global health	10	996	0.98 [0.49, 1.47]	Tau² = 0.52; Chi² = 6.74, df = 9 (P < 0.00001); I² = 90%	P < 0.00001
Cognitive functioning	8	918	0.28 [-0.03, 0.59]	Tau² = 0.14; Chi² = 27.73, df = 7 (P = 0.0002); I² = 75%	P = 0.08
Emotional functioning	8	891	0.55 [0.18, 0.92]	Tau² = 0.22; Chi² = 39.74, df = 7 (P < 0.00001); I² = 82%	P = 0.003
Physical functioning	10	1001	0.55 [0.37, 0.74]	Tau² = 0.01; Chi² = 10.75, df = 9 (P= 0.29); I² = 16%	P < 0.0001
Role functioning	8	928	0.29 [-0.02, 0.61]	Tau² = 0.15; Chi² = 29.36, df = 7 (P = 0.0001); I² = 76%	P = 0.07
Social functioning	8	918	0.33 [0.01, 0.65]	Tau² = 0.15; Chi² = 29.65, df = 7 (P = 0.0001); I² = 76%	P = 0.04

EORTC QLQ-C23					
Body imagem	3	622	0.22 [-0.29, 0.72]	Tau² = 0.16; Chi² = 9.90, df = 2 (P = 0.007); I² = 80%	P = 0.41
Arm symptoms	3	622	-0.64 [-1.41, 0.14]	Tau² = 0.42; Chi² = 21.49, df = 2 (P < 0.0001); I² = 91%	P = 0.11
Breast symptoms	3	622	-0.38 [-1.46, 0.70]	Tau² = 0.85; Chi² = 39.55, df = 2 (P < 0.00001); I² = 95%	P = 0.49
Sexual functioning	2	560	0.02 [-0.15, 0.18]	Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.89); I² = 0%	P = 0.84
Future pespective	2	560	0.19 [-0.36, 0.74]	Tau² = 0.12; Chi² = 4.22, df = 1 (P = 0.04); I² = 76%	P = 0.49
Sexual enjoyment	2	560	-0.03 [-0.19, 0.14]	Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%	P = 0.76
Side effect of treatment	2	560	-0.15 [-0.82, 0.53]	Tau² = 0.20; Chi² = 6.24, df = 1 (P = 0.01); I² = 84%	P = 0.67

k = number of studies; N = total number of participants evaluated; SMD - standardized mean difference; 95%CI = 95% confidence interval.

Table 3: Effect of aerobic exercise and aerobic exercise combined with strength training on quality of life, considering the domains of the SF-36 instrument.

Subscales	Aerobic exercise					Strength and Aerobic exercise				
	k	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**	***k***	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**
Physical functioning	5	784	0.26 [0.12, 0.40]	Tau² = 0.00; Chi² = 2.01, df = 4 (P = 0.73); I² = 0%	0.0002	5	458	1.02 [0.41, 1.63]	Tau² = 0.39; Chi² = 35.32, df = 4 (P < 0.00001); I² = 89%	0.0010
Roles: physical	4	197	0.22 [-0.14, 0.58]	Tau² = 0.05; Chi² = 4.63, df = 3 (P = 0.20); I² = 35%	0.23	5	509	0.80 [0.29, 1.31]	Tau² = 0.26; Chi² = 25.51, df = 4 (P < 0.0001); I² = 84%	0.002
Bodily pain	4	205	0.21 [-0.14, 0.56]	Tau² = 0.04; Chi² = 4.43, df = 3 (P = 0.22); I² = 32%	0.24	5	509	0.97 [0.36, 1.58]	Tau² = 0.40; Chi² = 36.39, df = 4 (P < 0.00001); I² = 89%	0.002
General health perceptions	4	197	0.19 [-0.42, 0.79]	Tau² = 0.29; Chi² = 12.75, df = 3 (P = 0.005); I² = 76%	0.55	5	509	0.57 [0.25, 0.90]	Tau² = 0.08; Chi² = 10.97, df = 4 (P = 0.03); I² = 64%	0.0005
Vitality	5	817	0.12 [-0.02, 0.26]	Tau² = 0.00; Chi² = 3.70, df = 4 (P = 0.45); I² = 0%	0.09	5	509	0.73 [0.39, 1.08]	Tau² = 0.10; Chi² = 12.04, df = 4 (P = 0.02); I² = 67%	< 0.0001
Social role functioning	4	197	-0.08 [-0.36, 0.20]	Tau² = 0.00; Chi² = 0.38, df = 3 (P = 0.94); I² = 0%	0.58	5	509	0.73 [0.34, 1.12]	Tau² = 0.13; Chi² = 14.98, df = 4 (P = 0.005); I² = 73%	0.0002
Role: emotion	4	197	0.16 [-0.13, 0.44]	Tau² = 0.00; Chi² = 0.28, df = 3 (P = 0.96); I² = 0%	0.28	4	426	0.52 [-0.07, 1.10]	Tau² = 0.30; Chi² = 21.65, df = 3 (P < 0.0001); I² = 86%	0.09
Mental functioning	4	197	0.15 [-0.13, 0.43]	Tau² = 0.00; Chi² = 0.48, df = 3 (P = 0.92); I² = 0%	0.30	5	509	0.51 [0.33, 0.68]	Tau² = 0.00; Chi² = 1.37, df = 4 (P = 0.85); I² = 0%	< 0.00001
Physical component score	1	32	0.79 [0.05, 1.53]	Not applicable	0.04	4	485	0.59 [0.21, 0.97]	Tau² = 0.11; Chi² = 11.63, df = 3 (P = 0.009); I² = 74%	0.002
Mental component score	1	32	0.16 [-0.56, 0.88]	Not applicable	0.66	4	485	0.42 [0.24, 0.60]	Tau² = 0.00; Chi² = 2.01, df = 3 (P = 0.57); I² = 0%	< 0.00001

k = number of studies; N = total number of participants evaluated; SMD - standardized mean difference; 95%CI = 95% confidence interval.

Table 4: Effect of aerobic exercise and aerobic exercise combined with strength on quality of life, according to the domains of the FACT instrument.

Subscales	Aerobic exercise					Strength and Aerobic exercise				
	k	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**	***k***	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**
FACT										
FACT - General	5	52	0.36 [0.03, 0.69]	Tau²= 0.07; Chi²= 7.56, df = 4 (P = 0.11); I²= 47%	0.03	4	295	0.85 [-0.11, 1.81]	Tau² = 0.88; Chi²= 43.84, df= 3 (P < 0.00001), I²= 93%	0.08
FACT - Breast	6	311	0.49 [0.20, 0.78]	Tau² = 0.05; Chi²= 7.75, df = 5 (P = 0.17); I² = 35%	0.0009	3	232	1.29 [0.58, 2.00]	Tau²= 0.32; Chi² = 12.28, df = 2 (P = 0.002); I² = 84%	0.0003
Physical well-being	7	372	0.28 [0.05, 0.52]	Tau² = 0.02; Chi²= 7.61, df= 6 (P = 0.27); I² = 21%	0.02	4	295	0.96 [-0.07, 1.85]	Tau² = 0.75, Chi² = 37.59, df= 3 (P < 0.00001); I²= 92%	0.03
Social/family well-being	7	372	0.20 [-0.07, 0.48]	Tau²=0.06 Chi²=10.35, df=6 (P=0.11); I²=42%	0.14	3	132	0.58 [0.05, 1.11]	Tau² = 0.16, Chi² = 7.72, df = 2 (P = 0.02), I²= 74%	0.03
Emotional well-being	7	372	0.24 [0.03, 0.44]	Tau²= 0.00; Chi²= 2.84, df = 6 (P = 0.83); I² = 0%	0.02	3	132	0,71 [0.29, 1.14]	Tau² = 0.09; Chi² = 4.99, df = 2 (P = 0.08); I²= 60%	0.001
Functional well-being	7	372	0.16 [-0.13, 0.45]	Tau² = 0.07; Chi² = 11.22, df= 6 (P = 0.08); I² = 47%	0.28	4	295	0.56 [-0.13, 1.25]	Tau² = 0.43, Chi²= = 24.70, df = 3 (P = 0.0001); I²= 88%	0.11
Breast cancer subscale	5	254	0.37 [0.06, 0.67]	Tau² = 0.03, Chi² = 5.55, df = 4 (P = 0.24); I² = 28%	0.02	3	222	0.71 [0.44, 0.98]	Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I²= 0%	<0,00001

k = number of studies; N = total number of participants evaluated; SMD - standardized mean difference; 95%CI = 95% confidence interval.

Table 5: Effect of aerobic exercise and aerobic exercise combined with strength training on quality of life, according to the domains of the EORTC QLQ-C30 and EORTC QLQ-C23 instruments.

Subscales	Aerobic exercise					Strength and Aerobic exercise				
	k	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**	***k***	**N**	**SMD [95%CI]**	**Heterogeneity**	**p-value**
EORTC QLQ-C30										
Global health	5	744	0.47 [0.01, 0.94]	Tau² = 0.22; Chi² = 24.23, df = 4 (P <0.0001); I²= 89%	0.05	4	262	1.47 [1.02, 1.91]	Tau² = 0.14; Chi² = 9.20, df = 4 (P = 0.06); I²= 57%	<0.00001
Cognitive functioning	5	744	0.02 [-0.24, 0.28]	Tau² = 0.04; Chi² = 7.65, df = 4 (P = 0.11); I² = 48%	0.87	3	184	0.65 [0.35, 0.94]	Tau² = 0.00; Chi² = 0.14, df = 2 (P = 0.93); I² = 0%	<0.0001
Emotional functioning	4	642	0.35[-0.11, 0.80]	Tau² = 0.16; Chi² = 14.33, df = 3 (P = 0.002); I² = 79%	0.13	4	149	0.75 [0.32, 1.19]	Tau² = 0.22. Chi² = 39.74 df = 3 (P <0.0001); I²= 82%	0.003
Physical functioning	5	739	0.41[0.16, 0.67]	Tau² = 0.02; Chi² = 5.25, df = 4 (P = 0.26); I² = 24%	0.002	5	262	0.73 [0.48, 0.98]	Tau² = 0.00 Chi² = 1.83, df = 4 (P = 0.77); I² = 0%	<0.00001
Role functioning	4	682	0.08[-0.19, 0.35]	Tau² = 0.04; Chi² = 5.62, df = 3 (P = 0.13); I² = 47%	0.57	4	246	0.50 [-0.05, 1.05]	Tau² = 0.24; Chi² = 13.30, df = 3 (P = 0.004); I² = 77%	0.07
Social functioning	5	734	0.29[-0.17, 0.76]	Tau² = 0.23; Chi² = 24.48, df = 4 (P<0.0001); I² = 84%	0.22	3	184	0.41 [0.11, 0.70]	Tau² = 0.00; Chi² = 0.01, df = 2 (P = 1.00); I² = 0%	0.006
EORTC QLQ-C23										
Body imagem	1	500	-0.06[-0.24,0.12]	Not applicable	0.50	2	122	0.41[-0.42, 1.23]	Tau² = 0.29; Chi² = 5.19, df = 1 (P = 0.02); I² = 81%	0.34

Arm symptoms	1	500	-0.01[-0.19,0.16]	Not applicable	0.89	2	122	-0.99[-1.37, -0.62]	Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%	<0.0001
Breast symptoms	1	500	0.08[-0.10, 0.25]	Not applicable	0.39	2	122	-0.64[-2.91, 1.63]	Tau² = 2.59; Chi² =33.12, df = 1 (P = <0.00001); I² = 97%	0.58
Sexual functioning	1	500	-0.03[-0.20, 0.15]	Not applicable	0.75	1	60	-0.01[-0.52, 0.49]	Not applicable	0.97
Future pespective	1	500	0.96[0.81, 1.15]	Not applicable	0.67	1	60	1.70[0.70, 2.10]	Not applicable	0.04
Sexual enjoyment	1	500	-0.03[-0.20, 0.15]	Not applicable	0.75	1	60	-0.01[-0.52, 0.49]	Not applicable	0.97
Side effect of treatment	1	500	0.16[-002, 0.33]	Not applicable	0.08	1	60	-0.54[1.05, -0.02]	Not applicable	0.04

k = number of studies; N = total number of participants evaluated; SMD - standardized mean difference; 95%CI = 95% confidence interval.

Figure 1: Flow diagram of the process of selecting studies for the review.

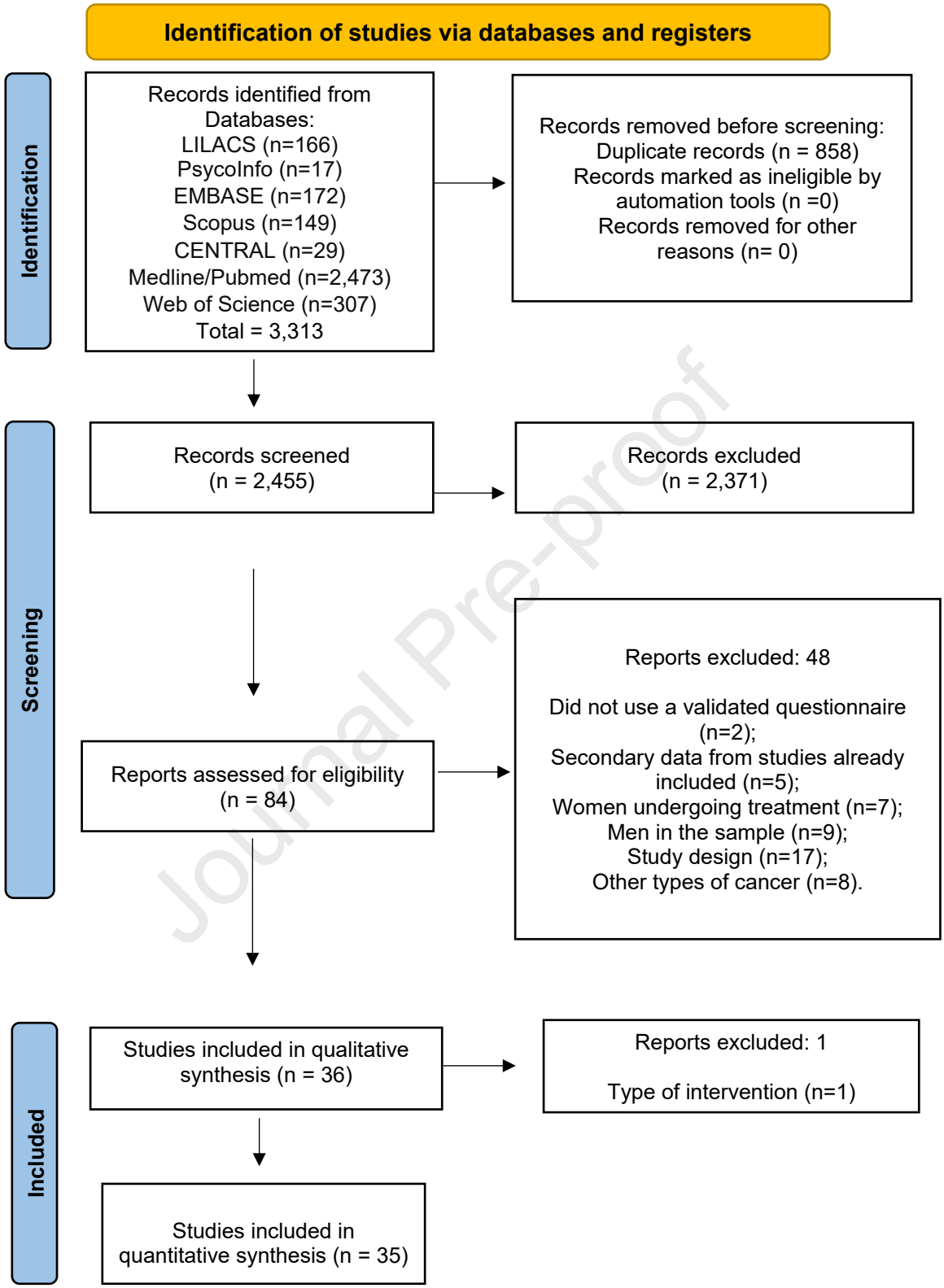
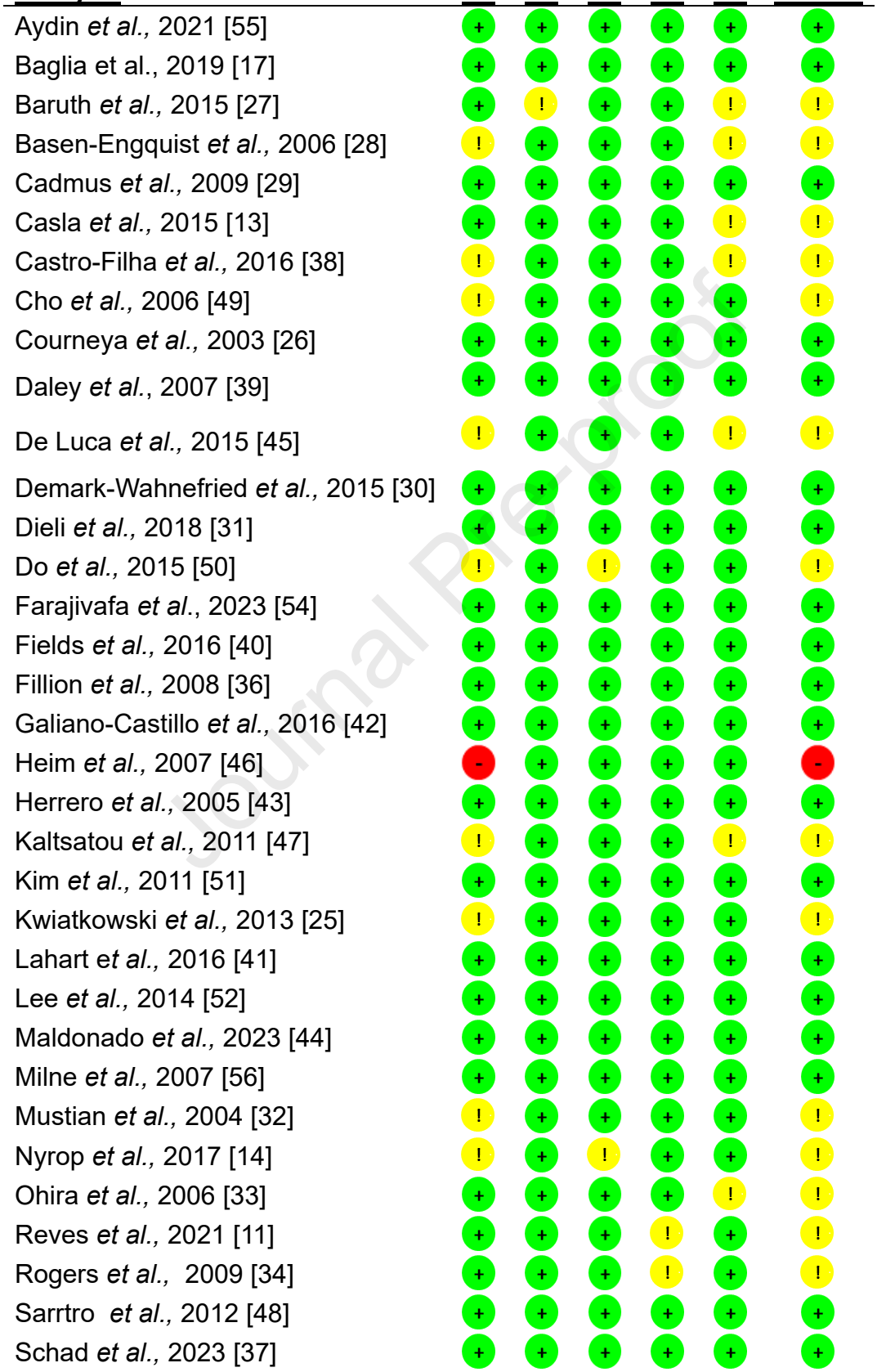


Figure 2: Analysis of the risk of bias of randomized clinical trials eligible for qualitative analysis, according to the RoB-2 instrument.



Legend: D1: Randomisation process; D2: Deviations from the intended interventions; D3: Missing outcome data; D4: Measurement of the outcome; D5: Selection of the reported result.