A Systematic Review of the Effectiveness of Physical Activity Interventions in Adults with Breast Cancer by Physical Activity Type and Mode of Participation

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Abstract:

Objectives: Engaging in physical activity following a diagnosis in breast cancer patients improves both survival rates and psychosocial health outcomes. The factors influencing the effectiveness of physical activity interventions for breast cancer patients remain unclear. This systematic review focuses on two questions: Are there differences in outcomes depending on; the mode of physical activity undertaken; and whether group-based, or individual, programmes are proposed.

Methods: Five databases were searched (PsycINFO, CINAHL, MEDLINE, EMBASE and Central). Randomised control trials were included if they reported an intervention aiming to increase physical activity amongst breast cancer patients. A total of 1561 records were screened with seventeen studies identified for final inclusion. Data extraction and risk of bias analysis were undertaken. A meta-analysis was not possible due to methodological differences between studies.

Results: Findings indicate no evident differences in outcomes based on exercise mode adopted. There are some indications that group interventions may have additional beneficial outcomes, in comparison to individual interventions, but this conclusion cannot be drawn definitively due to confounds within study designs, lack of group-based intervention designs and overall lack of long-term intervention effects.

Conclusions: Although there are no indications of negative intervention effects, only 6 of 17 trials demonstrated significant intervention effects were maintained. Greater transparency in reporting of interventions, and research enabling a comparison of physical activity delivery and mode is needed to determine optimum physical activity interventions to maintain patient physical activity and outcomes.

Keywords: Breast Cancer, Exercise, Oncology, Physical Activity, Quality of Life, Systematic Review

Background

According to the World Health Organisation[1], breast cancer is the most common cancer. Breast cancer survival rates vary greatly worldwide, ranging from below 40% in low-income countries to 80% or over in North America, Sweden and Japan[2]. Improvements in medical and behavioural treatments with breast cancer has led to a substantial number of individuals achieving a normal life expectancy[3] . Physical activity (PA) is one such intervention that can reduce breast cancer incidence and improve quality of life (QoL)[4-11]. PA interventions such as strength and resistance training, aerobic exercise and brisk walking following breast cancer diagnosis have been shown to be associated with improved survival rates and psychosocial health outcomes[12-15], increase levels of physical activity[16] and reduce fatigue[17]. Many health psychology theories such as the social cognitive theory, self-determination theory and the transtheoretical model are used to guide the design and evaluation of PA interventions amongst the targeted population so that the behavioural mechanisms through which behaviour change occurs can be identified and used to implement future behaviour change[18-20] . Previous reviews have demonstrated the effects of PA on breast cancer patients indicating that most interventions were effective in producing short-term behaviour changes in PA[21].

A systematic review of the effects of exercise on breast cancer patients and survivors[22] found exercise to be associated with small but statistically significant improvements in physical functioning, QoL and fatigue. Whilst, this review found promising results, it was based on a relatively small number of trials with wide variations in the population and intervention dose. More recently, Meneses-Echavez and colleagues explored the effects of supervised exercise on breast cancer survivors and demonstrated beneficial reductions in fatigue[23]. However, when supervised and non-supervised exercise were compared amongst breast cancer survivors, there were no significant group differences[24].

Although the benefits of PA for breast cancer patients are widely accepted, the importance of adherence to PA interventions remain unclear. Further, it has not been established whether there are differences in outcomes depending on the type of PA that individuals undertake, or whether the mode of PA intervention, is group-based, or individual. This is particularly relevant as a synthesis of qualitative research undertaken with breast cancer patients indicates that engaging in PA with peers with similar conditions, can facilitate participation[25]. Given the importance of the continuing need to increase the QoL and maintain positive outcomes/survival rates in this population, it is important to try and address this research gap. This systematic review will examine PA randomised trials amongst breast cancer patients and will specifically consider the effectiveness of PA interventions by exercise mode, and intervention type of group versus individual PA interventions. The review will focus on the effectiveness of PA interventions to improve health outcomes; however, the review summary will also show whether an increase in PA was achieved by interventions. The review summarises current evidence, assesses the research quality and identifies issues and recommendations for future research.

Method

This systematic review is reported in line with Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (PRISMA)[26]. The protocol was pre-registered in PROSPERO (registration number: CRD42017081324).

Eligibility Criteria

Studies eligible for inclusion included randomised trials that reported an intervention with the aim to increase PA amongst adult breast cancer patients. Studies were limited to published, peer reviewed articles written in English language. Studies could include adults who have been diagnosed with breast cancer including invasive carcinoma and in situ disease. Eligible comparators included different types of PA interventions.

Eligible Outcomes

The primary outcome of studies was self-reported levels of PA. Secondary outcomes included adherence, cardiorespiratory fitness, QoL, body mass index (BMI), weight and fatigue.

Search Strategy

The search strategy was based on the Cochrane handbook for systematic reviews of interventions[27] and PRISMA flow chart (Figure 1). A systematic literature search was performed across five electronic databases: PsycINFO, CINAHL, MEDLINE, EMBASE and CENTRAL. All studies available up to the end of December 2017 were included. The search strategy was developed using terms based on the population, intervention and outcomes. We used the Boolean operator 'OR' to combine similar keywords and 'AND' to combine key concepts. Search terms are provided in Appendix 1. The first author (SA) conducted the initial searches. The exclusion and inclusion of relevant studies based on titles and abstracts were reviewed independently by SA and the second author (JL). The full text of the remaining studies was reviewed independently by SA and JL based on the eligibility criteria. Any disagreements were resolved by discussion with the research supervisor. Additional reference lists of included studies and related systematic reviews were manually checked. To minimise unintentional publication bias and language bias, a search for unpublished data was conducted in the British Library, Conference Proceedings Citation Index and Open Grey. Searches of the Cochrane Library and the Centre for Reviews and Dissemination were also undertaken. Where original papers were not available contact was made to authors to request paper access or further clarification.

Data Extraction

Data were extracted on the country of origin, participant characteristics, intervention and study design, measures used to assess PA and the results of each paper in relation to PA in breast cancer patients. Selection bias was kept at a minimum, by requiring the three researchers to assess articles and extract data separately prior to discussion and final

agreement. Reasons for exclusion were agreed between researchers and are summarised in Figure 1. Data extraction was undertaken using The Cochrane Collaboration Data Extraction Form.

Risk Assessment of Included Studies

Cochrane's risk of bias tool was adopted to assess the risk for included studies[27]. The tool covers six domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases which are measured against 7 criteria to determine indications of high, low or unclear risks of bias. As well as providing indications of risk of bias in relation to each of the 7 criteria, an overall evaluation of risk of bias is then determined for each study assessed. Risk of bias was assessed independently by two researchers and no disagreements arose.

Synthesis of Results

Due to heterogeneity in population characteristics, intervention components, outcomes measures and the durations of interventions, a meta-analysis was not undertaken[28].

Results

The literature search yielded 1561 records. Following the removal of duplicates and applying the inclusion and exclusion criteria, a total of 1544 articles were excluded (see figure 1). A total of 17 randomised trials met the inclusion criteria and were included in the systematic review. No unpublished relevant studies were identified. Where trials were published across multiple papers, data were extracted and combined for inclusion. Table. 1 provides the detailed summary and main outcomes of eligible studies included within the review.

Study Characteristics

Seventeen randomised trials were identified with total of 2208 participants. Nine studies were undertaken across Europe, six studies in USA, one in Australia and other in

Canada and interventions were often implemented across a variety of settings. The modes of PA across the studies varied with all offering either non-specific aerobic/exercise programmes or walking interventions. Six studies included strength/resistance training, either independently or in combination, with broader cardiovascular exercise. Only five trials provided group-based exercise intervention. The length of reporting ranged from a minimum of 12 weeks[29,30] up to two years[31]. Six studies referred to a theoretical basis/model of behaviour change in relation to the intervention design however, only three studies[30, 32,33] stated a specific theory.

Summary of Effectiveness

To identify the effectiveness of increased health outcomes related to the increase in PA, the outcomes are described by grouping the studies as group versus individual PA interventions. The study effects are reported as p values as not all papers reported effect size. Effect sizes are reported where stated in the papers.

Risk of Bias

Risk of bias ratings are reported in Table 2. Following the assessment only one study, Travier et al., 2015[33], was identified as having a clear low risk of bias in all areas. Overall, nine of the studies were deemed as having a low risk of bias, with the risk of bias for the other trials being unclear. The blinding of participants and personnel was rarely reported. However, blinding participants may have been challenging given the nature of the study designs and populations being used. Allocation concealment was only demonstrated in five studies. Four studies[32, 34, 40,46] were assessed as having an unclear, or high risk of providing incomplete outcome data, with the majority of the studies reporting participants' data from the beginning of the intervention to completion. Overall, the risk of bias assessment does indicate that there are still areas of reporting where transparency in design, procedure and/or outcomes could be improved.

Group physical activity interventions. There were five randomised trials that implemented a group-based PA intervention amongst breast cancer patients[29, 33-36] with Campbell et al., (2005)[29] and Mutrie et al., (2007)[35] showing clear long-term positive intervention effects. The risk of bias assessment for all five of the group intervention studies indicated they were of low risk of bias. Therefore, in this instance risk of bias had no bearing on likelihood of significant results.

Three studies[29,33.35.] found significant intervention effects on physical functioning although across studies different measures were used: Campbell et al., (2005)[29] showed significantly higher physical functioning (p = .001); Mutrie et al, (2007)[35] found significant benefits for metres walked in 12 minutes (p <.0001) and shoulder mobility (p <.0001), whereas Travier et al (2015)[33] reported significant differences in aerobic capacity (effect size .31) and leg muscle strength.

A significant improvement in overall QoL was seen in one study[29] (p = .046) in addition, Mutrie et al, (2007)[35] only found an improvement in Breast Cancer QoL (p= .039) and positive affect (p=.0008) but not general quality of life (p = .053).

The support for intervention benefits on fatigue across studies was not strong. Travier et al (2015)[33] found the increase in physical fatigue was significantly lower for the intervention group compared to controls (effect size - .30). However, although the increase in general and mental fatigue was lower, and levels of activity higher in the intervention group, the difference was not statistically significant and therefore the change could be a result of chance. This was mirrored by Campbell et al., (2005)[29] where changes in fatigue favoured the intervention group but this change was not statistically significant.

In relation to the two studies where no significant intervention effects on health outcomes were seen there were no detrimental effects evident. Some positive changes were apparent such as; the exercise intervention mitigated against the decrease in PA seen in the control group during treatment and boosted levels of engagement in strength exercise post-

intervention[36] and a significant improvement in running time was seen amongst the intervention group (p = .001)[45].

Finally, qualitative data from one paper[37] indicated that the exercise group itself was important for achieving patient outcomes with exercise in standard settings not providing similar benefits.

Individual physical activity interventions. The studies examining individual physical activity interventions amongst breast cancer patients also had mixed results. Four of these studies were assessed as having a low risk of bias, whilst the remaining studies were unclear. Of the five trials showing significant positive intervention effects, three were assessed as having a low risk of bias[30, 38-39], and two[31,40] were assessed as having an unclear risk of bias.

Only five studies adopting individual-based physical activity interventions demonstrated some positive effects were maintained across the data collection period ranging from 6, 12, 18 and 24 months[30, 31, 38-40]. Three studies showed beneficial intervention effects on fatigue Baunmann et al., (2017)[31](p = .025), Gokal et al., (2016)[30] (p = .02) and Hayes et al., (2013)[39] (p <.05). All five of the studies[30, 31, 38-40] showed the intervention had beneficial effects on either physical function or physical activity although the nature of improvement reported was not consistent across studies. For example, Anderson et al., (2012)[38] demonstrated a significant improvement in physical function (p = .01) but no significant group differences for lymphedema whereas in the Mock et al., (2005) study[40], there were no significant intervention effects on physical function but positive impacts on performance within the 12-minute walk test (p = .02) and overall PA (p = .03). In relation to other primary health outcomes, one study showed beneficial intervention effects on quality of life[39] and one study[30] showed broader psychological benefits for the intervention group on self-esteem (p =.001) and mood (p = .03).

Of the remaining individual type interventions, some positive effects were evident but were either not maintained at follow up, or not significant for primary outcome measures. Interestingly, Chou, Dodd and Paul (2012)[41], who compared the timing of PA interventions during chemotherapy treatment, found individuals who started the intervention at the beginning of their chemotherapy significantly increased exercise duration and intensity ($p = .02$) during treatment compared to those who started after chemotherapy with initial indications that levels were sustained. However, an alternative trial paper[42] , found no intervention effects on fatigue or related cancer symptoms.

There were only three studies[34,43-44] which compared different modes and doses of exercise and they found contradictory results. Although Courneya et al., (2013)[43] found some sustained positive effects of higher dose exercise were indicated for pain and endocrine symptoms, Ligibel et al., (2016)[34] and Husebo et al, (2014)[44] found no significant group differences. Further, Courneya et al., (2013)[43] indicated that body mass index (BMI) moderated the intervention effects whereby those of a healthy weight (i.e., BMI< 25 kg·m2) responded better to the higher dose exercise than overweight/obese participants.

Although the mode of delivery within the Cadmus study[32] was individual exercise, one of the conditions offered supervised gym-based training within dedicated sessions (open to multiple participants) which may have provided some group/social benefits. Indeed, with this study there was a positive association shown between exercise and social functioning amongst individuals who reported low social functioning at baseline ($p < .05$).

Discussion

The seventeen trials included in this review found mixed evidence for the effectiveness of physical activity interventions in breast cancer patients and survivors across a range of outcomes. Overall, the findings again provide positive results of increasing PA amongst patients being treated for breast cancer in both individual and group-based interventions. No detrimental effects of physical activity were apparent across any trials. In

relation to the reviews specific aims to examine whether there are differences in efficacy of interventions depending on design (group or individual) or mode of PA, the findings are not definitive.

Engaging in group-based PA has been shown to help facilitate engagement and adherence with PA amongst breast cancer patients based on a meta-synthesis of qualitative research[25]. Based on this systematic review there are further indications that group PA may be effective both in increasing PA and improving quality of life amongst the targeted population[29, 35]. Further, both Schmidt et al, (2017)[36] and Travier et al., (2015)[33] indicated short-term benefits of PA interventions during treatment on fatigue, fitness and muscle strength, although effects were not maintained. One explanation for the lack of longer-term group differences is highlighted by Travier et al., (2015)[33], of there being a confound caused by high PA levels apparent within control groups, and was an issue across a number of papers, regardless of design[40,44, 46]. The argument being that either pre-diagnosis levels of PA are largely driving post-intervention levels of PA or, that following a diagnosis of breast cancer, individuals are more motivated to engage in healthier behaviour regardless of intervention. If the latter is the case, this emphasises why diagnosis/post-treatment are opportune moments for behaviour change intervention. Recent literature has continued the ongoing debate of whether cancer is a teachable moment through promoting long-term health after diagnosis[17, 21], smoking cessation in cancer patients[47] and physical activity after cancer treatment[48]. Future research may explore this argument to tailor interventions to those who are in greatest need.

If we compare the level of sustained positive outcomes from individual-based PA interventions to group-based PA interventions, the net results are similar, with 40% of studies showing positive intervention impacts at the final follow-up[30, 31, 38-40]. Most of the studies that implemented an individual intervention reported at least some short-term positive improvements in PA, including reduction in levels of fatigue, mood and increases in self-

esteem. Although no group differences were found amongst some individualised interventions e.g. Ligibel et al., 2016[34] and Husebo et al, 2014[44]. One study[41] reported engaging in PA at the start of chemotherapy was more effective than starting PA after completion of chemotherapy however, alternative literature has reported that fatigue levels for breast cancer patients peak immediately after chemotherapy[49] and therefore starting at this time-point may have been the most detrimental comparison option. Therefore, given the methodological quality and risk of bias with regards to Chou et al, (2012)[41], it is perhaps unwise to put substantial weight behind this finding. With several qualitative evidences reporting that a barrier to PA is fatigue[25, 50] and Cramp and Byron-Daniel, (2012)[51] arguing that aerobic exercise is beneficial in managing fatigue; it is clear that fatigue plays a role in cancer and adherence to PA. Engaging in PA is a huge barrier with evidence suggesting that being able to live well and engaging or re-engaging in activities such as PA is a complex and challenging issue[52] .

Clinical Implications

Overall, our review findings suggest that a definitive conclusion cannot be drawn on whether group-based PA intervention are more likely to produce more effective outcomes than individual-based PA interventions. Previous literature[53, 54] has demonstrated that the social element of interventions may provide motivation and improve adherence to the intervention programme through peer support. It is possible that in relation to some of the trials reviewed here e.g. Cornette et al., (2016)[55], the regular personal interaction and support individuals received from professionals, may have taken on a similar motivational aspect and helped with achieving the positive outcomes and strong adherence levels of participation. Barriers to engagement in physical activity such as low self -esteem, body image and intrusive thoughts about the illness, have been shown to deter individuals from partaking in group-based interventions[56]. But in contrast, an alternative synthesis indicated that if this is addressed and acknowledged by knowledgeable physical trainers, engaging in physical

activities with peers, who have similar experiences and fears, was a positive aspect of group-based PA[25,37]. The meta-synthesis highlighting however that regardless of whether individual or group-based PA was undertaken, women found taking part in PA acted both as a distraction from cancer and a means to increase self-esteem and body confidence.

In relation to conclusions over whether any type of exercise is more effective, the review indicates that PA type is largely irrelevant to determining efficacy of outcomes. Trials where comparison of exercise type and/or dosage of exercise were undertaken showed no significant group differences[32, 43]. However, a clear weakness of these studies was the lack of clear control i.e. non-physically active group comparison and possible cross-contamination within the trial groups. It must also be recognised that in most instances, the exact type of PA within trials is difficult to determine.

The included studies indicate that, perhaps unsurprisingly, individuals who engaged in PA before diagnosis are more motivated to exercise, and as a result more likely to show improvements to their quality of life. However, the findings highlighted that many survivors remained inadequately active, suggesting that continued motivation and support is required. It would be beneficial to consider the PA history of survivors when incorporating exercise amongst the daily routine of breast cancer survivors and tailor approaches to encourage sustainability of behaviour change.

Recommendations for Future Research

The evidence around the benefits of PA across breast cancer patients are widely accepted but the link between the type of PA interventions and breast cancer outcomes is still relatively poorly evidenced, highlighting a gap in the literature. A direct link of effectiveness in PA has not been established due to large differences across studies designs, risk of bias and findings. Future studies should use rigorous designs and transparent reporting to provide conclusive evidence around optimum PA interventions with breast cancer within the limits of their health system environment.

Only six studies of the included 17 made mention of psychological theory in the development of their interventions. Of those, three referred to a specific theoretical model of behaviour change, with two making a generic statement of "drawing on" models of behaviour change. Given the behaviour change element of PA interventions[58], this is particularly disappointing as numerous research has highlighted the effectiveness of physical activity amongst breast cancer patients using social cognitive theory[57] , the transtheoretical model[18] and self-determination theory[19]. Future research should embed psychology theory and framework when devising interventions using guidance as recommended by the Medical Research Council[59]. The capacity for this is clear with researchers able to draw on evidence-based models and framework purposefully suited for this[60-62].

Although the review suggests positive results, due to an unclear risk of bias across several criteria across 16 studies, and an overall low risk bias assessment for only 9 of 17 studies, the results do need to be considered in this regard. A clear challenge in assessing risk of bias is the lack of clarity within publications or alternatively, it is an accurate reflection of weaknesses in design/implementation and biases in reporting. It is clearly acknowledged that reporting bias is already likely to be apparent with non-significant findings less likely to obtain publication[27]. Although it is important to recognise the challenges of working within clinical practice and specific populations, the differences between studies and national health systems do naturally raise questions of generalisability. The effectiveness, and transferability, of interventions may be potentially limited due to differences across the globe in healthcare practices, policies and social norms. Therefore, in this field, there is still a clear need for replication of interventions and further refinement of intervention research and design.

Study Limitations

This review was limited to studies published in English Language, therefore relevant studies published in other languages may offer alternative findings. Furthermore, despite a comprehensive search of the literature across a wide range of databases, this review was only

able to access 17 randomised trials. It is not clear whether further trials occurred, as not all trials may have pre-published protocols, and therefore publication bias may be evident with interventions yielding a negative or insignificant outcome unpublished[63]. In addition, despite direct requests, some original trial papers were not forthcoming from authors, and although data from the trials were available in other publications (used here) it is the case that this may still have affected our analysis of risk of bias and access to trial results. Further, the high levels of heterogeneity across the studies (including the measures and outcomes) meant it was not possible to pool the data in to a meta-analysis.

This review investigated all types of PA across breast cancer patients such as cycling, walking and circuits. The differentiation, and lack of specificity, across the types of PA makes it difficult to reach a conclusion on the topic. Moreover, the primary outcome of inclusion in this review was self-reported physical activity outcomes, therefore, individuals may have over or under reported PA levels. Although two of the studies included did make comparisons on type and dosage of exercise and found no significant effects, it is still the case that the type of PA may influence the effectiveness of interventions. For example, exercise such as aerobics has been suggested to tone and strengthen body[64], whilst activities such as yoga often focus on physical and mental fitness[65] with both types of exercise shown to increase physical activity amongst the targeted population[66, 67]. It would be interesting if future research could make further comparisons between the efficacies of different types of PA and consider qualitative as well as quantitative outcomes in the overall assessment.

Conclusions

Current findings suggest that both group and individual PA interventions for individuals with breast cancer have positive outcomes. Although there are some indicators that group interventions may be more beneficial, for example with regards to psychosocial outcomes, this conclusion cannot be drawn definitively. The review could not establish whether there are differences in outcomes based on the type of PA. It would be beneficial for future

research to investigate whether specific types of physical activity are more, or less, beneficial in patients with breast cancer and impact on different outcomes. It is still apparent that clarity of reporting and a lack of use of theory in intervention design is still a concern. There appears to be minimal consideration evident of behavioural factors, such as individual motivation and intentions, or behaviour change techniques that may influence intervention efficacy. Further research underpinned by behaviour change theory and techniques is warranted, both in terms of developing effective PA interventions for this population across the range of treatment stages, and to aid researchers and clinical practitioners to draw well founded conclusions on the most effective approaches to take with this population.

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Ethical Approval

None Sought

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Table.1. *Descriptive information on eligible studies reviewed.*

Reference Location Intervention setting	**Demographics – N, Age**	**Intervention conditions**	**Measurement points.**	**Outcomes Measured**	**Adherence**	**Outcomes +, - or 0 diff for intervention (p value – where reported)**	**Interv. effect +/-/0**	**Behaviour Change Theory evident**	**Group (G) or Individual (I) PA**
1. Anderson et al., (2012) USA Research centre	I= N52 C= N52 Age= 53.6 (32-82)	I- Lymphedema Education + tailored walking, strength & resistance programme C- patient education	**Baseline** 3 months, 6 months 9 months 12 months 15 months **18 months**	QoL – FACT-B 6 min. walk test (MWT) Arm volume Self-efficacy in PA	79% completed 61% participated in 75% of PA sessions	- (.057) + (.0098) + (.054) + (.03)	+	None specified (NS)	I
2. Baumann et al., (2017) Germany	I= N111 C= N83 Age= I-53.8 (±8.6), C-58.2 (±9.4) (*p = .001)	I- 3-week Individual tailored exercise & rehab programme (residential) and home-based f/up programme C-standard 3-week rehab programme only & no f/up care	**Baseline** **4 months** **8 months** **12 months** **18 months** **24 months**	Physical Activity Fatigue QoL	68% I v 65% C completed	+ (.005) + (.025 0 (>.05)	+	NS	I
3. Cadmus et al., (2009) USA	Ia= N25 C= N25 Ib= N37 C= N38 Age= Ia (35-75)	Ia- 6-month Home based	**Baseline** **6 months**	Physical Activity Happiness Depression	90% Ia and 80% Ib	0 0 0	0	TPB TTM	I

	Ib (34-79)	walking/exercise programme Ib- 6-month Supervised GYM & home-based walking/exercise programme C- Usual Care		Anxiety Stress Self-esteem FACT-B SF-36	completion rates 67% of supervised sessions attended	0 0 0 0 0			
4. Campbell et al., (2005) UK	I= N12 C= N10 Age= I-48 (±10), C-47 (±5)	I- 12-week structured exercise and individual tailored maintenance programme C- usual care	**Baseline** **12 weeks**	FACT-B FACT-G Life satisfaction Fatigue Physical Activity 12 MWT	86% completed 70% of sessions attended	0 (.094) + (.046) 0 (.315) 0 (.115) + (.003) + (.001)	+	Non-specific model of behaviour change	G
5. Chou et al., (2012) USA**	Ia= N35 Ib= N31 Age= Ia- 48.8 (±8.5) C-49.5 (±9.5)	Ia -Home-based aerobic exercise programme from beginning of chemo Ib – Home-based aerobic exercise programme on completion of chemo	**Baseline** **Treatment completion** **Study completion**	Physical Activity (PA) frequency PA duration PA intensity	Ns	0 (>.05) + Ia (<.01) 0 (>.05)	0	NS	I
6. Cornette et al., (2016) france	I= N21 C=N21 Age= 18-75	I- 27-week tailored PA programme (home based) incl. motivational weekly calls.	**Baseline** **27 weeks** **End of chemo.** **27 weeks post chemo.**	Cardiorespiratory Fitness (CRF) 6MWT Muscular Strength Fatigue QoL	95% completed. 88% adherence to aerobic PA 46% adherence	+ (.049) >.05 @ T2 + (.03) 0 (.283) 0 (.157) 0 (.644) 0 (.453)	0	NS	I

		Aerobic (Cycling/Walking) and resistance training. C- usual care		Anxiety/Depression	to resistance PA				
7. Courneya et al., (2013) Canada**	N=301 Age= 50.0 (±8.9)	Ia- supervised higher intensity aerobic PA Ib- supervised combined higher intensity aerobic and resistance PA C- Supervised Standard PA	**Baseline** **During chemo** **3-4 weeks post chemo**	Physical Functioning Pain Fatigue Endocrine symptoms Aerobic Fitness	98.3% completed C 88% attendance Ia 82% attendance Ib 78% attendance 66% resistance PA attendance	0 (>.30) + Ia (.02) 0 Ia (.09) + Ia (.02) Ib (.009) 0 (.08)	0	NS	I
8. Gokal et al., (2016) UK	I= N25 C= N25 Age= I-52 (±11.7) C-52 (±8.9)	I- 12-week home based self-guided walking programme C- Usual care	Baseline **Pre-intervention** **12 weeks (post chemo)**	Fatigue Self-Esteem Mood Physical Activity Anxiety Depression	80% completed	+ (.02) + (.001) + (.03) + (.001) 0 (.35) 0 (.60)	+	TPB	I
9. Hayes et al., (2013) australia	Ia= N67 Ib= N67 C= N65 Age= 52 (29-70)	Ia – F2F 8-month tailored exercise intervention Ib – Telephone delivery 8-month tailored exercise intervention C – usual care	**Baseline** **6 months** **12 months**	QoL Physical Function Fatigue Anxiety Depression Pain Lymphoedema	93% completed Ia 88% attendance Ib 81% attendance	+ (.030) + .016) + (.032) 0 (>.20) 0 (>.20) 0 (.441) 0	+	NS	I
10. Husebo et al., (2014) norway	I= N33 C=N34	I – Home-based strength and walking	**Baseline** **Post Chemo** **6-months post**	Fatigue 6MWT Physical Activity	77.6% completed	0 (.970) 0 (.849) 0 (.398)	0	NS	I

	Age= I-50.8 (±9.7) C-53.6 (±8.8)	C – Maintain "normal" physical activity (Moderate)			I – 17% walking adherence 15% strength adherence			
11. Ligibel et al., (2016) usa	I= N48 C= N53 Age= I-49.3 (±9.6) C-50.7 (±9.4)	I – 16-week home-based moderate aerobic exercise C – wait list/usual care	**Baseline 16 weeks**	Physical Function Fitness – Treadmill test QoL Fatigue	75.2% completed	0 (.23) 0 (.35) 0 (.17) 0 (.63)	0	NS	I
12. Mock et al., (2001) usa**	N52 (group data unclear) Age- info unclear.	I- Variable length tailored walking programme C – usual care	**Baseline Post treatment**	Fatigue Physical Function 12MWT QoL Social Functioning	69% completed I – 33% non-adherence C – 50% engaging in moderated exercise	0 NB: results not reported by original intervention group due to adherence issues	0	NS – alternative theoretical framework referenced "Levine Conservation Model"	I
13. Mock et al., (2005) usa	I= N60 C= N59 Age= I-51.3 (±8.9) C-51.6 (±9.7)	I- Variable length home-based walking programme C- usual Care	**Baseline Post treatment**	Fatigue 12MWT Physical Function Physical Activity	91% completed I – 72% adherence C – 61% adherence	0 (.29) + (.02) 0 (.14) + (.03)	0	NS	I
14. Mutrie et al., (2007) uk	I= N91 C= N91 Age= I-51.3 (±10.3) C-51.8 (±8.7)	I- 12-week group aerobic and strength exercise and discussion programme C- usual care	**Baseline 12 weeks 6 months**	FACT-G FACT-B Depression Affect 12MWT Physical Activity Shoulder mobilisation	87% completed	0 (.053) + (.039) 0 (.064) + (.0008) + (<.0001) 0 (.23) + (<.0001)	+	Non-specific model of behaviour change	G

15. Saarto et al., (2012) finland	I= N302 C= N271 Age= I-52.3 (36-68) C-52.4 (35-68)	I- 12-month weekly group (aerobics and circuits) plus home-based programme. C- maintain existing PA practice.	**Baseline** 6 months **12 months**	Physical Activity 2km Walk Test Running Test QoL Fatigue Depression Menopausal symptom	87% completed I – on average participants attended 62% of group sessions 88% exercise 3 x per week.	0 (.97) 0 (.15) + (<.001) 0 (.43) 0 (.95) 0 (.50) 0 (>.05)	0	NS	G
16. Schmidt et al., (2017) germany	I= N114 C= N113 Age= I-53.9 (±9.5) C-55.3 (±9.3)	I- 12-week resistance exercise group C- relaxation wait-list control	**Baseline** **During** **3 months** **6 months** **12 months**	PA frequency PA duration PA intensity	87% completed I – on average participants attended 65% of group sessions 40% maintained attendance post-I C – 25% commence resistance groups during f/up	0 0 0	0	NS	G
17. Travier et al., (2015) netherlands	I= N102 C= N102 Age= I-49.7 (±8.2) C-49.5 (±7.9)	I- 18-week aerobic and strength group C- usual care	**Baseline** **Post-Intervention** **36 weeks**	Fatigue QoL Anxiety Depression Aerobic capacity Strength	80% completed I - 89% meeting PA levels C - 56% meeting PA levels	0 0 0 0 0 0	0	Bandura – cognitive behaviour theory	G

Note. Where measurement points are highlighted in **bold**, these are the time points reported in the publication. Outcome/Intervention effects are (+,-,0) are indicated at end of f/up reporting period. FACT-B = Functional Assessment of Cancer Therapy-Breast, FACT-G = Functional Assessment of Cancer Therapy-General, QoL = Quality of Life, PA = Physical Activity. ** = reflects data presented in table is from multiple papers published.

Table 2.

Summary of Risk Assessment of Bias (Higgins et al., 2011) for Randomised Controlled Trials Included in the Review

	Criteria*							
Study	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Overall Risk Assessment**
Anderson et al., (2012)	↓	-	↓	-	↓	-	↓	Low
Baunmann et al., (2017)	-	-	-	-	↓	-	-	Unclear
Cadmus et al., (2009)	↓	↓	-	-	↑	-	↓	Unclear
Campbell et al., (2005)	↓	↓	-	-	↓	↓	↓	Low
Chou et al., (2012)	-	-	-	-	↓	↓	-	Unclear
Cornette et al., (2016)	↑	-	-	-	↓	↓	↓	Unclear
Courneya et al., (2013)	↓	↓	-	-	↓	↓	-	Low
Gokal et al., (2016)	↓	-	-	-	↓	↓	↓	Low
Hayes et al., (2013)	↓	-	-	↓	↓	↓	↓	Low
Husebo et al., (2014)	↑	↓	-	-	↓	-	↓	Unclear
Ligibel et al., (2016)	-	-	↓	↓	-	↓	↑	Unclear
Mock et al., (2001)	↓	-	↓	-	↑	-	↑	Unclear
Mock et al., (2005)	↓	-	-	↓	↑	-	-	Unclear
Mutrie et al., (2007)	↓	-	↓	↓	↓	-	↓	Low
Saarto et al., (2012)	↓	-	↓	↑	↓	↓	↓	Low
Schmidt et al., (2017)	-	-	↓	-	↓	↓	↓	Low
Travier et al., (2015)	↓	↓	↓	↓	↓	↓	↓	Low
No of studies meeting criterion	10	5	8	5	15	11	11	-

Note. ↓ = Low risk, ↑ = High risk, - = unclear risk. *1) Random sequence generation, 2) Allocation concealment, 3) Blinding of participants and personnel, 4) Blinding of outcome assessment, 5) Incomplete outcome data, 6) Selective outcome reporting, 7) Other bias