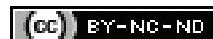


# Physiotherapy Interventions and Assessment Tools for Physical Function in Breast Cancer Patients: A Systematic Review and Meta-analysis

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## ABSTRACT

**Introduction:** Breast Cancer (BC) and its treatment impart a variety of physical impairments in body causing physical functional decline even after the completion of active treatment. Physiotherapy plays an important role in managing physical functional limitations. However, there is lack of data regarding efficacy of physiotherapeutic interventions in improving physical functional impairments and assessment tools used to evaluate Physical Function (PF) in individuals with BC.

**Aim:** To evaluate the efficacy of physiotherapy interventions on PF and analyse the assessment tools used for evaluating PF in BC.

**Materials and Methods:** Randomised Controlled Trials were searched in PubMed and Scopus databases, published from inception to December 2023, in which the effect of physiotherapeutic interventions on PF was evaluated in individuals with BC. Keywords used to search literature were: (BC) AND (physiotherapy intervention) AND (PF). The mean change in PF was primary outcome measure, and tools used to assess PF in included studies were also analysed. The quality of

the studies and the risk of bias were evaluated. A meta-analysis of included studies was done using Review Manager (Software, version 5.4).

**Results:** Overall 333 trials were retrieved, of which nine were included in systematic review. Four studies were included in meta-analysis, which used Short Form-36 (SF-36) and European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire's "Physical functioning" subscale as measures to evaluate changes in PF at the end of the study. The meta-analysis revealed statistically significant improvements in SF-36 "Physical functioning" subscale scores (Mean difference=2.87, 95% CI: 0.63 to 5.12,  $p=0.01$ ) and EORTC QLQ-C30 "Physical functioning" subscale scores (Mean difference=8.77, 95% CI: 3.31 to 14.24,  $p=0.002$ ), with low heterogeneity in treatment groups when compared to control group.

**Conclusion:** Physiotherapeutic exercise interventions are effective in improving PF in individuals with BC, and SF-36 questionnaire "Physical functioning" subscale was the most commonly used tool to assess PF in BC patients and survivors.

**Keywords:** Breast cancer, Physiotherapy interventions, Physical function

## INTRODUCTION

The BC is the most common malignancy among women globally and the leading cause of cancer-related deaths worldwide [World Health Organisation (WHO)] 2023 [1]. With advances in awareness programs, early screening, and treatment, the survival time in BC has significantly improved. However, BC and its treatment-related side effects impart a variety of short- and long-term impairments related to neuromuscular, musculoskeletal, lymphovascular, and cardiovascular systems, which cause functional decline in individuals with BC [2-6]. Other prevalent side effects of cancer and anti-cancer treatment, including anxiety, stress, depression, and fatigue, further add to functional morbidity in this patient population [7].

In literature, a clear and consistent definition of PF and related parameters are lacking. The definition most cited by professionals in literature is the one given by Painter P et al., as "the ability to perform the basic actions that are essential for maintaining independence and carrying out more complex activities" [8]. Here, the basic actions are basic physical movements like walking, lifting, carrying, pushing, and pulling, while complex activities combine basic movements that are essential for self-care (ADLs and IADLs), role/obligatory and discretionary activities [8]. An adequate level of PF is required to perform activities of daily living, for adaptation to the environment, and live independently and safely in society, particularly for older people. Some determinants of PF have been enumerated including level of physical fitness (cardiorespiratory fitness, muscle function, and flexibility), disease-specific clinical

factors, and sensory, environmental, and behavioural factors; many of which are adversely affected in patients with BC even after completion of active treatment [6,8-10]. Advanced age, co-morbidities, higher Body Mass Index (BMI), smoking, and lower educational and socioeconomic status are considered possible predictors of subsequent decline in physical functioning in BC [11,12]. An association between deterioration of PF and premature mortality has been found in BC survivors [13-15]. Impairment in PF have been reported to reduces work participation, cause increased workplace changes, and result in more sick leaves among BC survivors who returned to work post-BC treatment [16].

Positive effects of exercises have been reported on various aspects of PF in BC patients and survivors and physiotherapeutic exercises are seen as an effective management strategy for cancer related decline in physical functioning [17-22]. In light of the knowledge about negative effects of impaired physical functioning on an individual's independence in society and health-related quality of life, there is need for focussed efforts to evaluate and manage such limitations in individuals with BC. To present knowledge, there is no published systematic review and meta-analysis of RCTs in humans that evaluates the impact of physiotherapeutic interventions on PF, as well as assessment tools used to evaluate PF in individuals with BC. To address this gap in knowledge, this systematic review seeks to synthesise the available evidence to answer the following research question: What is the efficacy of physiotherapeutic interventions in improving PF in individuals with BC, and which assessment tools

are used to evaluate PF in BC? The objectives of the current review were to evaluate the efficacy of physiotherapeutic interventions in improving PF in individuals with BC; and to analyse the assessment tools used to evaluate PF in individuals with BC.

MATERIALS AND METHODS

The elements of the Population, Intervention, Comparison, Outcome (PICO) framework are provided in [Table/Fig-1]. The current systematic review and meta-analysis has been conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) 2015 statement. The detailed protocol for this systematic review has been registered on PROSPERO (Identification No. CRD42023470883).

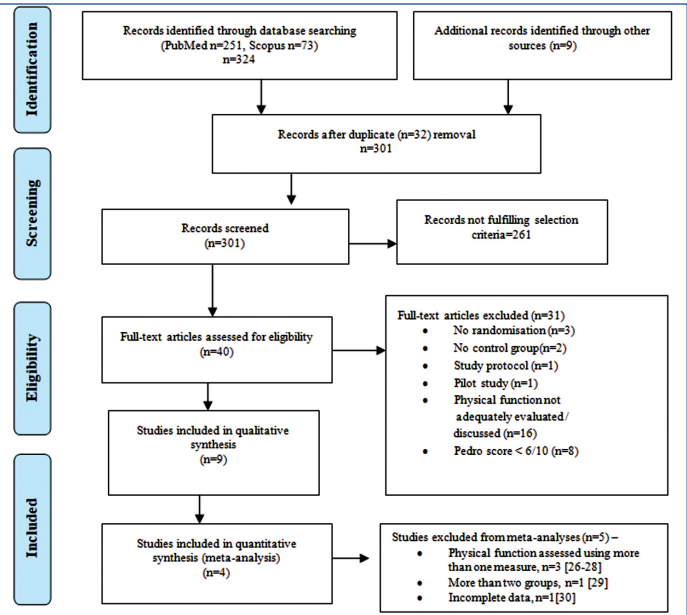
Population	Breast Cancer (BC) patients and survivors (both male and female) with age equal to or more than 18 years
Intervention	Physiotherapeutic interventions used alone or in combination with other interventions
Comparator	Standard treatment, usual care or placebo group
Outcome	Physical Function (PF)

[Table/Fig-1]: Elements of Population, Intervention, Comparison, Outcome (PICO) framework.

**Inclusion and Exclusion criteria:** Inclusion criteria for eligible studies were: RCTs conducted on BC patients and survivors that evaluated the effect of physiotherapeutic interventions on PF; published in English language; and published from inception to December 2023. All reviews, systematic reviews, meta-analyses, case reports, editorials, letters, and comments were excluded from the study. Studies involving other cancer types, where the majority of study population was of cancer type other than BC, were excluded.

Study Procedure

**Search strategy:** The search was undertaken from February to March 2024. PubMed and Scopus databases were searched for the relevant studies from commencement to December 2023. The algorithm used was: (BC) AND (physiotherapy intervention) AND (PF). The detailed search strategy of this systematic review has been explained in the flow diagram [Table/Fig-2]. Two authors (SM, PK) independently searched the databases for eligible studies through multistep approach involving title and abstract reading, and full-text assessment according to inclusion criteria.



[Table/Fig-2]: PRISMA flow diagram showing selection of studies.

**Data extraction:** Two reviewers (SM, PK) extracted the data for analysis independently. The extracted information was compared, and any disparity was resolved by discussion with third reviewer (AS).

Any unclear or missing data were cleared by contacting corresponding author of the article, followed by data summarisation and tabulation. The information collected from each study included: study ID (first author and year), study location, sample size, age, intervention, duration of intervention, outcome measures used to evaluate PF, and results (change in PF). To evaluate treatment efficacy, mean change in PF was included in meta-analysis.

**Assessment of quality and risk of bias:** The methodological quality of the studies was assessed using the Physiotherapy Evidence Database (PEDro) quality scale, which has 11 items that address external validity, internal validity, and interpretability of the study results [23]. The studies rating 6 or more on PEDro scale were included in the review. The risk of bias for the RCTs was assessed using the Cochrane Collaboration tool [24]. Information regarding random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias was retrieved from the articles. Included studies were evaluated independently by the three authors to classify the risk of bias as a 'high-risk,' 'low-risk,' or 'unclear-risk.'

STATISTICAL ANALYSIS

To determine the treatment efficacy, the mean change in PF score from baseline to end of the study was compared between experimental and comparison groups. For the efficacy of exercise interventions, the mean differences were calculated with standard deviations for the outcome variable and assessed as continuous variables using weighted mean differences and 95% confidence interval. The I<sup>2</sup> statistics was used to evaluate the heterogeneity of the studies: "0-25% was considered low heterogeneity, 26-75% as moderate heterogeneity, and 76-100% as substantial heterogeneity" [25]. Sensitivity analysis was not done, as low heterogeneity was observed in meta-analysis. To perform the meta-analysis, the random-effects model was used. The results were considered statistically significant at p≤0.05. Forest plots were generated using the Review Manager 5.4 software. Funnel plots were not generated, as number of included studies in meta-analysis (n=2) was less for both PF outcome measures.

RESULTS

**Search results:** The PubMed and Scopus electronic database search yielded 333 citations (PubMed=251, Scopus=73, and 9 from other sources). Thirty-two duplicates were removed, and 301 articles were assessed through multistep approach involving title and abstracts reading, followed by full-text assessment. Nine studies fulfilled the selection criteria of the review [26-34]. Five out of nine selected studies were excluded from the meta-analysis of PF [26-30]. The remaining four studies, consisting of 500 participants in treatment group and 505 in comparison group, were included for meta-analysis of PF. The details of the study selection are presented in [Table/Fig-2].

**Study characteristics:** Characteristics of the included studies are summarised in [Table/Fig-3] [26-34]. Nine studies met the inclusion criteria. The included studies were conducted in the USA (four), Spain (two), Belgium (one), Germany (one), and Australia (one). The majority of the trials were conducted on BC survivors (n=7). Two studies had mixed cancer population, with majority of cancer survivors being of BC [31,32]. Four studies had patient population ≥60 years [27,29,31,32], while five had less than 60 years of age [26,28,30,33,34].

Studies evaluated effect of physiotherapeutic exercise interventions only (n=6) [26,27,29,30,33,34], physiotherapeutic interventions with added telephonic counseling and dietary recommendations (n=2) [31,32], and pain neuroscience education on PF [28]. Physiotherapeutic exercise interventions given in trials were resistance/strengthening exercises, aerobic exercises, endurance exercises, aqua fitness exercises and balance exercises, and flexibility exercises. Resistance or strengthening exercise were the most commonly used intervention in trials, primarily focused on strengthening major muscle groups of upper and lower body.

Authors name/ Year/Place of the study	No. of participants	Study population	Age (years) (mean±SD)	Intervention and settings	Study duration	Outcomes	Physical Function (PF) measure	Findings
Brown JC and Schmitz KH, 2015 [30] USA	TG=148 CG=147	Breast Cancer (BC) survivors	TG-55.3±8.5 CG-56.7±9.1	TG-weight lifting exercises CG-usual care -Supervised	12 months	PF	SF-36 Questionnaire 'physical functioning subscale'	Reduced incident deterioration of PF in treatment group when compared to control group
Cormie P et al., 2013 [26] Australia	TG 1=22 TG 2=21 CG=19	BC Survivors with BC related lymphoedema	TG 1-56.1±8.1 TG 2-57.0±10.0 CG-58.6±6.7	TG 1-high load resistance exercises TG 2-low load resistance exercises CG-usual care -Supervised	3 months	Lymphoedema status, Symptom severity, PF, health related quality of life	Strength and endurance of major muscles, flexibility shoulder, elbow and wrist	Significant improvement noted in muscle strength and endurance in both treatment groups when compared to control group
Dams L et al., 2023 [28] Belgium	TG=92 CG=92	BC patients who had undergone BC surgery	TG-55.4±11.5 CG-55.2±11.4	TG-pain neuroscience education, standard physiotherapy CG-biomedical education, standard physiotherapy home-based and supervised	12 months	Pain related disability, Pain intensity, physical and emotional functioning	Physical activity level using accelerometer Upper limb function using DASH questionnaire	No significant difference in PF between treatment and control group
Denmark- Wahnefried W et al., 2006 [32] USA	TG=89 CG=93	Breast and prostate cancer survivors	TG-71.5±4.4 CG-71.9±5.6	TG-diet and exercise program (strength, endurance, balance and flexibility exercises) of telephone counselling and tailored mailed material CG-general health information home-based	6 months	PF, physical activity level, and diet quality	SF-36 Questionnaire 'physical functioning subscale'	No significant difference in physical functioning between experimental and control group
Galiano-Castillo N et al., 2016 [33] Spain	TG=40 CG=41	BC survivors	TG-47.9±9.6 CG-49.2±7.9	TG-terehabilitation (resistance and aerobic exercises) CG-basic recommendations for exercise home-based	8 weeks	Health related quality of life, pain, grip strength, muscle strength, fatigue level	EORTC QLQ-C30 Questionnaire 'physical functioning subscale'	Tererehabilitation group had statistically significant improvements in PF scores when compared to control group
Garcia-Soidan JL et al., 2020 [29] Spain	STG=79 AFG=79 AEG=79 CG=79	BC survivors	STG-63±7 AFG-62±6.8 AEG-64±7.1 CG-63±4.6	STG- strength training exercises AFG AEG CG-usual care -Supervised	24 months	Functional fitness, health related quality of life	SF-12 Questionnaire 'physical functioning subscale'	Significant improvements found in PF in all three treatment groups (Strength, aqua-fitness and aerobic exercise group) when compared to control group. Among intervention groups, aqua fitness found more effective than others in improving PF
Morey MC et al., 2009 [31] USA	TG=319 CG=322	Breast, prostate and colorectal cancer survivors	TG-73.0±5.0 CG-73.1±5.1	TG- home-based telephone counselling and tailored mailed material promoting exercises and diet CG-wait listed	12 months	PF, lower extremity function, physical activity level, health related quality of life	SF-36 Questionnaire 'physical functioning subscale'	Less decline in PF scores in treatment group when compared to control group
Schmidt ME et al., 2015 [34] Germany	TG=52 CG=49	BC patients receiving adjuvant chemotherapy	TG-52.2±9.9 CG-53.3±10.2	TG=Resistance exercises CG=Relaxation exercises -Supervised	12 weeks	Fatigue, health related quality of life	EORTC QLQ-C30 Questionnaire 'physical functioning subscale'	Less deterioration of physical functioning in treatment group when compared to control group
Winters-Stone KM et al., 2022 [27] USA	AEG=37 STG=39 CG=38	BC survivors	AET-71.1±4.6 ST-70.6±5.4 CG-70.9±5.4	AETG STG-resistance exercise training CG-stretching exercise Home-based and supervised	12 months	Aerobic capacity, muscle strength, PF	Objective measure-SPPB, 6-minute walk distance. Subjective measures- SF-36 Questionnaire 'physical functioning subscale', Late Life Function and Disability Index	Significant improvement in PF in treatment groups when compared to control group. Resistance exercises more beneficial in improving PF when compared to other two groups

**[Table/Fig-3]:** Major characteristics of the included studies [26-34].

TG: Treatment group; CG: Control group; SF-36 questionnaire: Short form-36 questionnaire; SF-12 questionnaire: Short form-12 questionnaire; EORTC QLQ-C30 questionnaire- European organisation for research and treatment of cancer QLQ-C30 questionnaire; STG: Strength training group; AFG group: Aqua-fitness training group; AEG: Aerobic exercise training group; DASH: Disabilities of arm, shoulder and hand

Trials varied in terms of number of repetitions and sets per session, frequency of exercise interventions, and duration of exercise sessions. Trials were home-based, supervised, or combination of both, performed individually or in group, with protocol duration ranging from eight weeks to 24 months.

Majority (n=7) of the included studies used valid and reliable health-related quality of life tools, including - Short Form-36 (SF-36) Questionnaire (n=4, [27,30-32]), European Organisation for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) questionnaire (n=2) [33,34]. Short Form-12 (SF-12) questionnaire

(n=1) [29], with 'physical functioning' as subscale. One study assessed primary components affecting PF, such as 'muscle strength' using dynamometer, 'muscle endurance' using repetition maximum test of major muscle groups, and 'flexibility' in upper limb using standard goniometer [26], and one study assessed 'physical activity level' (using accelerometer) and 'upper limb function' (using DASH questionnaire) as a measures of physical functioning [28]. Outcome measures used in trials were subjective (n=6) [29-34], objective (n=1) [26], or a combination of both (n=2) [27,28].

In majority of the trials included in systematic review, exercise interventions were found to improve physical functioning in treatment group when compared to control group [26,27,29-31,33,34]. Three of these trials involving older BC survivors [27,29,31], and one trial involving BC patients undergoing adjuvant chemotherapy [34], exercise interventions alone or with diet and counselling interventions, were found effective in improving or reducing incident decline in PF in treatment groups when compared to control groups. However, pain neuroscience education and standard physiotherapy were not found to be more effective in improving PF in treatment group compared to control group, which received pain biomedical education and standard physiotherapy [28]. In one study including home-based diet and exercise program, supplemented by telephone counseling and tailored mailed material, conducted on older breast and prostate cancer survivors no statistically significant difference in self-reported physical functioning between treatment group and control group was found at the end of the study [32].

Eight of the nine reviewed randomised controlled trials commented on relative safety and adverse events during treatment duration [26,27,29-34]. No serious adverse events during study duration were reported in six of the included studies [26,27,29,30,33,34]. Two trials involving older breast, prostate, and colorectal cancer survivors reported adverse events directly attributable to study intervention [31,32]. However, in these studies, no difference in total number of events between the groups was noted.

**Quality assessment:** All included studies ranked high on PEDro score, scoring six or more points out of ten [Table/Fig-4] [26-34]. Four studies had 6/10 rating [27,30-32], four studies had 7/10 [26,28,29,34], and one study had 8/10 score [33] on PEDro scale. Therefore, it can be inferred that all the included studies were of high quality.

**Assessment of risk of bias:** The risk of bias assessment was carried out using the Cochrane tool [24] and compiled in [Table/Fig-5] [26-34]. Random sequence generation was conducted in all included studies. Allocation concealment was implemented in five studies [26,27,29,33,34]. Blinding of participants occurred in one study [28], while blinding of the therapist was not conducted in any of the studies. Blinding of outcome assessment was described in six studies [27-31,33]. A low attrition rate ( $\leq 15\%$ ) was reported in seven of the nine included studies. Two studies had an attrition rate greater than 15% [27,30].

**Meta-analysis:** Four studies included in the meta-analysis used the Short Form-36 (SF-36) Questionnaire - 'physical functioning' subscale (n=2) and European Organisation for Research and Treatment of Cancer Quality of Life - C30 (EORTC QLQ-C30) Questionnaire 'physical functioning' subscale (n=2) as outcome measures to evaluate the efficacy of various exercise protocols in improving PF in the experimental group compared to the control group [31-34]. Two studies included in systematic review, which also used the SF-36 Questionnaire - 'physical functioning' subscale to evaluate PF [27,30], were excluded from meta-analysis due to use of more than one measure to evaluate physical functioning [27] and inadequate data [30].

Two studies conducted on older cancer survivors used SF-36 'Physical functioning' subscale as an outcome measure to evaluate the efficacy of exercise protocols in improving PF in treatment group compared to control group [31,32]. The differences were statistically significant ( $p=0.01$ ), with a mean difference of 2.87 (95% CI: 0.63 to 5.12) and low heterogeneity ( $I^2=0\%$ ,  $p=0.75$ ) [Table/Fig-6] [31,32], suggesting that a tailored exercise program were beneficial in improving SF-36 Physical functioning scores.

Two of the studies incorporated in meta-analysis [33,34] used EORTC QLQ-C30 'Physical functioning' subscale as outcome measure to evaluate the efficacy of exercise protocols in improving PF in intervention group when compared to control group. The differences were statistically significant ( $p=0.002$ ), with a mean difference of 8.77 (95% CI: 3.31 to 14.24) and low heterogeneity ( $I^2=12\%$ ,  $p=0.29$ ) [Table/Fig-7] [33,34], suggesting that physiotherapeutic exercises interventions were beneficial in improving EORTC QLQ-C30 'Physical functioning' scores.

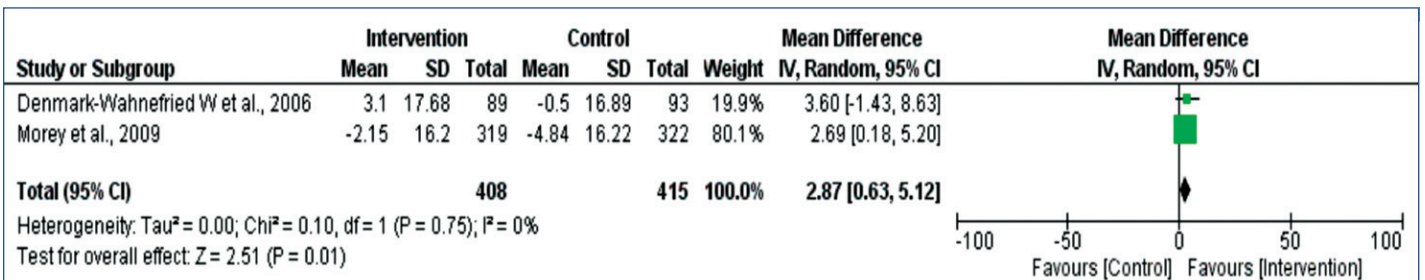
S. No.	Authors name/year of the study	Specified eligibility criteria	1	2	3	4	5	6	7	8	9	10	Total score
			Random allocation	Concealed allocation	Similar baseline	Subject blinding	Therapist blinding	Assessor blinding	Measures of key outcomes from more than 85% of subjects	Intention to Treat analysis of key outcome	Statistical comparisons between groups of key outcomes	Variability for at least one outcome	
1.	Brown JC et al., 2015 [30]	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6/10
2.	Cormie P et al., 2013 [26]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
3.	Dams L et al., 2023 [28]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	7/10
4.	Denmark-Wahnefried W et al., 2006 [32]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
5.	Galiano-Castillo N et al., 2016 [33]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
6.	Garcia-Soidan JL et al., 2020 [29]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
7.	Morey MC et al., 2009 [31]	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
8.	Schmidt ME et al., 2015 [34]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
9.	Winters-Stone KM et al., 2022 [27]	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	6/10

[Table/Fig-4]: Assessment of quality of studies by PEDro scoring [26-34].

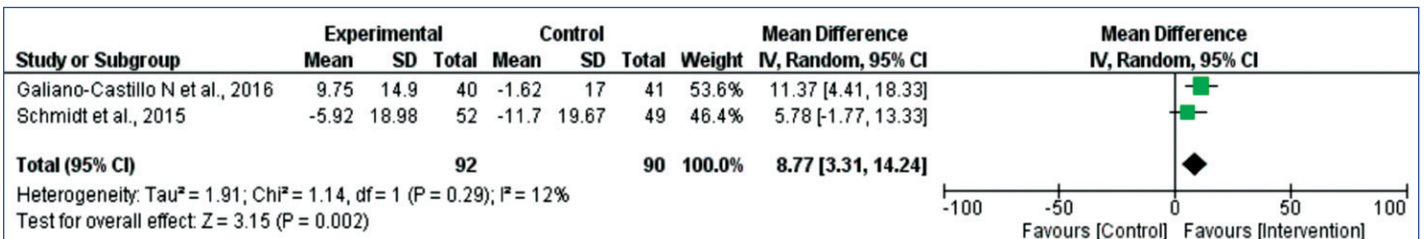


	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Brown JC et al., 2015	+	+	+	+	+	+	+
Cormie P et al., 2013	+	+	+	+	+	+	+
Dams L et al., 2023	+	+	+	+	+	+	+
Denmark-Wahnefried W et al., 2006	+	+	+	+	+	+	+
Galliano-Castillo N et al., 2016	+	+	+	+	+	+	+
Garcia-Soldan JL et al., 2020	+	+	+	+	+	+	+
Morey et al., 2009	+	+	+	+	+	+	+
Schmidt et al., 2015	+	+	+	+	+	+	+
Winters-Stone KM et al., 2022	+	+	+	+	+	+	+

**[Table/Fig-5]:** Risk of bias summary. Studies in green or (+) are at low-risk of bias, red or (-) high-risk of bias and rest are unclear-risk of bias [26-34].



**[Table/Fig-6]:** Forest plot showing effect of physiotherapy interventions on Physical Function (PF) (change in SF-36 'PF' subscale scores) [31,32].



**[Table/Fig-7]:** Forest plot showing effect of physiotherapy interventions on Physical Function (PF) (change in EORTC QLQ-C30 'PF' subscale scores) [33,34].

## DISCUSSION

Physical impairments involving neuromuscular, musculoskeletal, lymphovascular, and cardiovascular systems cause decline in physical fitness, functioning, and quality of life among patients with BC, more so in case of older and frail [2-6]. Physiotherapeutic exercises have beneficial effects on physiology, body composition, PF, psychological outcomes, and quality of life in patients with BC [21,22]. Current systematic review and meta-analysis evaluated the effects of physiotherapeutic interventions on PF and assessment tools used to evaluate PF in individuals with BC.

In current meta-analysis, SF-36 and EORTC QLQ-C30 'physical functioning' subscales were used as outcome measures to evaluate the level of PF. Scores improved for both SF-36 and EORTC QLQ-C30 'physical functioning' subscales in treatment groups when compared to control groups. Meta-analysis revealed low heterogeneity in studies for both SF-36 and EORTC QLQ-C30 measures, which suggests that the results are reliable. Therefore, current systematic review and meta-analysis corroborate that physiotherapeutic exercise interventions can result in statistically significant improvement in physical functioning in individuals with BC. Substantial evidence has previously indicated that various parameters affecting PF e.g., muscle strength and endurance, flexibility, aerobic capacity, fatigue and associated clinical factors can be improved with physiotherapeutic exercise interventions in individuals with breast cancer [8,17-22,35,36]. Improvement found in PF in this meta-analysis can be attributed to improvement in these parameters. Present findings are in agreement with many previously published researches in which physiotherapeutic exercise

interventions were found effective in improving PF [26,27,29-31,33,34,36-39]. However, some previous studies contradict present results [28,32].

In current systematic review, resistance exercise training to major muscle groups of body was found to be the most used exercise intervention. In older BC survivors, exercise interventions were effective in reducing decline in PF when compared to a control or comparison group. No serious adverse events were reported in majority ( $n=6$ ) of the studies, suggesting that with appropriate screening, exercise interventions can be safely administered to improve PF.

In present review, a few observations regarding measurement tools used to evaluate PF in individuals with BC have been made. First, majority of the included studies ( $n=7$ ) used general health related quality of life tools to measure level of physical function, with SF-36 Questionnaire being the most used tool ( $n=4$ ), followed by EORTC QLQ-C30 questionnaire ( $n=2$ ) and SF-12 questionnaire ( $n=1$ ).

The SF-36 questionnaire has a 10-item subscale for 'physical functioning,' and the EORTC QLQ-C30 has a five-item subscale on PF, which includes questions about the participants' ability to perform a variety of physical tasks [40,41].

However, BC patients and survivors experience some treatment-specific unique impairments (e.g., reduced flexibility and strength, lymphedema, and cardiopulmonary and neurological impairments) that adversely impact their level of physical functioning. These impairments might not be captured adequately by general health-related quality of life assessment tools or general PF assessment tools. Secondly, the majority of studies in the current review used patient-reported subjective measures to evaluate PF, while discrepancies between self-reported symptoms and the results of objective physical examinations have been reported in patients with BC [42,43]. Therefore, this systematic review has observed a lack of specific PF assessment tools for individuals with BC. In literature, dearth of specific assessment tools for evaluating PF in cancer research has been reported [44-46]. Harrington SE et al., in a scoping review, reported that SF-36 and EORTC QLQ-C30 questionnaires were the most commonly used measures of PF in cancer rehab research [47].

This review had a number of notable strengths. As per the available information, this is the first review that has evaluated the efficacy of physiotherapy interventions and assessment tools used to assess PF in individuals with BC. Present review included only RCTs, which are considered as gold standard in experimental studies, and all included studies were of high quality.

However, this systematic review and meta-analysis also had few limitations. Present review searched only two databases and was limited to RCTs published in English language. RCTs published in other languages were not included in this review. Meta-analysis had limited sample size, as few trials had to be excluded from meta-analysis for the reason that more than one outcome measure was used in the study to evaluate PF, or sufficient data was not available. There was clinical heterogeneity in included trials in terms of diversity in exercise prescription and blinding of participants was done in only one of the included studies.

The present systematic review and meta-analysis have significant implications for individuals with BC. Although survival time in BC has improved with advances in treatment facilities, patients still suffer from variety of short- and long-term physical impairments causing physical functional limitations, particularly in case of old, or those having co-morbidities. Physiotherapeutic exercise interventions can result in significant improvement in PF, and structured exercise protocols should be prescribed to prevent and treat such limitations in individuals with BC.

## CONCLUSION(S)

Based on the findings of this systematic review and meta-analysis, we conclude that physiotherapeutic exercise interventions can result in significant improvement in PF in individuals with BC during and after active cancer treatment. Physiotherapeutic exercise interventions were found to reduce decline in physical functioning in older BC survivors. Therefore, it can be suggested that structured exercise protocols can be an effective measure to improve PF and should be prescribed to improve or reduce decline in physical functioning in individuals with BC. The PF has been predominantly evaluated using general health-related quality of life tools, with SF-36 questionnaire being the most used tool to evaluate PF in individuals with BC. A lack of specific tools to evaluate PF in BC was observed in this review. There is need to develop specific and sensitive PF assessment tool for BC patients which takes into consideration all unique impairments experienced by this patient population and which may ideally include subjective and objective measures of assessment under one umbrella.

**Authors' contribution:** All authors contributed to the conceptualisation and designing of the study. Literature search, data extraction and reporting were done by SM (Primary researcher) and PK (Supervisor). AS (Co-supervisor) compared the data and resolved any disparity. All authors contributed to analysis, interpretation of the data, and preparation of tables and figures. SM wrote the main manuscript text, PK and AS did critical revisions in draft of this manuscript.

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